Palladium-Catalyzed Synthesis and Transformations of Organometallic Compounds

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Abstract

This thesis is focused on two important fields of palladium catalysis: the development of electrophilic allylic substitution reactions via bis-allylpalladium intermediates; and application of palladium pincer-complexes in the synthesis and transformations of organometallic compounds.

Palladium-catalyzed electrophilic allylation of aldehyde and imine substrates could be achieved using readily available allyl chlorides and acetates by employing hexamethylditin or bis(pinacolato)diboron reagents. The reaction proceeds under mild and neutral reaction conditions with high regioselectivity, providing the branched homoallylic products. The stereoselectivity of the reaction depends on the steric and electronic effects of the allylic substituents of the substrates. DFT modeling of the electrophilic attack on the bis-allylpalladium intermediate of the reaction revealed the origin of the regio- and stereoselectivity of the reaction.

Palladium pincer-complexes were employed as catalysts in a variety of reactions such as stannylation, selenylation, allylation, and cross coupling reactions with various electrophiles. Allylic stannylation in the presence of hexamethylditin was achieved by use of an NCN palladium pincer-complex catalyst. In contrast to the reactions catalyzed by traditional palladium catalysts, isolation of functionalized allyl stannanes was possible due to the special features of the pincer-complex catalyst. Extension of the scope of the palladium pincer-complex catalyzed electrophilic allylation reactions was achieved by using potassium trifluoro(allyl)borate instead of allyl stannanes. In addition, asymmetric electrophilic allylation of sulfonimines was achieved by employment of novel BINOL-based palladium pincer-complexes. The enantioselectivity of the pincer-complex catalyst was fine-tuned by employment of substituted analogs of BINOL.

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List of Papers

This thesis is based on the following papers referred to by their roman numerals **I-IX**.

I. O. A. Wallner, K. J. Szabó:
Regioselective Palladium-Catalyzed Electrophilic Allylic Substitution in the Presence of Hexamethylditin. *Org. Lett.* **2002**, Vol. 4, 1563-1566

II. O. A. Wallner, K. J. Szabó:
Palladium-Catalyzed Electrophilic Allylic Substitution of Allyl Chlorides and Acetates via Bis-allylpalladium Intermediates. *J. Org. Chem.* **2003**, *68*, 2934-2943

III. O. A. Wallner, K. J. Szabó:
Origin of the Regio- and Stereoselectivity in Palladium-Catalyzed Electrophilic Substitution via Bis-allylpalladium Complexes. *Chem. Eur. J.* **2003**, *9*, 4025-4030

IV. S. Sebelius, O. A. Wallner, K. J. Szabó:
Palladium-Catalyzed Coupling of Allyl Acetates with Aldehyde and Imine Electrophiles in the Presence of Bis(pinacolato)diboron. *Org. Lett.* **2003**, Vol. 5, 3065-3068

V. O. A. Wallner, K. J. Szabó:
Palladium Pincer Complex-Catalyzed Allylic Stannylation with Hexaalkylditin Reagents. *Org. Lett.* **2004**, Vol. 6, 1829-1831

VI. N. Solin, O. A. Wallner, K. J. Szabó:
Palladium Pincer-Complex Catalyzed Allylation of Tosylimines by Potassium Trifluoro(allyl)borates. *Org. Lett.* **2005**, Vol. 7, 689-691

VII. O. A. Wallner, V. J. Olsson, L. Eriksson and K. J. Szabó:
Synthesis of New Chiral Pincer-Complex Catalysts for Asymmetric Allylation of Sulfonimines. *Inorg. Chim. Acta. In Press.*

VIII. O. A. Wallner and K. J. Szabó:
Employment of Palladium Pincer-Complexes in Phenylselenylation of Organohalides. *J. Org. Chem.* **2005**, *70*, 9215-9221

IX. J. Kjellgren, J. Aydin, O. A. Wallner, I. V. Saltanova, and K. J. Szabó:
Palladium Pincer Complex Catalyzed Cross-Coupling of Vinyl Epoxides and Aziridines with Organoboronic Acids. *Chem. Eur. J.* **2005**, *11*, 5260-5268

List of Abbreviations

Bs	- Benzenesulfonyl
Cat	- Catalyst, catalytic amount
DFT	- Density functional theory
d.r.	- Diastereomeric ratio
E	- Electrophile
ee	- Enantiomeric excess
L	- Ligand
L_n	- Unspecified number of ligands
Lg	- Leaving group
M	- Metal
Nu	- Nucleophile
PES	- Potential energy surface
R	- Substituent
R_n	- Unspecified number of substituents
TFA	- Trifluoroacetate
Ts	- Toluene-4-sulfonyl
TS	- Transition state
ZPV	- Zero point vibration energy

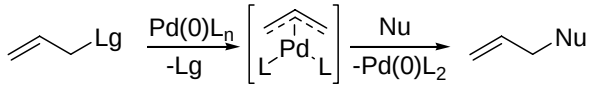
1. Introduction

Palladium-catalyzed transformations is one of the most studied areas of transition metal catalysis. Studies in palladium catalysis have resulted in a wide variety of important organic transformations such as redox-, substitution-, carbonylation-, and cross-coupling reactions,[1-4] and new reactions are continually being developed.

This thesis is mainly focused on the development of palladium-catalyzed substitution and addition reactions involving allylic compounds. Most of the research is aimed towards extending the scope of different palladium-catalyzed transformations for synthesis of densely functionalized organic and organometallic compounds. In many reactions, palladium pincer-complex catalysts are employed in order to improve/alter the reactivity and selectivity of commonly used palladium catalysts. The synthesis and application of novel pincer-complex catalysts for asymmetric allylation reactions is also presented.

1.1 Nucleophilic allylation via (mono)allylpalladium intermediates

Nucleophilic allylic substitution is a widely used transformation in palladium catalysis.[1-8] This reaction involves substitution of readily available substrates such as allyl acetates, allyl halides and their congeners (Scheme 1). The reaction proceeds through mono-allylpalladium complexes (**1**) generated by oxidative addition of the palladium(0) catalyst to the allylic precursors. The mono-allylpalladium complex is subsequently attacked by nucleophiles resulting in an allylated nucleophile and regenerated palladium(0) catalyst.



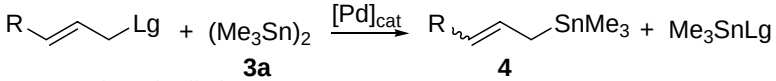
1

Lg = OAc, Halide, OCOOR, etc.
Nu = malonate, enolate, amine

Scheme 1. Palladium-catalyzed nucleophilic allylation.

1.2 Palladium-catalyzed synthesis of allyl stannanes

Beletskaya and co-workers[9] described a useful method for the palladium-catalyzed synthesis of trimethylallylstannanes (Scheme 2). In this procedure, allyl chlorides or allyl acetates were reacted with hexamethylditin (**3a**) in the presence of a palladium catalyst to afford the corresponding allyl stannane product (**4**).



3a **4**

R = H, Phenyl, alkyl
Lg = Acetate, halide
$[Pd]_{cat}$ = $[(\eta^3\text{-allyl})PdCl]_2$, $Pd(PPh_3)_4$

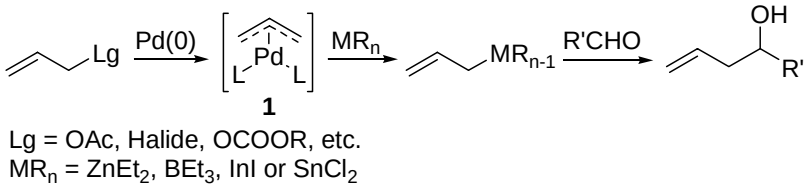
Scheme 2. Palladium-catalyzed synthesis of trimethylallylstannanes.

It was shown that this reaction proceeds through mono-allylpalladium intermediates (c.f. Scheme 1) and that the reactive nucleophile is generated from hexamethylditin. The authors found that the catalytic reaction with allyl chloride precursors could be performed under

phosphine-free conditions by employment of η^3-allylpalladium chloro dimer (**1a**) as catalyst. However, for allyl acetates, $Pd(PPh_3)_4$ (**2a**) had to be used in order to avoid deactivation of the catalyst.

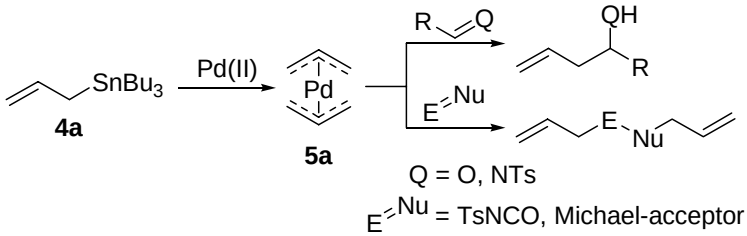
1.3 Umpolung of the π-allylpalladium reactivity

Although palladium-catalyzed nucleophilic allylic substitution reactions make up a well established, broad area in palladium catalysis, the use of electrophilic reagents has attracted considerable attention.[10-34] Application of electrophilic reagents in allylic substitutions requires umpolung of the electrophilic reactivity of the allyl moiety of the η^3-allylpalladium complexes. There are two major strategies to achieve this umpolung of the reactivity of the allyl functionality; the first strategy involves transformation of the electrophilic η^3-allylpalladium intermediates into nucleophilic allyl-metal species by treatment with low-valent metal reagents (such as $ZnEt_2$, BEt_3, InI or $SnCl_2$) (Scheme 3).[10-19] These highly reactive species subsequently directly react with electrophiles, such as aldehydes. The second approach is based on the generation of bis-allylpalladium intermediates (**5a**) from allyl stannanes followed by a nucleophilic attack of one of the allyl moieties on various types of electrophiles (Scheme 4).[20-36]



Scheme 3. Electrophilic allylation by generation of a reactive allyl metal species.

There is a very important difference between the two processes. In the latter process (Scheme 4), the electrophile reacts directly with the allyl moiety of the bis-allylpalladium complex (**5a**), while in the former case (Scheme 3), the highly reactive allyl-metal species attacks the electrophile without any assistance from palladium. This mechanistic difference leads to a different reactivity and selectivity in catalytic applications.



Scheme 4. Electrophilic allylation via a bis-allylpalladium complex.

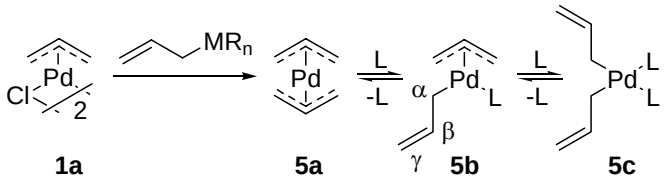
Employment of easily accessible allyl chloride and allyl acetate precursors allows for a very broad synthetic scope in palladium-catalyzed processes involving highly reactive allyl-metal species (Scheme 3). On the other hand, a wide range of electrophilic reagents can be used in the catalytic reactions proceeding via bis-allylpalladium complexes (Scheme 4). However, the poor availability of functionalized allyl stannane substrates imposes a limitation on the

synthetic scope of the bis-allylpalladium-catalyzed reactions, which in its original form was mainly applied to the alkylation of the parent or simple alkyl-substituted allylic precursors.[20] Therefore, it would be highly desirable to conduct the reactions employing stable and readily available allylic substrates in place of the corresponding allyl stannanes. Examples of such reactions are given in Chapter 2 in this thesis.

1.4 Structure and reactivity of bis-allylpalladium complexes

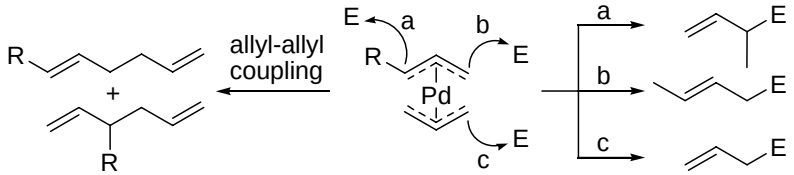
As mentioned above, the palladium-catalyzed electrophilic substitution of allyl stannanes with electrophiles proceeds via bis-allylpalladium complexes (Scheme 4). These complexes can be prepared by reacting mono-allylpalladium complexes (**1**) with reactive organometallic species such as allyl stannanes or allyl magnesium chloride (Scheme 5).[20,37,38]

Bis-allylpalladium complexes may exist in at least three different forms. In the η^3,η^3-bis-allylpalladium complex (**5a**) both allyl groups are η^3-coordinated.[20,37,38] These η^3,η^3-coordinated complexes can easily be converted to the η^1,η^3-forms (**5b**) by coordination of external ligands such as phosphines (L = PR_3).[39,40] A third form is the η^1,η^1-bis-allylpalladium complex (**5c**) which is formed using excess ligands or by employment of a bidentate phosphine ligand.[28,41,42]



Scheme 5. Formation of bis-allylpalladium complexes.

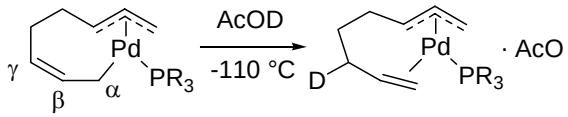
Although **5a-c** and their analogs have been observed and characterized,[20,37-41,43-45] isolation of bis-allylpalladium complexes is much more difficult than isolation of the mono-allylpalladium complexes (**1**), as bis-allylpalladium complexes are very unstable. The dynamic properties of the bis-allylpalladium complexes impose considerable synthetic limitations: for example it is difficult to control the regioselectivity of the electrophilic attack when an unsymmetrically substituted bis-allylpalladium complex is formed (Scheme 6).[26,27,32-34] Furthermore, in the presence of external ligands, the bis-allylpalladium complexes can undergo allyl-allyl coupling forming hexadiene derivatives.[28,41,42]



Scheme 6. Reactivity of an unsymmetrical substituted bis-allylpalladium complex.

It is well documented in the literature[20-29,31-36,46,47] that bis-allylpalladium complexes react with electrophiles. Mechanistic studies by Jolly an co-workers showed[46] that bridged η^1,η^3-

complex **5d** (PR_3 = PCy_3) is deuterated with acetic acid at low temperature (-110 °C) selectively at the γ-carbon of the η^1-allyl moiety (Scheme 7).



