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Investigation of the Palladium Catalyzed *C*-Allylation of Phenols

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1. Introduction

It has always been a great desire of chemists to take advantage of catalysis for their applications, inspired by essential catalysis in our body and environment.[1] Several catalytic reactions exert an incredible impact on mankind, especially the *Haber-Bosch* process.[2] With this invention production of ammonia from air nitrogen became possible. Cultivation of agriculture was then practiced in such an extensive amount, that experts consider this process as the key enabling factor for the demographic growth in the last century.[3] Not without reason was the *Nobel Prize* awarded to Fritz Haber in 1918.[4]

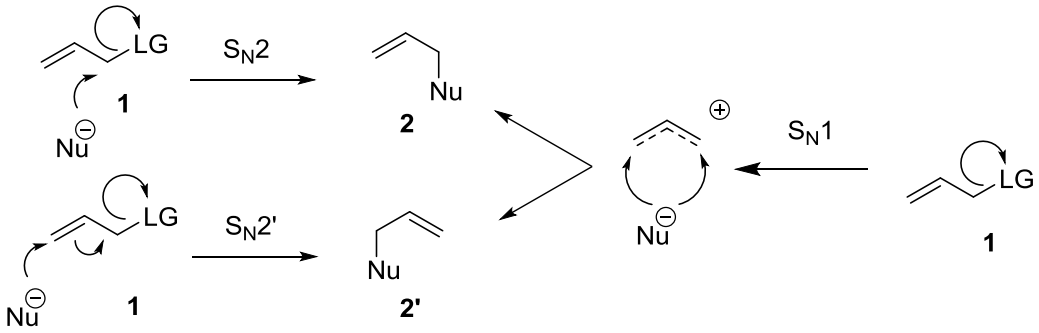
Throughout the years other catalytic systems have received increasing attention. The most promising topics for basic research belong homogeneous catalysis and *C*-*C* coupling of organic molecules. In the early 1970's *Heck et al.* discovered homogeneous palladium-catalyzed coupling reactions.[5] Soon after, other chemists like *Sonogashira et al.* (1975), *Negishi et al.* (1977), *Stille et al.* (1978) and *Suzuki et al.* (1979) also developed *C*-*C* coupling reactions that are now well established.[6-12] Consequently, Heck, Negishi, and Suzuki have been awarded with the 2010 *Nobel Prize* in chemistry for their work on "*palladium-catalyzed cross couplings in organic synthesis*".[13] Since the 1970's, many scientists focused on palladium-catalyzed research. There is a huge number of several new coupling reactions with palladium, f. i.: *Hiyama* coupling, *Buchwald-Hartwig* amination or *Liebeskind-Srogl* coupling.[14-16] One of the underestimated early palladium-catalyzed reactions is the *Tsuji-Trost* reaction. It enables the substitution of a leaving group (LG) in allylic position with a nucleophile. Although, *Trost et al.* have solved enantioselectivity problems,[17] some aspects remain poorly explored. One of those poorly explored aspects of the *Tsuji-Trost* reaction is the *C*-coupling of allylic groups onto electron rich aromatic molecules. Herein, an intensive investigation of *ortho*- or *para*-selective allylation of phenol via the *Tsuji-Trost* strategy was considered as a scientific challenge and was assumed for this Master Thesis.

2. Theory

2.1 Reactions with Allyl-Reagents

2.1.1 Nuclephilic Attack on Allylic Compounds

Nucleophilic attack on allylic compounds is the simplest way to introduce an allylic function. There are three different mechanisms for this reaction. All of them (S_N1, S_N2 and S_N2') should lead to the same product (Scheme 1). The S_N2 mechanism includes an attack on σ* to release the leaving group wherein in a S_N2' mechanism the attack takes place on π*.

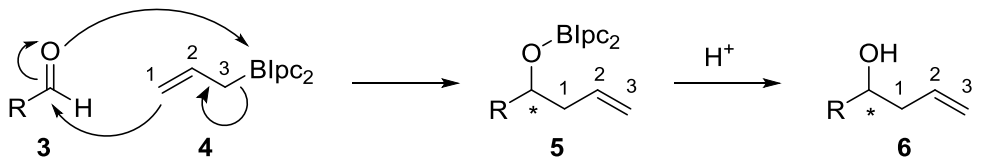


Scheme 1: Possible mechanisms for the attack of nucleophiles on allylic molecules.

Both mechanisms, S_N2 and S_N2' seem reasonable. If a prenyl compound is used, the S_N2 mechanism becomes more favored due to increased steric hindrance. Using a compound that is more similar to an allyl function, only one methyl at *C1*, shows ambiguous reactivity. Preference for either S_N2 or S_N2' has to be determined for each case. However, the S_N1 mechanism can be considered as a reasonable mechanism too. Each case has to be discussed individually, especially considering derivatization on *C1* and the leaving group. Therefore, it is hard to determine which mechanism is preferred in which case. Other experiments confirmed a "soft" generalization: S_N2 or S_N2' are depending on the starting material and copper compounds can favor the S_N2' pathway.[18]