5d, PR_3 = PCy_3
5e, PR_3 = PPhMeCy

Scheme 7. Electrophilic attack on a η^1,η^3-bis-allylpalladium complex at the γ-carbon.

Structures from X-ray crystallography[43] of **5e** (PR_3 = PPhMeCy) revealed that the dihedral angle Pd-C_α-C_β-C_γ is approximately 100°, which would allow hyperconjugation of the σ(Pd-C_α) and π*(C_β-Cγ) orbitals resulting in nucleophilic character at the γ-carbon. The reactivity of bis-allylpalladium complexes has also been the subject of DFT-modeling studies,[48] which confirmed that the η^1-allyl moiety of **5b** has a nucleophilic character, and the γ-carbon of the allyl moiety can react with electrophiles with a low activation barrier.

1.5 Palladium pincer-complexes

Palladacycles[49-55] are a special class of palladium complexes that incorporate palladium in a cyclic structure with at least one carbon-metal bond intramolecularly stabilized by at least one donor atom. A subclass of the palladacycles are the so-called palladium pincer-complexes which comprise an anionic terdentate ligand with one carbon-metal bond and two donor atoms of the general formula $[2,6\text{-}(ACH_2)_2C_6H_3]^-$ (Figure 1).

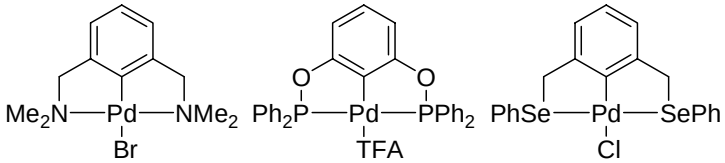


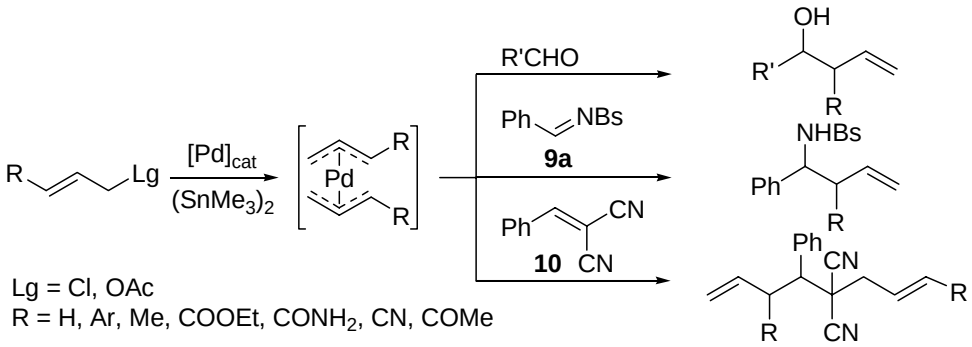
Figure 1. Examples of palladium pincer-complexes.

Palladium pincer-complexes are classified according to the heteroatoms on the side arms of the pincer-ligand. Hence, **6a**[56] is called an NCN complex whereas **7a**[57] and **8a**[58] is referred to as PCP and SeCSe complexes respectively. The topology of the ligand furnishes the palladium pincer-complexes with several attractive features: (i) the strong terdentate ligand-metal interaction makes the complexes highly stable and robust even at elevated temperatures; (ii) coordination of the terdentate ligand restricts the number of easily accessible coordination sites for external ligands to a single one; and (iii) under ambient conditions, the oxidation state of palladium is largely restricted to +2.

The above-mentioned characteristics (i-iii) of palladium pincer-complexes offer some useful features for new catalytic applications. Thus, several catalytic processes have been catalyzed by palladium pincer-complexes, including cross-couplings, aldol-condensations, Michael-additions, hydroamination, and nucleophilic substitution and addition reactions.[49-55,59-63]

2. Palladium-Catalyzed Electrophilic Substitution of Allyl Chlorides and Acetates (Papers I-IV)

As mentioned in the introduction, the poor availability of functionalized allyl stannanes imposes a severe synthetic limitation onto the palladium-catalyzed electrophilic allylic substitution reaction (Scheme 4). The synthetic scope of this reaction could be considerably extended by using easily available functionalized allylic substrates, such as allyl chlorides or allyl acetates. However, employment of these precursors requires *in situ* preparation of allyl stannanes, which are necessary for the generation of the bis-allylpalladium intermediate of the reaction (Scheme 4). We have found that this process can be accomplished by using palladium-catalyzed generation of the transient allyl stannanes from hexamethylditin and allyl chlorides or allyl acetates (c.f. section 1.2).

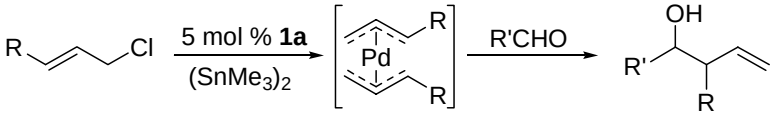


Scheme 8. Overview of the studied electrophilic substitution reactions.

Thus, palladium-catalyzed electrophilic substitution of functionalized allyl chlorides and allyl acetates could be achieved in the presence of hexamethylditin using various electrophiles (Scheme 8), such as aldehydes, N-benzylidene-benzenesulfonamide (**9a**), and benzylidenemalonitrile (**10**).

2.1 Palladium-catalyzed electrophilic substitution of allyl chlorides with aldehydes

The electrophilic allylation of aldehydes by allyl chlorides in the presence of a stoichiometric amount of hexamethylditin proceeds under mild conditions (generally at 40 °C) affording homoallylic alcohols (Scheme 9, Table 1). The reactions were conducted in THF using 5 mol % of η^3-allylpalladium chloro dimer (**1a**) as catalyst. It was found that in many cases, the addition rate of hexamethylditin has a great influence on the yield of the reaction; a rapid addition often leads to precipitation of colloidal palladium(0) deactivating the catalyst before full conversion of the allylic substrates can be achieved. With slow addition, the catalyst can be kept in solution, improving the yield of the reaction.



Scheme 9. Palladium-catalyzed allylation of aldehydes.

Functional group tolerance. As shown in Table 1, various allylic functionalities, including COOEt, COMe, CN, NO_2, and Br, are tolerated in the catalytic reactions due to the neutral and mild reaction conditions. The tolerance of the allylic carbonyl functionality (Table 1, entry 4) is particularly important. This functionality remains intact under the applied reaction conditions indicating that the catalytic transformation is highly chemoselective, since an aldehyde functionality (**12c**) can be manipulated in the presence of an allylic keto-group (**11c**). A further important aspect of the applied reaction conditions is that the organometallic reagent ($(SnMe_3)_2$) and the transient allyl stannanes contain tin in a high oxidation state, and accordingly, undesired reduction of the substrates can be avoided. Therefore, we could use nitro-benzaldehyde (**12a** and **12c**) as electrophile, in which the nitro-functionality is sensitive for reduction by low-valent metals (such as $SnCl_2$, Scheme 3).[64] Furthermore, under basic conditions, nitro-benzaldehyde easily undergoes Cannizzaro and Tischenko reactions[65] or other decomposition processes, all of which are avoided under these neutral reaction conditions. Other aldehydes, such as acrolein (**12b**), react selectively at the carbonyl functionality. Reduction of the double bond due to attack at the γ-position was not observed (Table 1, entry 2).

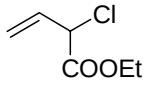
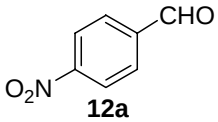
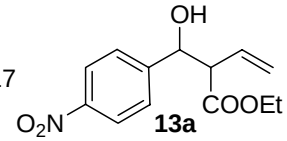
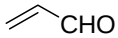
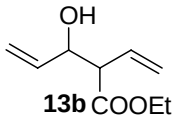
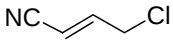
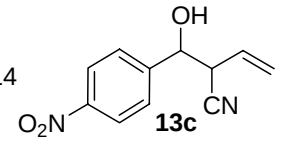
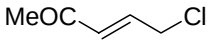
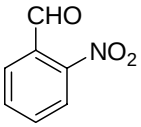
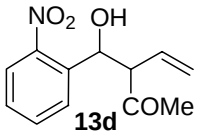
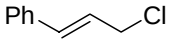
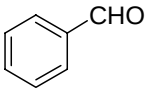
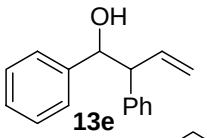
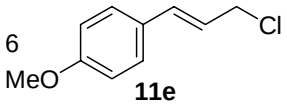
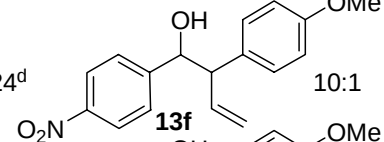
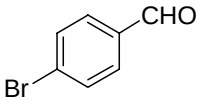
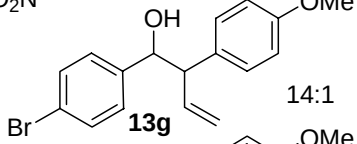
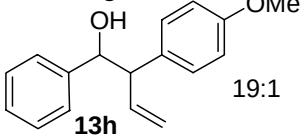
Regioselectivity of the reaction. The catalytic substitution reactions proceed with excellent regioselectivity. In the presented reactions, only a single regioisomer was formed, in all cases corresponding to the branched homoallylic product (**13a**-**h**). It is important to note that this regioselectivity is in sharp contrast with that of nucleophilic attack on η^3-allylpalladium complexes, which usually takes place at the less substituted allylic terminus.[66-73]

Stereoselectivity of the reaction. The stereoselectivity of the reaction is dependent on the particular allyl chloride and electrophile combination. Precursors with bulky allylic substituents, such as cinnamyl chloride (**11d**), and benzaldehyde (**12d**) react with a high diastereoselectivity (Table 1, entry 5), and the stereoselectivity is still fairly good in the reaction of **11a** with **12a** as electrophile (entry 1). However, as the steric bulk of the allylic substituents decreases (**11b** and **11c**) the stereoselectivity of the reaction is lowered (Table 1, entries 3 and 4). According to Table 1, the following trend can be envisaged for the influence of the allylic functionalities on the stereoselectivity of the reaction: Ph > COOEt > COMe > CN. A similar trend was observed for the substituent effects of the aldehyde electrophiles. Going from the bulky aryl substituent (Table 1, entry 1) to a vinyl substituent (Table 1, entry 2), the stereoselectivity drops, when **11a** is used as allylic precursor.

Comparison of the diastereoselectivity of the reactions of methoxycinnamyl chloride (**11e**) with different aldehydes (entries 6-8) reveals that the stereoselectivity is also influenced by electronic effects. The diastereomeric ratio in these reactions varies from 10:1 to 19:1 and the major diastereomer is always the *anti* isomer. Activated aldehydes react with lower stereoselectivity (entries 6 and 7) than benzaldehyde itself (entry 8). The above electrophilic substitutions could be performed under phosphine-free conditions using **1a** as catalyst source

(Scheme 9). Addition of phosphine ligand does not inhibit the reaction; however we found that the stereoselectivity of the electrophilic addition then is lowered.

Table 1. Selected examples of palladium-catalyzed allylation reactions of aldehydes in the presence of hexamethylditin.[a]

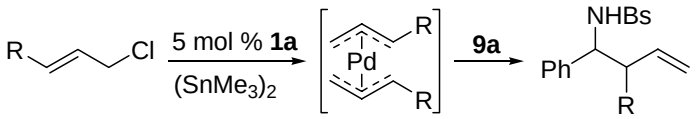
Entry	Allyl	Electrophile	Cat.	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	 **11a**	 **12a**	**1a**	20/17	 **13a**	4:1	88
2	**11a**	 **12b**	**1a**	40/4	 **13b**	1:1	60
3	 **11b**	**12a**	**1a**	40/14	 **13c**	1:1	79
4	 **11c**	 **12c**	**1a**	0/3	 **13d**	2:1	57
5	 **11d**	 **12d**	**1a**	40/24[d]	 **13e**	14:1	80
6	 **11e**	**12a**	**1a**	40/24[d]	 **13f**	10:1	78
7	**11e**	 **12e**	**1a**	40/24[d]	 **13g**	14:1	80
8	**11e**	**12d**	**1a**	40/24[d]	 **13h**	19:1	60

[a] All reactions were conducted using 5 mol % Pd-catalyst in THF solvent. [b] Diastereomeric ratio (*anti*:*syn*). [c] Isolated yield. [d] Hexamethylditin was added slowly over 12h.

2.2 Electrophilic substitution of allyl chlorides with imines

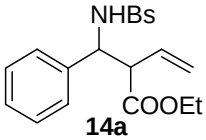
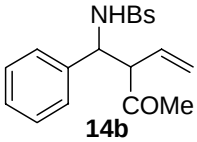
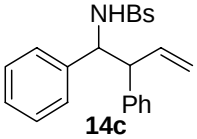
A great advantage of the allylation reactions proceeding through bis-allylpalladium intermediates is that imines can also be used as electrophiles.[20] We have found that N-benzylidene-benzenesulfonamide (**9a**) readily reacts with allyl chlorides (**11a**, **11c** and **11d**) under mild reaction conditions affording homoallylic amines (Scheme 10, Table 2). The benzenesulfonyl substituent appears to be important for the substitution reaction to proceed at

a satisfactorily high rate. When N-phenyl and N-benzyl analogs were used in place of **9a**, a very slow reaction with low conversion was seen.



Scheme 10. Palladium-catalyzed allylation of N-benzylidene-benzenesulfonamide.

Table 2. Selected examples of palladium-catalyzed allylation reactions of N-benzylidene-benzenesulfonamide.[a]

Entry	Allyl	Electrophile	Cat.	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	**11a**	**9a**	**1a**	40/15	 **14a**	sd[d]	57
2	**11c**	**9a**	**1a**	0/30	 **14b**	1:2	54[e]
3	**11d**	**9a**	**1a**	40/16	 **14c**	sd[d]	58

[a] All reactions were conducted using 5 mol% Pd-catalyst in THF solvent. [b] Diastereomeric ratio (*anti*:*syn*). [c] Isolated yield. [d] A single diastereomer (*syn*) was obtained. [e] Compound **14b** and its allylic isomer were formed in a 12:1 ratio.

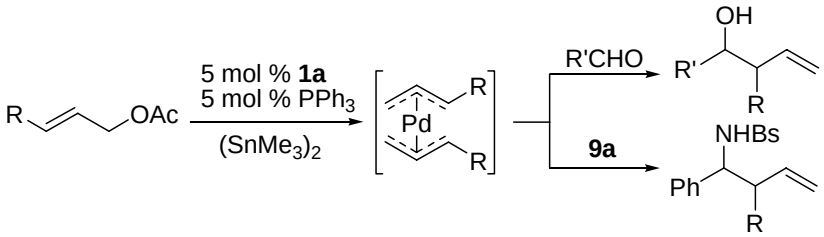
Stereoselectivity of the reaction. Comparison of entries 1 and 3 in Table 2 with entries 1 and 5 in Table 1 reveals that the imine electrophile **9a** reacts with higher stereoselectivity than do aldehydes. Thus, reaction of **11a** or **11d** with **9a** results in a single stereoisomer as product (**14a** and **14c**).

2.3 Palladium-catalyzed electrophilic substitution of allyl acetates

Allyl acetates (**15a-d**) react with aldehyde (**12a**) and imine (**9a**) electrophiles under mild conditions similarly to the allyl chloride precursors (Scheme 11, Table 3). The high regioselectivity of the reaction is maintained (Table 3) providing the branched allylic products. However, the stereoselectivity of the reactions and the isolated yields are usually lower with allyl acetate precursors than with allyl chlorides. For example, allyl chloride **11a** reacts with imine **9a** providing a single diastereomer of **14a** (Table 2, entry 1), while the corresponding reaction with the allyl acetate precursor (**15d**) provides the same product with poor stereoselectivity (Table 3, entry 4). On the other hand, product **13i** with allylic amide functionality is formed with a fairly high stereoselectivity (Table 3, entry 2). It is also interesting to note that in this reaction, the amide-functionality remains intact.

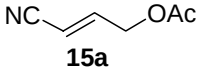
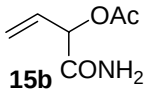
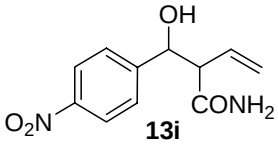
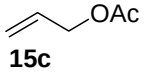
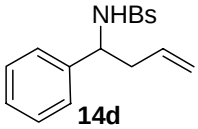
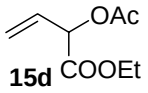
When allyl acetates were used as allylic precursors, it was necessary to add a phosphine co-catalyst to the reaction; in the absence of phosphine, colloidal palladium(0) precipitated upon

addition of hexamethylditin (c.f. section 1.1). As mentioned above (section 2.1), the use of a phosphine co-catalyst usually leads to a decrease in the diastereoselectivity, which may explain the fact that the reaction with acetates proceeds with a low stereoselectivity.



Scheme 11. Palladium-catalyzed electrophilic substitution of allyl acetates.

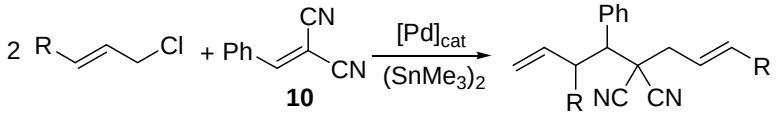
Table 3. Selected examples of palladium-catalyzed electrophilic allylic substitution reactions of allyl acetates.[a]

Entry	Allyl	E	Cat.	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	 **15a**	**12a**	$Pd(PPh_3)_4$ **2a**	40/4	**13c**	1:1	58
2	 **15b**	**12a**	**2a**	25/4	 **13i**	3:1	56
3	 **15c**	**9a**	**1a** + PPh_3	60/9	 **14d**	-	50
4	 **15d**	**9a**	**1a** + PPh_3	40/16	**14a**	2:3	40

[a] All reactions were conducted using 5 mol% Pd-catalyst in THF solvent. [b] Diastereomeric ratio (*anti*:*syn*). [c] Isolated yield.

2.4 Tandem bis-allylation reactions

Bis-allylpalladium intermediates display a unique ambiphilic reactivity under catalytic conditions (c.f. section 1.3).[22,27,32-34] Yamamoto and co-workers have shown[22] that this reaction proceeds through an initial electrophilic attack on one of the allyl moieties of the bis-allylpalladium intermediate followed by a nucleophilic attack on the mono-allylpalladium intermediate of the reaction.

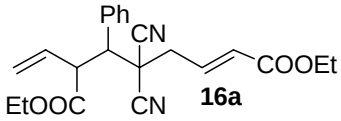
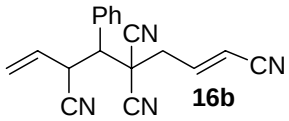
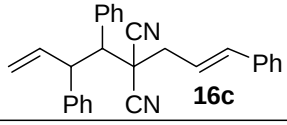


Scheme 12. Tandem bis-allylation of benzylidenemalonitrile.

In previous applications, this reaction had been performed by employing a 1:1 mixture of the allyl stannane and allyl chloride components.[22,27,32,33] However, using hexamethylditin as co-reactant, bis-allylation of benzylidenemalonitrile (**10**) can be performed with allyl chloride alone (Scheme 13). Substituted allyl derivatives **11a**, **11b**, and **11d** were reacted with **10**

(Table 4) providing a single regioisomer (**16a**, **16b** and **16c** respectively) out of the four possible products in all cases. The structures of **16a-c** clearly demonstrate the contrasting regioselectivity of the initial electrophilic attack and the subsequent nucleophilic attack. The phenyl-substituted electrophilic carbon in **10** is attached to the branched allylic position of the substrate (**11a**, **11b** and **11d**), while the nucleophilic dinitrile substituted carbon in **10** is bound to the unsubstituted allylic terminus of **11a**, **11b** and **11d**. Thus, starting from a particular allylic precursor, the two subsequent allylation processes occur with opposite regioselectivity to give a single regioisomer of the product.

Table 4. Palladium-catalyzed tandem bis-allylation reactions of benzylidenemalonitrile.[a]

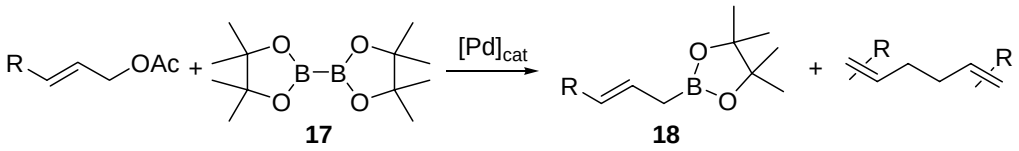
Entry	Allyl	E	Cat.	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	**11a**	**10**	**2a**	40/15	 **16a**	2:1	70
2	**11b**	**10**	**1a** + PPh_3	40/17	 **16b**	1:1	66
3	**11d**	**10**	**1a** + PPh_3	60/16	 **16c**	2:1	60

[a] All reactions were conducted in THF using 5 mol% Pd-catalyst. [b] Diastereomeric ratio. [c] Isolated yield.

In this tandem allylation reaction, we used **1a** together with 5 mol% of PPh_3 as co-catalyst or $Pd(PPh_3)_4$ (**2a**). Without a phosphine co-catalyst, the double allylation process does not occur. The reaction with **11a** and **11b** proceeded under mild conditions, however, the reaction with **11d** required a relatively high reaction temperature (60 °C) and an elongated reaction time (17 h). The phosphine co-catalyst is probably necessary for the activation of the mono-allylpalladium intermediate in the nucleophilic attack of the reaction. This nucleophilic attack may also require high temperature under these reaction conditions.

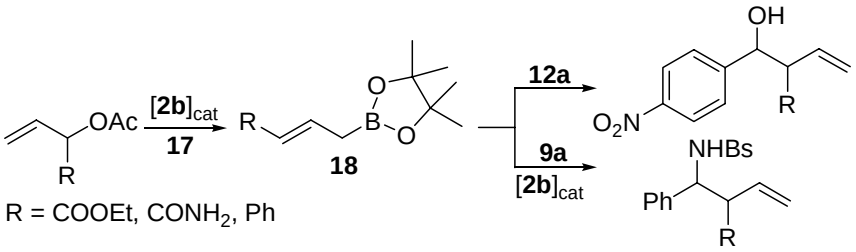
2.5 Palladium-catalyzed electrophilic substitution of allyl acetates in the presence of bis(pinacolato)diboron

Allyl boranes represent an important class of organic reagents because of the high stereoselectivity of their coupling reactions with electrophiles. Synthesis of functionalized allyl boron compounds, however, is a challenging task since allyl boranes are relatively unstable and most synthetic routes involve harsh reaction conditions. Miyaura and co-workers,[74] however, have shown (Scheme 13) that allyl acetates react with bis(pinacolato)diboron (**17**) under mild reaction conditions in a palladium-catalyzed transformation to afford allyl boronates (**18**). It was found that the transformation is accompanied by the formation of hexadiene products, which are presumably formed via a bis-allylpalladium complex (c.f. Scheme 6).



Scheme 13. Palladium-catalyzed formation of allyl boronates.

The possible involvement of a bis-allylpalladium intermediate in the coupling of **17** with allyl acetates[74] prompted us to extend the scope of the electrophilic substitution of allylic substrates by employment of **17** in the palladium-catalyzed coupling of allyl acetates with aldehyde and imine electrophiles (Scheme 14). The reaction of allyl acetates with aldehyde and imine electrophiles in the presence of **17** proceeds under mild reaction conditions in DMSO usually at 20 °C, employing 6 mol % of $Pd_2(dba)_3$ (**2b**) as catalyst.



Scheme 14. Palladium-catalyzed electrophilic coupling of allyl acetates

A wide variety of functional groups were tolerated under the applied reaction conditions, including COOEt, Ph, $CONH_2$, and NO_2 (Table 5). The reaction provides the branched homoallylic products with high diastereoselectivity; the reaction with aldehyde **12a** afforded *anti*-products as the major diastereomers whereas the reactions with **9a** afforded the corresponding *syn*-products. Interestingly, the reactions employing **17** generally proceeded with much higher diastereoselectivity than the electrophilic allylation reactions of allyl chlorides and acetates conducted in the presence of **3a** (c. f. sections 2.1 - 2.3).

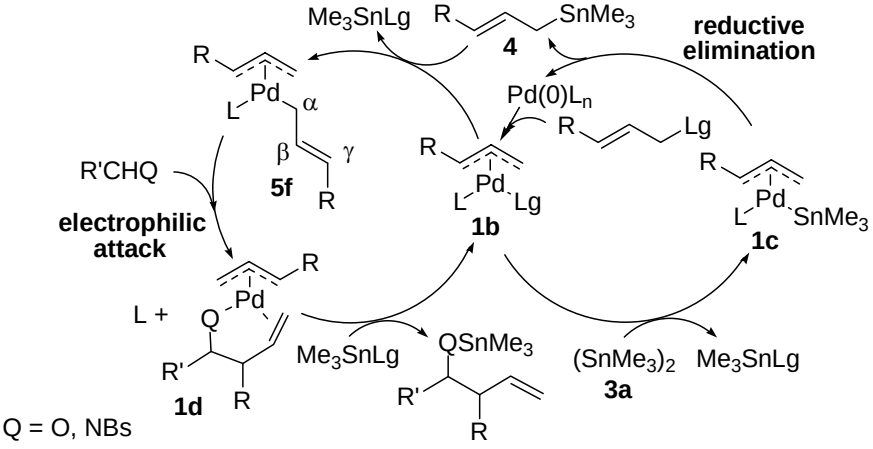
Table 5. Selected examples of the palladium-catalyzed electrophilic coupling of allyl acetates in the presence of bis(pinacolato)diboron.[a]

Entry	Allyl	Electrophile	Cat.	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	**15d**	**12a**	$Pd_2(dba)_3$ **2b**	20/21	**13a**	8:1	75
2	Ph, OAc **15e**	**12a**	**2b**	40/21	OH, O_2N, Ph **13j**	33:1	86
3	**15b**	**12a**	**2b**	20/21	**13i**	8:1	61
4	**15e**	**9a**	**2b**	20/72	**14c**	s.d.[d]	91
5	**15d**	**9a**	**2b**	20/21	**14a**	1:11	55

[a] All reactions were conducted in DMSO using 6 mol % of **2b** as catalyst. [b] Diastereomer ratio *anti*:*syn*. [c] Isolated yield. [d] A single diastereomer (*syn*) was obtained.

2.6 Mechanism of the electrophilic allylation reactions

The catalytic process of the electrophilic allylic substitution reaction using allyl chlorides (or acetates) in the presence of **3a** can be divided into two main cycles (Scheme 15); the first cycle provides the transient allyl stannane species (**4**); and the second cycle involves the formation and reaction of the bis-allylpalladium intermediate (**5f**). In the catalytic reactions we employed hexamethylditin and allyl chlorides/acetates for formation of the transient allyl stannanes. This reaction using simple allylic substrates (such as allyl chloride, **11d**, and **15c**) was first reported by Bumagin and Beletskaya.[9] Formation of the allyl stannane is initiated by oxidative addition of the allylic substrate to the palladium(0) catalyst to generate **1b**, followed by transmetalation with hexamethylditin to form **1c**. This process is probably affected by the leaving group of the allylic substrate. In case of allyl chlorides, intermediate complexes **1b** and **1c** are stabilized by chloride coordination. However, when allyl acetates are used as substrates, these intermediates are probably unstable, which is indicated by precipitation of palladium-black immediately after addition of hexamethylditin to the corresponding reaction mixture. We have found that precipitation of amorphous palladium(0) can be avoided by addition of at least 5 mol % PPh_3 co-catalyst, which probably thermodynamically stabilizes **1b** and **1c**. Similar behavior has been reported[75,76] for the allylpalladium intermediates formed in the palladium-catalyzed synthesis of allyl silanes from allyl acetates and $(SiMe_3)_2$. It was shown that in this silylation process, a trimethylsilyl group coordinates to palladium and by cis-migration is inserted into the η^3-allyl moiety. Formation of the allyl stannane product **4** from **1c** may proceed by the same mechanism.

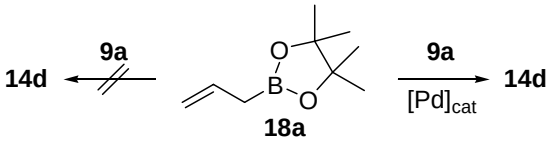


Scheme 15. Plausible mechanism for the palladium-catalyzed electrophilic allylation in the presence of hexamethylditin.

The bis-allylpalladium complex (**5f**) formed in the transmetalation step may exist in different isomeric forms (Scheme 5) and it has been shown[20,46] that bis-allylpalladium complexes readily react with electrophiles (section 1.4). The electrophilic attack on **5f** is probably the most important step of the entire catalytic cycle since this step determines the regio- and stereoselectivity of the catalytic process (vide supra). Electrophilic attack with

aldehyde and imine electrophiles provides **1d**, which after decomplexation gives the final reaction product (Scheme 15).

The reactions via transient allyl boronates (Section 2.5) are probably initiated by a similar mechanism as above (Scheme 15, right hand cycle). However, it is well known[77-79] that allyl boron compounds react with aldehydes without involvement of palladium, therefore we reason that formation of transient allyl boronates is a palladium-catalyzed transformation whereas the coupling to aldehydes is a direct allylation process. To determine if the coupling of allyl boronates with imine **9a** requires palladium catalysis, a series of experiments were undertaken (Scheme 16). The coupling of allyl boronate **18a** with **9a** in the presence of **2b** resulted in smooth formation of **14d**, however, no reaction occurred in absence of palladium catalyst. Therefore we conclude that the coupling of allyl acetates with imines involves bis-allylpalladium intermediates similarly to the coupling of allyl stannanes with imines[20] in accordance with Scheme 15. It is interesting to point out that this is the first report of formation of bis-allylpalladium species from allyl borane substrates.



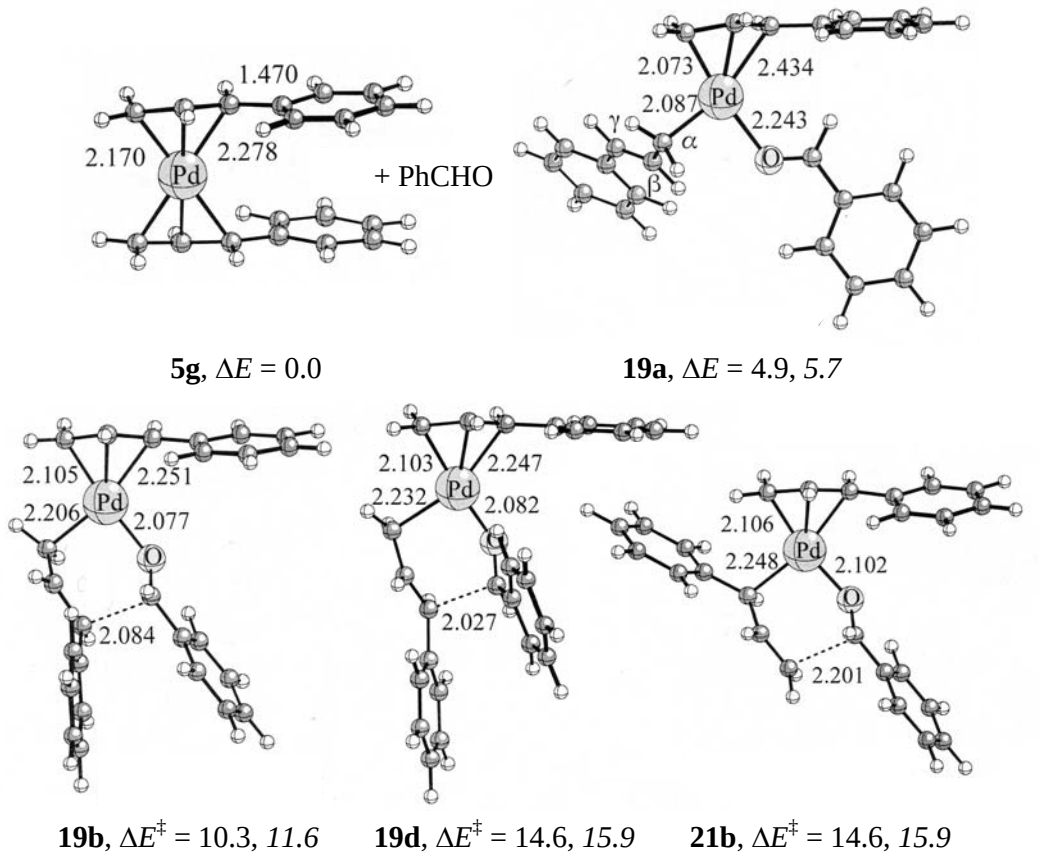
Scheme 16. Coupling of **18a** with **9a** in the presence and absence of palladium catalyst.

2.7 Theoretical studies on the origin of the regio- and stereoselectivity

The electrophilic attack on the bis-allylpalladium intermediate (Scheme 15) determines the regio- and stereochemical outcome of the catalytic transformation. Understanding the nature of the steric and electronic effects governing this process is particularly important, since the mechanistic aspects of the development of regio- and stereoselectivity in palladium-catalyzed electrophilic substitution has not been studied before. Therefore, we have performed theoretical studies on the selectivity-determining step of the above described reaction. As a model reaction, we have chosen the electrophilic substitution of cinnamyl chloride (**11d**) with benzaldehyde (**12d**), which give homoallylic alcohol **13e** with high regio- and stereoselectivity (Table 1, entry 5).

Computational methods. All geometries were fully optimized employing a Becke-type[80] three-parameter density functional model B3PW91 using a double-ζ(DZ)+P basis constructed from the LANL2DZ basis[81-84] by adding one set of d-polarization functions to the heavy atoms and one set of diffuse d-functions on palladium.[85] Harmonic frequencies have been calculated at the level of optimization for all structures to characterize the calculated stationary points and to determine the zero-point vibration energies (ZPV). Fully optimized transition state structures have been characterized by a single imaginary frequency, while the rest of the optimized structures possess only real frequencies. All calculations were carried out using the Gaussian 98[86] program package.

Structure and stability of the η^3,η^3-coordinated complexes. In case with one phenyl substituent on each allyl moiety, four different η^3,η^3-coordinated bis-allylpalladium complexes are expected to form. Interestingly, in the most stable isomer (**5g**, Figure 2) the phenyl substituents are located on the adjacent allylic termini. The phenyl substituent has a relatively large effect on the metal-carbon bonding; the palladium-carbon bond to the substituted allylic terminus is considerably longer (2.28 Å) than the corresponding bond to the unsubstituted terminus (2.17 Å).



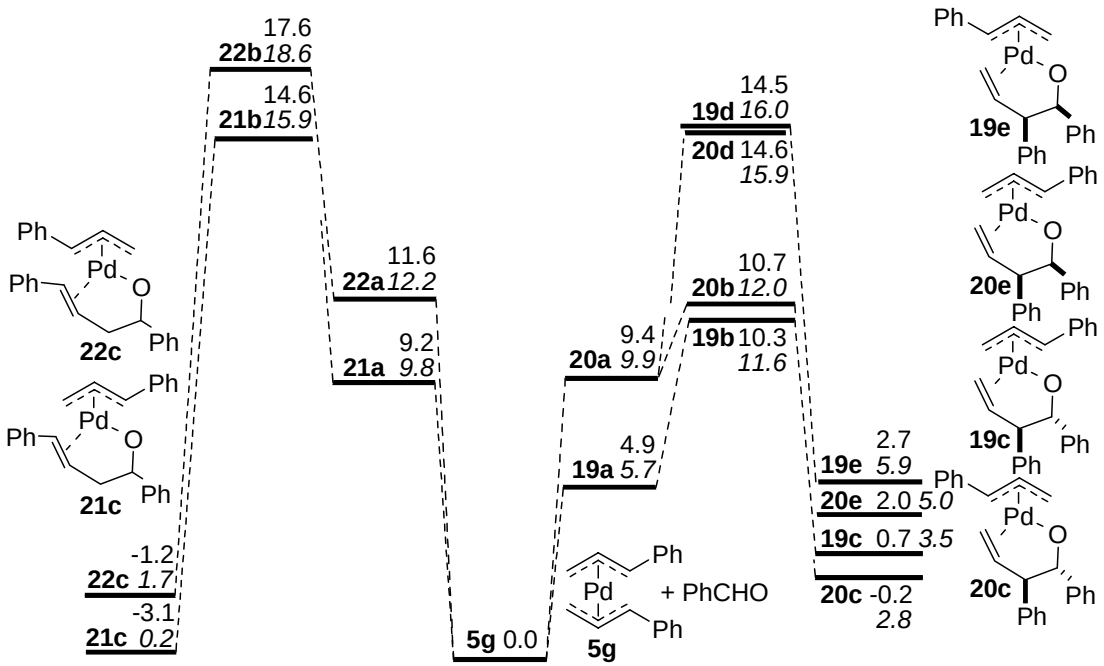
5g, ΔE = 0.0 **19a**, ΔE = 4.9, *5.7*

19b, $\Delta E^{\ddagger}$ = 10.3, *11.6* **19d**, $\Delta E^{\ddagger}$ = 14.6, *15.9* **21b**, $\Delta E^{\ddagger}$ = 14.6, *15.9*

Figure 2. Calculated structures and relative energies of selected bis-allylpalladium species. The energy values are given in kcal mol^{-1}, and the ZPV corrected energies are given in italics.

Structure and stability of the η^1,η^3-coordinated complexes. It is well established that η^1,η^3-coordinated complexes are easily formed from their η^3,η^3-coordinated analogs by coordination of an external ligand.[39,40] The catalytic reactions were conducted in the absence of strongly coordinating ligands (such as phosphines), under so called "ligand free" conditions (Table 1, entry 5). However, the DFT calculations indicate that the electrophilic substrates have fairly good coordination affinity for palladium. Formation of the η^1,η^3-complexes by coordination of benzaldehyde to **5g** is an endothermic process. In the most stable form (**19a**, ΔE = 5.7 kcal mol^{-1}), the η^1-allyl moiety has its phenyl substituent attached to the γ-carbon, and the phenyl group on the η^3-allyl ligand is attached to the allylic terminus *trans* to the η^1-allyl group (Figure 2).

Regioselectivity of the electrophilic attack. The electrophilic substitution reactions take place through six-membered cyclic transition states, in which the distance between the carbons forming the new carbon-carbon bond varies between 2.1-2.2 Å. The lowest energy path (11.6 kcal mol^{-1}) involves **19b** (Figure 2), bearing the phenyl substituent at the γ-position of the η^1-allyl moiety. This reaction path leads to slightly endothermic (3.5 kcal mol^{-1}) formation of the branched allylic product **19c** (Scheme 17). Formation of the linear product **21c** via TS **21b** (Figure 2) has a much higher activation barrier (15.9 kcal mol^{-1}), which can be explained by steric repulsion between the phenyl group of the η^1-allyl moiety and the η^3-allyl moiety. When the phenyl group of the η^3-allyl ligand is located on the same side of the complex as the η^1-allyl moiety, the reaction profiles (**20a** → **20b** → **20c** and **22a** → **22b** → **22c**) are similar to the above, however, the energy for formation of the η^1-η^3-bis-allylpalladium complexes (**20a** and **22a**) and the activation energies are higher (Scheme 17) than path **19a** → **19b** → **19c**.



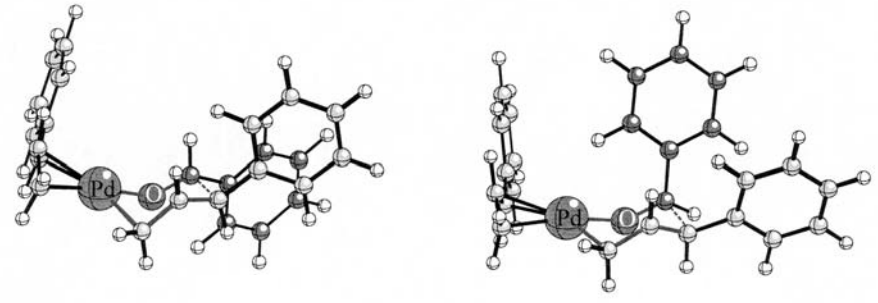
Scheme 17. Reaction profile for the palladium-catalyzed electrophilic allylation of benzaldehyde. The energy values are given in kcal mol^{-1}, and the ZPV corrected energies are given in italics.

It is interesting to note that the formation of the branched allylic product (**19c** and **20c**) requires a lower activation barrier (**19b** and **20b**) than the formation of the linear products (**21c** and **22c**), however the thermodynamic stability of **21c** and **22c** is higher than that of **19c** and **20c**. This indicates that the regioselectivity of the electrophilic substitution reaction is under kinetic control.

Stereoselectivity of the electrophilic attack. Formation of the branched allylic products may proceed via four different complexes. The process discussed above leads to **19c**, in which the phenyl groups are in an *anti* configuration. However, changing the relative orientation of

the η^1-moiety and the benzaldehyde molecule, two other products can be obtained (**19e** and **20e**) in which the phenyl groups are mutually *syn*. Formation of *syn* complexes **19e** and **20e** proceeds through TS structures **19d** (Figure 2) and **20d**, respectively. The activation barrier (Scheme 17) for the formation of these *syn* products is considerably higher (by 3.9-4.4 kcal mol^{-1}) than the activation barrier (**19b** and **20b**) for the formation of the *anti* products (**19c** and **20c**). This result is in good agreement with the experimental results (Table 1, entry 5), i.e. that the major product of the palladium-catalyzed electrophilic substitution is the branched allylic product with *anti* stereochemistry.

Inspection of the reoriented TS geometries (Figure 3) reveals the underlying substituent effects governing the stereochemistry of the reaction. The TS structures of **19b** and **19d** show a pronounced chair conformation. In **19b**, leading to the *anti* product **19c**, the phenyl groups are in a *trans*-diequatorial position across the newly forming carbon-carbon bond, while in TS structure **19d** (providing the *syn* product **19e**), the phenyl group of benzaldehyde is axial and the η^1-allylic phenyl group is equatorial. Thus, in **19d**, the axial phenyl group is involved in a destabilizing steric interaction with the η^3-allyl moiety of the complex, which explains its low stability. It is interesting to point out that the energy difference between the activation barriers (**19b** vs. **19d**) is considerably higher (4.4 kcal mol^{-1}) than the energy difference between the corresponding stereoisomeric products (**19c** and **19e**, 2.4 kcal mol^{-1}). Hence, the kinetic control enhances the stereoselectivity of the electrophilic substitution process.



19b **19d**

Figure 3. Side view of the TS structure of the electrophilic attack.

2.8 Conclusions

Palladium-catalyzed allylic substitution of functionalized allyl chlorides and allyl acetates with various electrophiles could be achieved by employment of hexamethylditin. This efficient one-pot procedure involves palladium-catalyzed formation of transient allyl stannanes followed by generation of a bis-allylpalladium intermediate that subsequently reacts with electrophiles. Using this catalytic transformation, various aldehyde and imine electrophiles could be allylated, providing densely functionalized homoallylic alcohols and amines. Furthermore, tandem bis-allylation reactions could be performed by using benzylidenemalonitrile as substrate. Employment of bis(pinacolato)diboron in place of

hexamethylditin allowed the in situ formation of functionalized allyl boronates which was coupled to aldehyde and imine electrophiles.

It was found that the electrophilic allylic substitution proceeds with excellent regioselectivity to provide the branched allylic product. In the tandem bis-allylation reactions the regioselectivity of the electrophilic and the subsequent nucleophilic attack could be fully controlled. The stereoselectivity of the reaction depends on the steric and electronic effects of the allylic substituents. The stereoselectivity of the electrophilic allylation in the presence of bis(pinacolato)diboron was generally higher than the corresponding reactions in the presence of hexamethylditin.

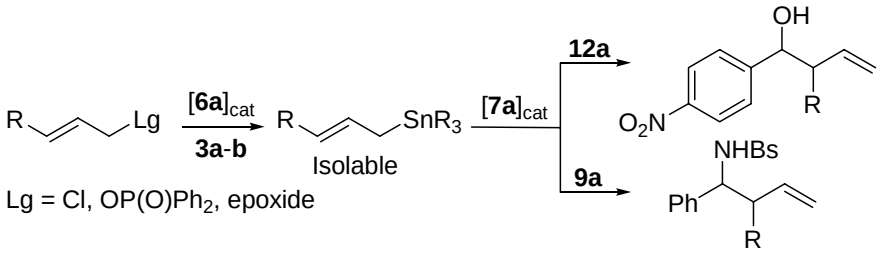
Density functional calculations were undertaken in order to study the regio- and stereoselectivity of the electrophilic allylation reaction. The theoretical results show that the two most important factors controlling the selectivity are: the location of the phenyl functionality in the η^1-moiety of the bis-allylpalladium intermediate; and the relative configuration of the phenyl substituents in the cyclic six-membered transition state of the reaction. The lowest energy path corresponds to formation of the branched allylic isomer, in which the phenyl groups are in an *anti* configuration. These computational results are in excellent agreement with the experimental catalytic results presenting the same regio- and stereoselectivity for the formation of the product.

3. Application of Palladium Pincer-Complex Catalysts in the Synthesis and Transformations of Organometallic Species (Papers V-IX)

Employment of pincer-complexes offers an attractive synthetic route to the preparation of organometallic compounds (section 1.5). Recent studies have shown that palladium pincer-complexes are robust and effective as catalysts in these processes, which is reflected by their high functional group tolerance and broad synthetic scope.[61-63]

3.1 Palladium pincer-complex catalyzed allylic stannylation (Paper V)

The Szabó group have shown[61,62] that palladium pincer-complex **6a** can be employed as an efficient catalyst in the coupling of **3a** with propargylic substrates to afford allenyl stannanes. In this process, the reactivity of pincer-complexes is completely different from the reactivity of commonly used palladium-catalysts[87,88] such as $Pd(PPh_3)_4$ and $Pd_2(dba)_3$.



Scheme 18. Electrophilic allylic substitution in the presence of palladium pincer-complex catalysts.

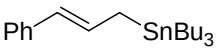
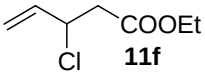
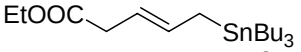
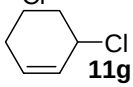
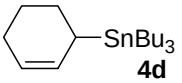
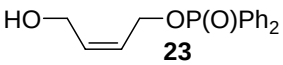
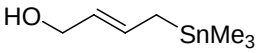
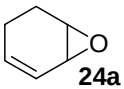
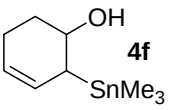
These findings inspired us to investigate the possibility of employing palladium pincer-complex catalysts for allylic stannylation, which would open a convenient route to functionalized allyl stannanes. We have found that palladium pincer-complex **6a** does indeed catalyze the coupling of hexamethyl- (**3a**) and hexabutylditin (**3b**) with a wide variety of allylic substrates generating allyl stannane products (Scheme 18). Moreover, allylation of aldehyde and imine substrates with allyl chlorides can be realized in the presence of **3a** by simultaneous employment of two different palladium pincer-complex catalysts (**6a** and **7a**).

The NCN-pincer-complex **6a** efficiently transfers a trialkyltin-group from **3a** or **3b** to a variety of allylic substrates including allyl chloride, -phosphonate, and -epoxide (Table 6). The mild and neutral reaction conditions applied allow the presence of functionalities such as COOEt, CN, and unprotected OH groups. The stannylation with **3b** requires higher reaction temperature than the corresponding reaction with **3a**, probably due to the sterically more bulky alkyl-groups in **3b** (butyl) compared to **3a** (methyl). The allyl stannanes **4b-f** are sensitive toward protonation and therefore the isolated yields are lowered by partial decomposition during silica-gel chromatography. The regioselectivity of the reaction is high, as both branched and linear allylic substrates afford the corresponding linear allyl stannane (entries 1, 2, and 4).

We have also attempted to prepare allyl stannanes bearing strongly electron-withdrawing substituents in the allylic position by employing **11a** or **11b** as substrates, however, the

corresponding allyl stannane products rapidly decomposed upon purification. Nevertheless, we were able to combine the stannylation process with allylation of aldehyde and imine electrophiles (see also section 2.1).[59,60] In this reaction, the in situ formed allyl stannanes (entries 6-8) are allowed to react with the electrophiles. The allylation reaction (Scheme 18) could be performed as a one-pot sequence by employment of catalysts **6a** (1 mol %) and **7a** (2 mol %) as well as the appropriate electrophile (**12a** or **9a**) in the presence of **3a**. As we reported recently,[59,60] catalyst **6a** is characterized by a very low activity in the allylation of aldehydes and imines. In fact, this low reactivity allows the isolation of allyl stannanes **4b-f** when using solely catalyst **6a** (entries 1-5). Employment of catalyst **6a** alone leads to a very slow allylation reaction with a low conversion and a poor yield under the applied reaction conditions. On the other hand, PCP catalyst **7a** efficiently facilitates the allylation of **12a** and **9a** without catalyzing the stannylation process.

Table 6. Selected results of the palladium pincer-complex catalyzed allylic stannylation.[a]

Entry	Allyl	Ditin	E	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	**11d**	**3b**	-	60/15	 **4b**	-	57
2	 **11f**	**3b**	-	60/7	 **4c**	-	62[d]
3	 **11g**	**3b**	-	60/15	 **4d**	-	72
4	 **23**	**3a**	-	40/15	 **4e**	-	59[e]
5	 **24a**	**3a**	-	0/17	 **4f**	4:1	68[f]
6	**11a**	**3a**	**12a**	20/18	**13a**	2:1	95
7	**11b**	**3a**	**12a**	20/18	**13c**	1:1	96
8	**11a**	**3a**	**9a**	40/18	**14a**	1:4	56

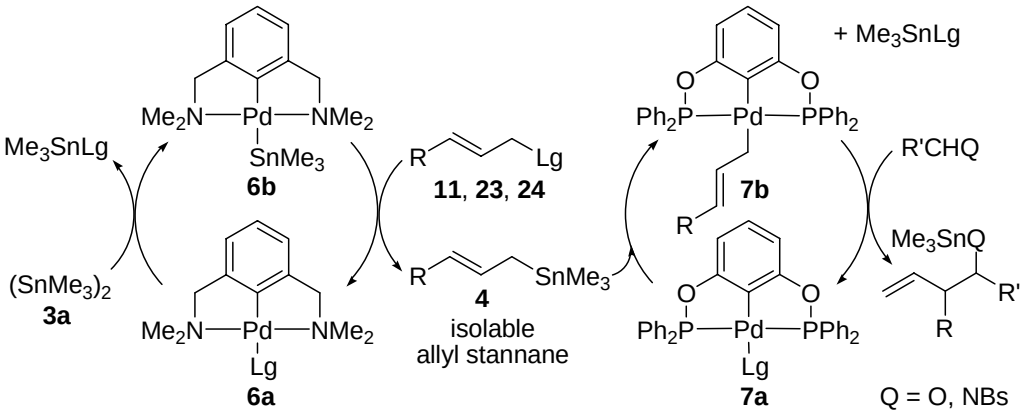
[a] All reactions were conducted using 2 mol % **6a** (entries 1-5) or 1 mol % **6a** and 2 mol % **7a** (entries 6-8) in THF solvent. [b] Diastereomeric ratio (*anti*:*syn*). [c] Isolated yield. [d] *E*/*Z* ratio = 9:1. [e] *E*/*Z* ratio = 5:3. [f] About 20% of the 1,4-substituted isomer was also formed.

The above one-pot substitution reaction works smoothly with substrates bearing electron-withdrawing carbethoxy (**11a**) and cyano (**11b**) substituents in the allylic position (entries 6-8). The reaction proceeds with high regioselectivity to provide the branched homoallylic product (**13a**, **13c**, and **14a**), however, the stereoselectivity of the reaction is poor, affording the *anti* product in the reactions with **12a** (entries 6-7) and the corresponding *syn*-product in the reaction with **9a** (entry 8).

Mechanistic considerations. Previous studies[61,62] revealed that hexamethylditin (**3a**) readily reacts with palladium pincer complex **6a** to afford mono-stannyl complex **6b**. The formation of complex **6b** is probably also the first step of the allylic stannylation reaction

(Scheme 19). The next step is a direct transfer of the trialkyl-stannyl group to the allylic substrate to afford allyl stannane **4**. Since there is only a single coordination site available on palladium, the displacement of the allylic leaving group takes place via a metal-induced S_N2 (e.g., **11d** and **23**) or S_N2' (e.g., **11f**) reaction,[62] affording linear products (**4b**, **c**, and **e**) from functionalized substrates.

The Szabó group has previously shown[59,60] that PCP complexes (such as **7a**) readily undergo transmetalation with allyl stannanes, and also efficiently catalyze the electrophilic substitution of allyl stannanes. The reactions conducted in the presence of electrophiles and catalyst **7a** will probably proceed via complex **7b** (Scheme 19) generated by transmetalation of **7a** with allyl stannane **4**. Subsequently, **7b** will undergo electrophilic allylation affording the branched homoallylic products.



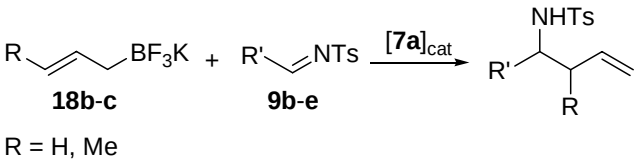
Scheme 19. Mechanism of the palladium pincer-complex catalyzed allylic substitution.

There are two interesting mechanistic features of this catalytic process (Scheme 19): the first is that allyl-palladium complexes are not involved in the formation of the allyl stannanes because of the lack of free coordination sites on palladium; the second is that the allylic substitution reaction does not involve a change in the oxidation state of palladium, since it is restricted to +2 for the whole process. A clear advantage of the palladium pincer-complex catalyzed stannylation reaction is that formation of bis-allylpalladium complexes (such as **5a**) is prohibited because of the firm terdentate coordination of the pincer-ligand. Furthermore, under the applied reaction conditions, NCN complex **6a** does not react with the allyl stannane product, and therefore these products (**4b-f**) can be isolated in relatively good yield.

3.2 Palladium pincer-complex catalyzed electrophilic allylic substitution of potassium trifluoro(allyl)borates (Paper VI)

As mentioned in section 2.5, allyl boranes and boronates are relatively unstable species, which limits their use as reagents in organic synthesis. Recently, however, Batey and co-workers[89] presented a new class of stable allyl boronates: potassium allyl- and crotyl trifluoroborate. As indicated in sections 2.5 and 2.6, allyl boronates can be employed as allylic precursors in the palladium-catalyzed allylation of imines (Scheme 14). This gave us

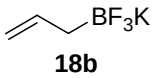
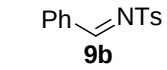
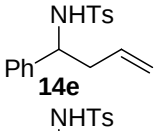
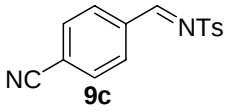
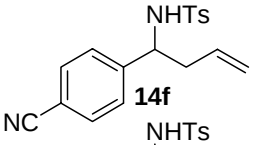
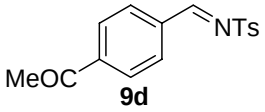
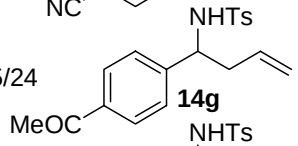
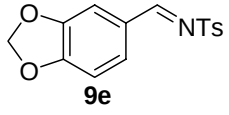
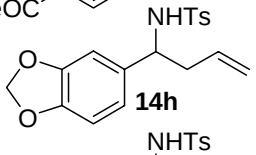
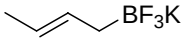
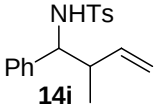
the idea to employ potassium trifluoro(allyl)borate as an allylic substrate in the pincer-complex catalyzed allylation of tosylimines (Scheme 20).



Scheme 20. Palladium pincer-complex catalyzed electrophilic allylation with potassium trifluoro(allyl)borates.

We found that **7a** catalyzes the coupling of potassium trifluoro(allyl)borate (**18b**) with tosylimines (**9b-e**), affording homoallylic amines in high yields (Scheme 20, Table 7). The mild reaction conditions allow the presence of a wide variety of functional groups including cyano, keto, and acetal functionalities (entries 2-4). The reaction is usually conducted at 40 °C, however, activated imine **9d** was successfully allylated at 25 °C, and deactivated imine **9e** required heating to 50 °C in order to achieve full conversion.

Table 7. Selected examples of the palladium pincer-complex catalyzed allylation of tosylimines.[a]

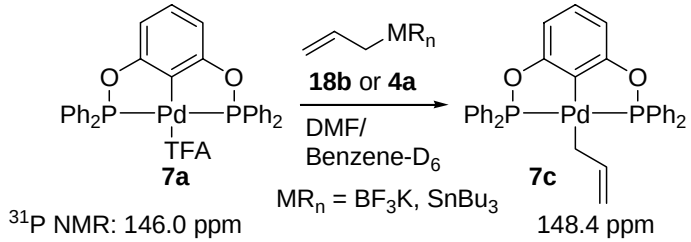
Entry	Allylborate	Tosyl imine	t [°C]/Time [h]	Product	d.r.[b]	Yield[c] [%]
1	 **18b**	 **9b**	40/24	 **14e**	-	95
2	**18b**	 **9c**	40/24	 **14f**	-	88
3	**18b**	 **9d**	25/24	 **14g**	-	79
4	**18b**	 **9e**	50/24	 **14h**	-	95
5	 **18c**	**9b**	40/48	 **14i**	35:65	40

[a] All reactions were conducted in DMF in the presence of 5 mol % **7a**. [b] Diastereomeric ratio (*anti*:*syn*). [c] Isolated yield.

To assess the stereoselectivity of the reaction, we employed potassium trifluoro(*E*-crotyl)borate (**18c**) in the reaction with **9b**. The reaction required a prolonged reaction time (48h) and afforded the branched homoallylic amine in poor yield (40%) and with low selectivity (35:65) for the *syn* product (entry 5).

Mechanistic considerations. We investigated the reaction of potassium trifluoro(allyl)borate (**18b**) with **7a** in order to elucidate the reactive intermediate of the allylation reactions with trifluoro(allyl)borate salts **18b-c**. When monitoring the reaction of

18b with **7a** in a DMF/Benzene-D_6 mixture by ^{31}P-NMR spectroscopy, the signal from **7a** (146.0 ppm) disappeared and a new peak at 148.4 ppm appeared, clearly indicating a reaction between **7a** and **18b**. To clarify the nature of this reaction product, **7a** was reacted with allyl stannane **4a** in a DMF/Benzene-D_6 mixture, and once again, we observed a downfield shift by 2.4 ppm in the ^{31}P-NMR spectrum (Scheme 21).



Scheme 21. Stoichiometric reactions monitored by ^{31}P-NMR.

The active allylating agent in the coupling reaction of allyl stannanes with aldehydes or sulfonimines has been investigated,[60] and it was shown that the product of transmetalation of allyl stannane **4a** with palladium pincer-complex **7a** is the η^1-(mono)allylpalladium complex **7c** (Scheme 21). The fact that **4a** and **18b** afford the same product in the reaction with **7a** indicates that the reactions of **18b** with tosylimines **9b**-**e** presented above proceed via the common intermediate **7c**.

3.3 Synthesis of chiral palladium pincer-complex catalysts for the asymmetric allylation of sulfonimines (Paper VII)

As shown above, PCP pincer complexes are efficient catalysts for the allylation of imines (sections 3.1 and 3.2) using allyl stannane and boronate substrates. As the reaction generates a new stereogenic carbon, asymmetric electrophilic allylation is expected to occur with chiral palladium pincer-complex catalysts. The development of such a reaction is synthetically important, since there are only a few reports in the literature on the asymmetric allylation of imines.[23,24,29-31,90-92]

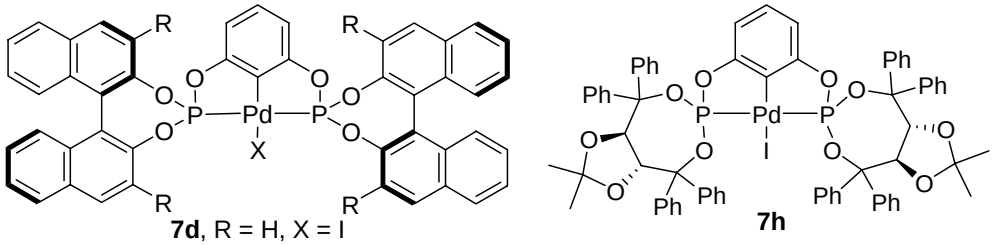
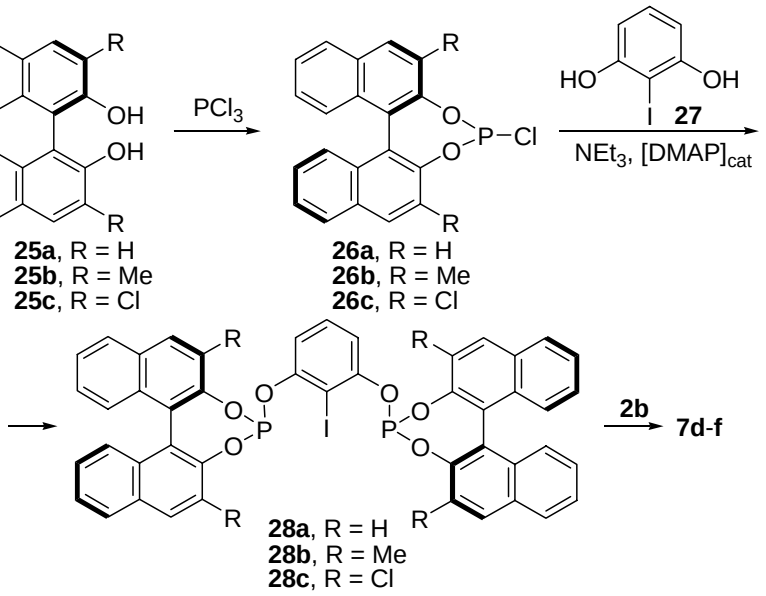


Figure 4. Chiral palladium pincer-complexes.

The new chiral pincer-complex catalysts were designed considering two important requirements for the chiral precursors: (i) easy access to both enantiomers; and (ii) the possibility for fine-tuning of the steric and electronic properties of the ligand. We expected that BINOL (**25a**) and TADDOL (**29**) would fulfill these requirements, as both enantiomers

are commercially available for both compounds, and substituted derivatives are readily accessible.[93,94]



Scheme 22. Synthesis of BINOL-based pincer-complexes.

The synthesis of BINOL-based palladium pincer-complexes **7d** (Figure 4) started from R-(+)-BINOL (**25a**), which was treated with an excess of PCl_3 to provide phosphorochloridite **26a** (Scheme 22). Compound **26a** is sensitive to moisture, and therefore it was used without purification in the reaction with iodo-resorcinol (**27**), affording pro-ligand **28a**, which was immediately reacted with $Pd_2(dba)_3$ (**2b**) to afford BINOL-based complex **7d** in 89% yield.

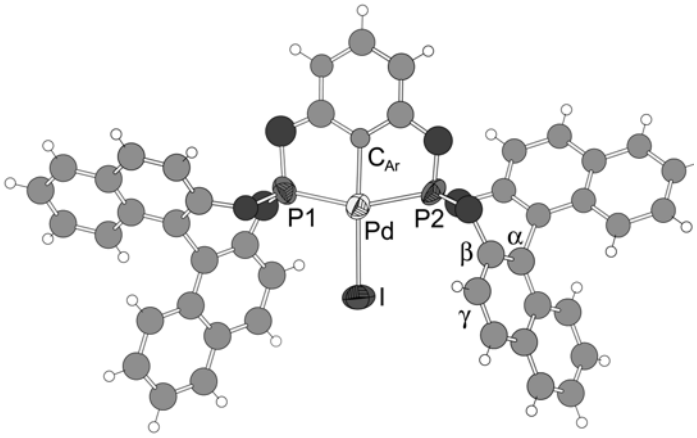


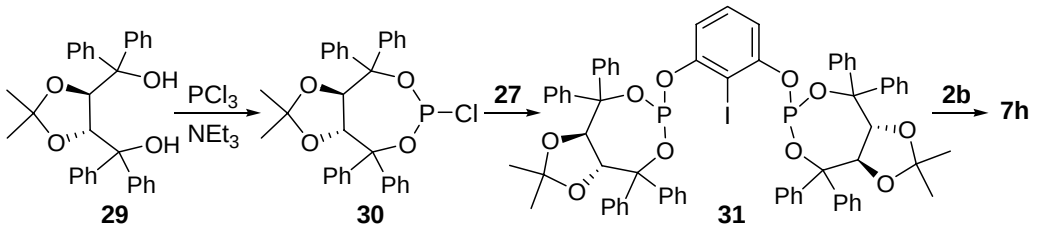
Figure 5. X-ray structure of **7d**. Selected bond lengths (Å) and angles (°): Pd-C_{Ar}, 1.985(6); Pd–P1, 2.251(5); Pd–P2, 2.249(5); Pd–I, 2.631(18); P1–Pd–C_{Ar}, 80.2(4); P1–Pd–C_{Ar}, 77.4(4); P1–Pd–P2, 166.32(18).

Inspection of the X-ray structure of **7d** (Figure 5) reveals that the palladium complex has a C_2-symmetry with short Pd-P and Pd-C bond lengths (2.25 Å and 1.99 Å respectively) indicating a tight coordination of the pincer-ligand to palladium. The complex is characterized by a well-defined chiral environment surrounding the palladium atom. The X-ray structure clearly shows that one of the γ-hydrogens of each BINOL moiety is located relatively close to

palladium. This topology allows fine-tuning of the chiral environment on the central atom by employment of γ,γ'-disubstituted BINOL derivatives.

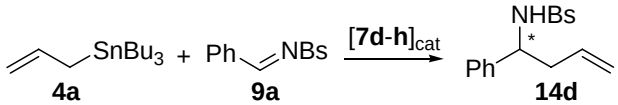
As precursors for synthesis of substituted BINOL complexes **7e** and **7f** (Figure 4), we used the previously reported[93] γ,γ'-dimethyl-BINOL (**25b**) and γ,γ'-dichloro-BINOL (**25c**) derivatives. The synthesis of **7e-f** could be accomplished by the same synthetic strategy as the synthesis of **7d** (Scheme 22), however, the isolated yields of the complexes were lower: 18% and 26% respectively. The previous report[60] on palladium pincer-complex catalyzed allylation of aldehyde and imine electrophiles showed that application of pincer-complexes with weakly coordinating ions, such as trifluoroacetate (**7a**), leads to high catalytic activity. Therefore, we also prepared TFA-complex **7f** by ligand-exchange of complex **7d** with Ag(TFA).

In order to vary the chiral backbone of the pincer-complex catalysts, we synthesized TADDOL-based pincer complex **7h** (Figure 4) as well. Thus, TADDOL (**29**) was reacted with PCl_3 to give phosphorochloridite **30** (Scheme 23). In contrast to the synthesis of BINOL derivatives (**28a-c**), **30** could be coupled directly with **27**, and thus the synthesis of pro-ligand **31** could be performed as a one-pot sequence. Subsequently, compound **31** was reacted with $Pd_2(dba)_3$ (**2b**) to give **7h** in 34% isolated yield.



Scheme 23. Synthesis of the TADDOL-based palladium pincer complex.

Catalytic asymmetric allylation of sulfonimines. The palladium pincer-complex catalyzed allylation of **9a** with **4a** was reported[59,60] to proceed relatively slowly when pincer-complexes with halogenide counter-ions were employed. Indeed, we found that the iodo-complex **7d** catalyzes the coupling of **4a** with **9a** at 20 °C in 72 h. This reaction (Scheme 24) afforded homoallylic amine **14d** in 70 % yield (Table 8, entry 1), albeit with poor enantioselectivity (20 % ee). On the other hand, employment of TFA-complex **7g** (entry 2) resulted in a much faster allylation reaction (17 h) with a high yield of the product (90 %) in accordance with the previous results,[59,60] however, the enantiomeric excess of the product was only 5%.



Scheme 24. Catalytic asymmetric allylation of sulfonimine.

Further studies showed that the enantioselectivity of the catalyst could be increased by substitution on the γ- and γ´-position of the BINOL moiety. Thus, tetramethyl substituted complex **7e** afforded **14d** with a higher ee (59 %) than the parent complex, even though a longer reaction time (90 h) was required to afford a high yield (entry 3). Also tetrachloro-substituted complex **7f** gave a higher ee (34 %) than unsubstituted complex **7d** (entry 4) in the

reaction of **9a** with **4a**. The TADDOL-based catalyst **7h** had a reactivity similar to **7d-f** (entry 5), however, the enantioselectivity obtained by this catalyst was very low (5 %).

Table 8. Catalytic asymmetric allylation of **9a** with **4a**.[a]

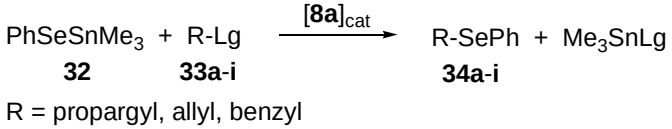
Entry	Cat.	Time [h]	ee[b] [%]	Yield[c] [%]
1	**7d**	72	20	70
2	**7g**	16	5	90
3	**7e**	90	59	74
4	**7f**	72	34	65
5	**7h**	72	5	60

[a] All reactions were conducted in DMF at 20 °C. [b] Determined with chiral-phase HPLC. [c] Isolated yield.

In summary, we have shown that BINOL-based palladium pincer-complexes are promising catalysts for the enantioselective allylation of sulfonimines. The enantioselectivity of the catalyst can be fine-tuned by employment of easily accessible substituted BINOL-derivatives.

3.4 Palladium pincer-complex catalyzed selenylation of organohalides (Paper VIII)

Palladium pincer-complexes are known to catalyze the transfer of organostannyl and -silyl groups to electrophiles from dimetallic trimethyltin reagents[61,62] (see also section 3.1). In these reactions the most electronegative metal of the dimetallic reagent is transferred to the electrophile. Considering this observation we expected that trimethylstannylphenylselenide (**32**) can be employed as selenylating reagent in pincer-complex catalyzed formation of organoselenides.[88,95-97]



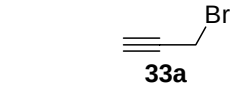
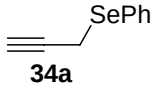
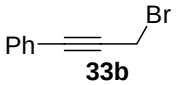
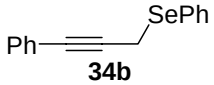
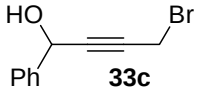
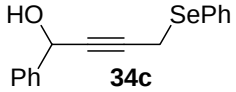
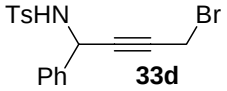
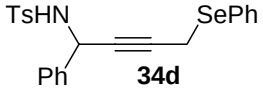
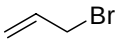
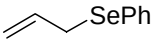
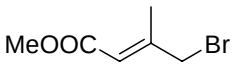
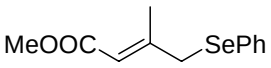
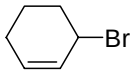
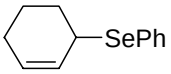
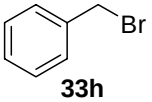
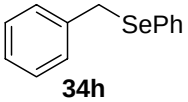
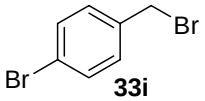
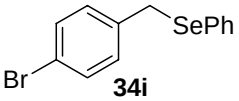
Scheme 25. Palladium pincer-complex catalyzed selenylation.

Indeed, we found that various organic substrates, including propargyl-, allyl-, and benzyl halides (**33a-i**), readily undergo halogen-selenium exchange in the presence of **32** (Scheme 25) and catalytic amounts (2 mol %) of **8a**, affording organoselenides **34a-i** in good to excellent yield (Table 9). On the other hand, in the absence of catalyst **8a**, only traces of the selenylated products were formed. The reactions were conducted under mild and neutral conditions without using an inert gas atmosphere. We did not observe formation of trimethylstannanes in any of the reactions, indicating that **8a** transfers exclusively the phenylselenyl group from **32** to the electrophile. The reaction displays a remarkably high functional group tolerance, as COOMe, TsNH, aryl bromide and OH groups are tolerated. The regioselectivity of the substitution involving allylic and propargylic substrates is excellent, as only products resulting from the direct substitution of the halogenated carbon are formed.

Thus, propargyl bromides **33a-d** afforded propargyl selenides **34a-d** (entries 1-4) in good to excellent yields. When unsubstituted propargyl bromide **33a** was used as electrophile, traces (about 2%) of allenyl selenide product was also observed in the crude reaction mixture. The

predominant formation of propargyl selenides from propargyl bromides **33a**, **33c** and **33d** (entries 1, 3 and 4) is in sharp contrast to the corresponding palladium pincer-complex catalyzed stannylation and silylation reaction of propargyl chlorides, which afforded the corresponding allenyl stannane and silane products.[61,62] Allyl bromides **33e-f** reacted also with high regioselectivity affording primary allyl selenides **34e-f** as the sole product in high yields (entries 5-6). Secondary allyl bromide **33g** could also be used as an electrophile (entry 7), however, this substitution reaction was sluggish, even at 60 ºC, and therefore an elongated reaction time was required. Benzyl bromides (**33h-i**) were also effective as electrophiles, affording benzyl selenides (**34h-i**) in high yields (entries 8-9), however, **33h-i** reacted somewhat slower than propargyl and allyl bromides **33a-f**.

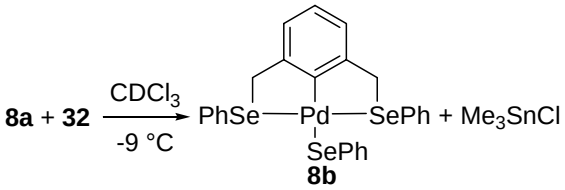
Table 9. Selected results of the palladium pincer-complex catalyzed selenylation.[a]

Entry	Electrophile	t [°C]/Time [h]	Product	Yield[b] [%]
1	 **33a**	20/15	 **34a**	90
2	 **33b**	20/5	 **34b**	66
3	 **33c**	20/17	 **34c**	95
4	 **33d**	20/17	 **34d**	91
5	 **33e**	20/15	 **34e**	80
6	 **33f**	20/3	 **34f**	85
7	 **33g**	60/24	 **34g**	87
8	 **33h**	20/17	 **34h**	89
9	 **33i**	20/17	 **34i**	90

[a] All reactions were conducted in THF using 2 mol % of **8a**. [b] Isolated yield.

Stoichiometric reactions. Previous studies have shown[61,62] that pincer complexes such as **6a** do not react with propargyl or allyl halides at ambient temperature. On the other hand, dimetallic organostannanes, such as $(Me_3Sn)_2$ or $Me_3SnSiMe_2Ph$, undergo transmetalation with **6a** to provide the corresponding organometal (tin or silicon) coordinated pincer complex, which could be observed by ^{129}Sn- or ^{29}Si-NMR spectroscopy, respectively. Thus, in order to elucidate the mechanism of the organoselenium transfer reaction, we conducted a series of

stoichiometric experiments for the reaction of SeCSe complex **8a** with **32**, monitored by ^{1}H-NMR and ^{77}Se-NMR at -9 °C (Scheme 26). When the pale yellow solution of **8a** was treated with 1.1 equivalents of **32** in $CDCl_3$, the color of the reaction mixture immediately turned to dark orange. The ^{1}H-NMR spectrum of **8a** also underwent substantial changes upon addition of **32**, as the characteristic signals from the methylene groups of **8a** (4.73, 4.72, 4.32, and 4.27 ppm) were considerably broadened. Unfortunately, extensive line-broadening (50 Hz) hindered the identification of the product of the stoichiometric reaction. We also analyzed the reaction mixture of the stoichiometric reaction of **8a** with **32** using ^{77}Se-NMR spectroscopy. The ^{77}Se-NMR spectrum of pure **8a** displayed two signals at 427.1 and 424.9 ppm, indicating the presence of two diastereomeric forms,[58] while the selenium atom of pure **32** resonated at 0.5 ppm. When **32** was added to **8a**, the ^{77}Se-NMR signal of **32** (0.5 ppm) vanished, and at the same time, the two signals of **8a** (427.0 and 424.9 ppm) were broadened and shifted downfield to 432.9 and 425.7 ppm respectively, and a new peak appeared at 83.8 ppm. Once again, the extensive line-broadening of the ^{77}Se-NMR signals did not allow clear identification of the product. Our further efforts to isolate and purify the product of the stoichiometric reactions were fruitless, because of its low stability.



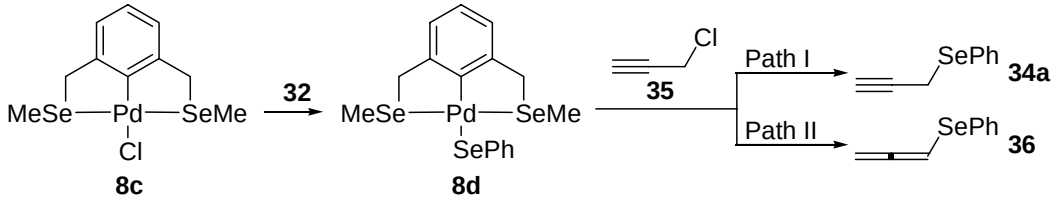
Scheme 26. Stoichiometric reaction studied by NMR spectroscopy.

Although the NMR studies clearly indicated that in the above stoichiometric process, **32** was consumed and that the NMR spectrum of **8a** underwent substantial changes, conclusive results as to the identity of the reaction product could not be obtained from these experiments. However, our previous studies[61,62] with $(Me_3Sn)_2$ or $Me_3SnSiMe_2Ph$ clearly indicated that transmetalation of these dimetallic reagents occurs with pincer-complex **6a**, and therefore we assume that the stoichiometric reaction of **8a** and **32** results in formation of a phenyl-selenium coordinated complex **8b** (Scheme 26).

DFT modeling of the phenylselenyl transfer reaction. Based on the assumption that the initial step of the pincer-complex catalyzed reaction is the formation of **8b**, we performed DFT modeling studies to explore the mechanism of the organoselenium group transfer from the palladium atom to the organic substrate. In these studies, we investigated the potential energy surface of the organoselenium transfer to a propargylic substrate (c.f. entries 1-4). The computational methods are described in section 2.7, except that Gaussian 03[98] was used for all calculations.

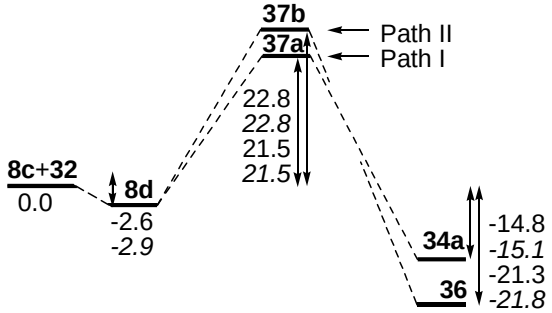
Reaction profile for the selenium transfer process. Because of computational limitations, we employed slightly simplified model systems to describe the mechanism of the experimentally studied reaction of **33a** with **32**. Accordingly, we approximated (Scheme 27) the phenylselenyl groups in palladium pincer-complex **8a** and **8b** by methylselenyl groups (**8c**

and **8d**) and the bromine atom of **33a** was approximated by a chlorine atom (**35**). Using these model systems, we investigated two different pathways (Scheme 27) for the palladium-catalyzed phenylselenylation of propargyl chloride **35**. Path I involves transfer of the phenylselenyl group from pincer-complex **8d** to give propargyl selenide **34a**, while the second pathway (Path II) is the corresponding reaction affording allenyl selenide **36**.



Scheme 27. Reactions studied by DFT modeling.

According to the DFT results, the reaction between **8c** and **32** is exothermic by 2.9 kcal mol^{-1}, affording **8d** (Scheme 28), which is the active selenylating agent in the selenium transfer process. The fact that **8d** is such a stable species also supports our assumption that the stoichiometric reaction (Scheme 26) of **8a** with **32** resulted in selenium-coordinated complex **8b**. The reaction of **8d** with **35** affording propargyl selenide **34a**, proceeds through TS **37a** (Path I), which require an activation energy of 21.5 kcal mol^{-1}. The subsequent formation of propargyl selenide **34a** is strongly exothermic by 15.1 kcal mol^{-1} (Scheme 28).



Scheme 28. PES of the palladium-catalyzed phenylselenylation reaction. The energy values are given in kcal mol^{-1}, and the ZPV corrected energies are given in italics.

The second pathway (Path II) leads to formation of allenyl selenide **36** via TS structure **37b** and requires a somewhat higher activation energy (22.8 kcal mol^{-1}) than Path I, resulting in **34a**. Interestingly, although the activation barrier of Path II is higher than that of Path I, formation of allenyl selenide **36** is more exothermic (-21.8 kcal mol^{-1}) than formation of the propargyl product **34a** (-15.1 kcal mol^{-1}). These results are in agreement with our experimental findings that the palladium-catalyzed reaction of **32** with **33a** leads predominantly to propargyl product **34a** (entry 1).

Inspection of the calculated structures of complexes **8c** and **8d**, as well as TS structures **37a-b** (Figure 6) reveals some interesting mechanistic details. In the palladium pincer-complex **8c**, the palladium-carbon bond is relatively short (2.0 Å), while the palladium-selenium bond lengths are somewhat longer (2.4 Å). These characteristics are preserved in complex **8d** and TS's **37a-b**, which means that the selenylation reaction takes place at a single coordination

site on palladium (Figure 6). In TS **37a**, the distance of the propargylic carbon (C_α) to the selenium atom is 2.482 Å and the C_α-Cl bond is 2.504 Å, indicating that the formation of the carbon-selenium bond and the cleavage of the carbon-chlorine bond is a concerted process. Furthermore, the Se-C_α-Cl bond angle is 151.9°, which is close to the characteristic displacement angle of the S_N2-reactions (180°). The geometrical features of TS structure **37a** indicate that the selenium atom is involved in an S_N2-type displacement of the leaving group (Cl), initiated by the lone-pair electrons of the selenium atom. The alternative TS structure (**37b**), where the selenium atom displaces the chlorine in an S_N2' fashion, leading to the allenyl selenide **36**, incorporates similar structural features. These results indicate that the palladium atom increases the nucleophilicity of the selenium without being directly involved in the Se-Cl substitution process.

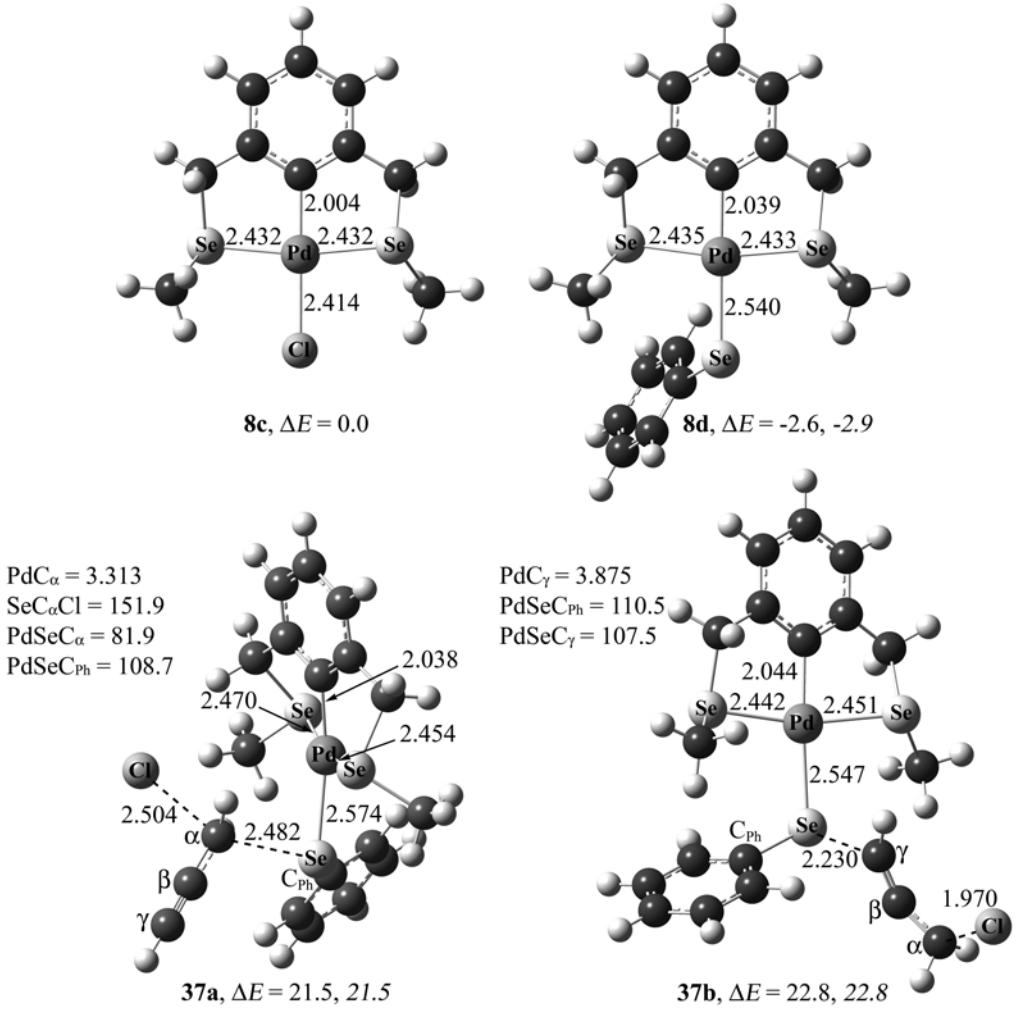
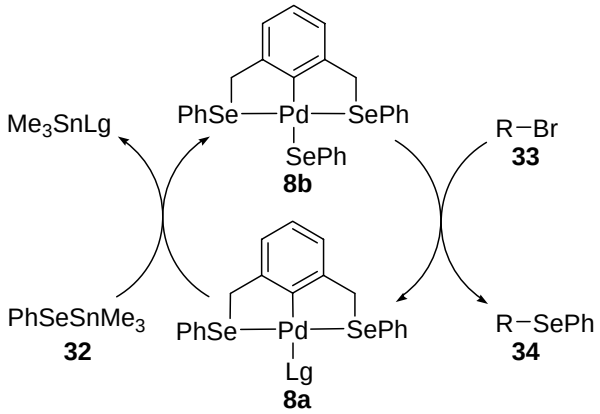


Figure 6. Calculated geometries of **8c** and **8d** and the TS's of the selenylation reactions (**37a-b**). Bond lengths are given in Å, angles in degrees, energies in kcal mol^{-1} and the ZPV-corrected energies in italics.

The catalytic cycle of the phenylselenyl transfer reaction. Based on the above results, we propose a catalytic cycle for the palladium pincer-complex catalyzed phenylselenyl transfer from **32** to the organic substrates (Scheme 25). Thus, the catalytic cycle of the substitution

reaction is initiated by the formation of intermediate **8b** via transmetalation of **32** with **8a** (Scheme 29). In the transmetalation process, the phenylselenyl group is transferred to palladium. Formation of **8b** is then followed by an S_N2-type displacement of the bromide leaving-group of **33** by the lone-pair electrons of selenium, regenerating catalyst **8a**.

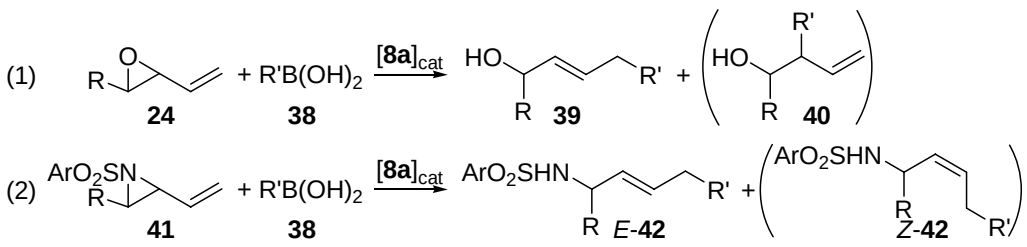


Scheme 29. The catalytic cycle of the phenylselenylation reaction.

An interesting feature of this catalytic cycle is that the catalytic process occurs at a single coordination site of palladium. Also, the oxidation state of palladium is restricted to +2. These features are in contrast to the corresponding Pd(0) catalyzed processes where redox processes occur, and therefore the mild reaction conditions employed in the reaction described above represents and alternative to the Pd(0) catalyzed and other transformations of selenium-tin reagents.[99-104]

3.5 Employment of palladium pincer-complexes in the cross-coupling of vinyl epoxides and vinyl aziridines with organoboronic acids (Paper IX)

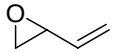
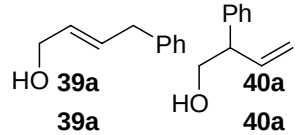
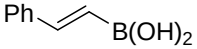
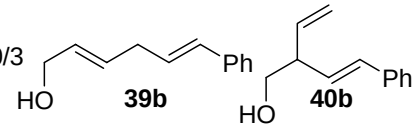
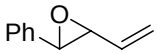
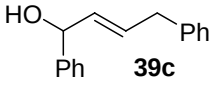
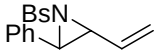
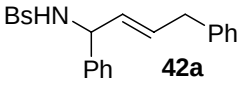
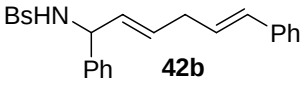
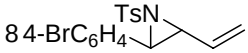
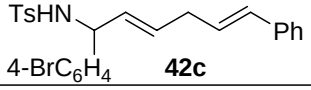
Palladium-catalyzed coupling of organoboronic acids with unsaturated substrates (Suzuki-Miyaura cross-coupling) is an important process in organic chemistry.[105-109] However, the literature of cross-coupling reactions of organoboronic acids with vinyl epoxides and aziridines is surprisingly scarce. As far as we know, only a single example of a palladium-catalyzed carbon-carbon coupling of vinyl epoxides with alkenylboranes has been reported to date.[110] As an extension of the above studies (sections 3.1-3.4), we decided to explore the synthetic potential of palladium pincer-complex catalysts in the cross-coupling of vinyl derivatives of three-membered rings and organoboronic acids. We found that such reactions can be achieved by employment of **8a** as catalyst (Scheme 30).



Scheme 30. Palladium pincer-complex catalyzed coupling of organoboronic acids with (1) vinyl epoxides and (2) vinyl aziridines.

The coupling processes are conducted under the typical conditions of the Suzuki-Miyaura cross-coupling reactions, with the use of base (Cs_2CO_3 or CsF) and water as additives. The coupling of butadiene monoxide (**24b**) with phenyl boronic acid (**38a**) proceeded smoothly at 0 °C (Table 10, entry 1) and afforded mainly the 1,4-addition product (**39a**) together with a small amount of 1,2-addition product (**40a**).

Table 10. Selected examples of palladium pincer-complex catalyzed cross-coupling reactions.[a]

Entry	Substrate	Boronic acid	Cat.	t [°C]/Time [h]	Product	Ratio[b]	Yield[c] [%]
1	 **24b**	$PhB(OH)_2$ **38a**	**8a**	0/16	 **39a** **40a**	11:1	94
2	**24b**	**38a**	**2b**	0/16	**39a** **40a**	7:3	95
3	**24b**	 **38b**	**8a**	0/3	 **39b** **40b**	9:1	95
4	**24b**	**38b**	**2b**	0/3	**39b** **40b**	3:2	95
5	 **24c**	**38a**	**8a**	20/9	 **39c**	>20:1	79
6	 **41a**[d]	**38a**	**8a**	20/18	 **42a**	>20:1	95[e]
7	**41a**[d]	**38b**	**8a**	20/3	 **42b**	>20:1	95[e]
8	 **41b**[d]	**38b**	**8a**	20/3	 **42c**	>20:1	95[e]

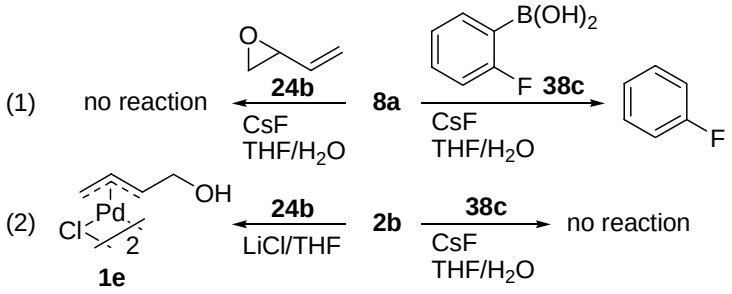
[a] All reactions were performed in a THF/H_2O mixture using 2.5 mol % **8a** in the presence of Cs_2CO_3 (Entries 1-5) or CsF (Entries 6-8). [b] 1,4:1,2 addition-product ratio, determined by ^{1}H-NMR. [c] Isolated yield. [d] *E*/*Z* ratio 2:1. [e] About 5% of the *Z*-product was also formed.

Alkenylboronic acid **38b** reacted much faster than **38a** in the reaction with **24b** (entry 3) and afforded the corresponding products **39b** and **40b** in excellent yields in 3 h. The ratio of 1,4-:1,2-addition product was slightly lower for the reaction of **38b** with **24b** than the reaction of **38a** with **24b**. We also employed commonly used palladium(0) catalysts such as $Pd_2(dba)_3$ (**2b**), in the reaction of **24b** with **38a** and **38b**. The catalyst displayed a high level of activity in the reactions (entry 2 and 4), however, the regioselectivity was poor as the 1,4-, and 1,2-addition products were formed in a 7:3 and 3:2 ratio respectively. On the other hand, the use of phenyl-substituted vinyl epoxide **24c** in the reaction with **38a**, catalyzed by **8a**, resulted in exclusive formation of 1,4-addition product **42c** (entry 5).

The use of vinyl aziridines (**41a**-**b**) as electrophiles in the cross-coupling with organoboronic acids resulted in the formation of 1,4-addition products **42a**-**c**; 1,2-addition products were not observed in any of the reactions. Interestingly, the products (**42a**-**c**) from

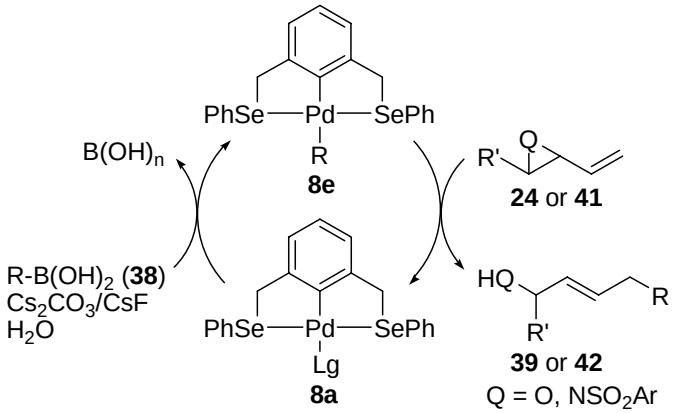
the reactions with organoboronic acids **38a-b** consisted of mainly of the *E*-isomer, even though the vinyl aziridine starting materials used had consisted of a 2:1 mixture of *E*- and *Z*-aziridines.

Mechanistic considerations. The mechanism of the reaction described above was explored by a series of stoichiometric reactions (Scheme 31). Monitoring the reaction of 2-fluorophenylboronic acid (**38c**) with **8a** by ^{1}H- and ^{19}F-NMR under the same conditions as the catalytic reactions revealed that fluorobenzene was formed after 20 min. Under the same reaction conditions using **24b** instead of **38c**, the reactants remained unchanged even after a prolonged reaction time.



Scheme 31. Stoichiometric reactions studied by NMR involving reactions of **8a** (1) and **2b** (2) with **24b** or **38c**.

We also carried out stoichiometric experiments with $Pd_2(dba)_3$ (**2b**) and **38c** or **24b** under the same reaction conditions as above. We did not observe any reaction between **2b** and **38c**. However, the reaction of **24b** and **2b** in the presence of LiCl resulted in allylpalladium complex **1e**, which could be isolated. The process without LiCl led to consumption of **24b**, however, the corresponding allylpalladium complex could not be isolated probably because of its instability.



Scheme 32. Catalytic cycle of the palladium pincer-complex catalyzed cross coupling reaction.

The stoichiometric reactions clearly indicate that the reaction of **8a** with **38c** or **24b** differs from the reaction employing **2b**. Previous studies showed[61,62] that a transmetalation of pincer-complex **6a** with **3a** resulted in a palladium-tin complex (see also Scheme 19). Considering that **8a** did react with **38c**, we assume that the initial step is transmetalation of the boronic

acid with **8a**, resulting in the formation of complex **8e** (Scheme 32). Prior to this process, the boronate-group is converted to a better leaving group by application of Cs_2CO_3/CsF and H_2O.[105] In the next step, the R group (R = aryl, vinyl) of complex **8e** is transferred to the electrophilic substrates (**24** or **41**) in an S_N2' (or S_N2) type process. The nucleophilic character of the transferred group (R) in **8e** is ensured by the electron donating selenium-based pincer-ligand.

3.6 Conclusions

We have shown that palladium pincer-complexes are highly selective catalysts for the synthesis and transformations of organometallic compounds. The use of NCN complex **6a** allowed the transfer of a trimethylstannyl group to allylic substrates, which could be employed for synthesis of functionalized allyl stannanes. Furthermore, the allylic stannylation could be efficiently coupled to electrophilic allylation of aldehyde and imine electrophiles by the simultaneous employment of NCN and PCP palladium pincer-complex catalysts. The palladium pincer-complex catalyzed electrophilic allylation reaction has been extended to involve coupling of potassium trifluoro(allyl)borate with tosylimines. New BINOL-based palladium pincer-complexes were synthesized that proved to be promising catalysts for asymmetric allylation of sulfonimines. The enantioselectivity of the catalyst could be fine-tuned by using substituted analogs of BINOL.

Selenylation of organohalides was accomplished using trimethylstannylphenylselenide in the presence of SeCSe palladium pincer-complex catalyst. The reaction has a high functional group tolerance and proceeds with high regioselectivity. Mechanistic studies suggest that the reactive intermediate is a selenium-coordinated palladium pincer-complex which transfers the selenium group via an S_N2 reaction to the organic substrate. Palladium pincer-complexes can also be applied for cross-coupling reactions of organoboronic acids with vinyl epoxides and aziridines. This reaction has a broad synthetic scope and it proceeds with an excellent regioselectivity. Mechanistic studies indicate that the organic group is transferred to the electrophile via the palladium pincer-complex in a nucleophilic substitution process.

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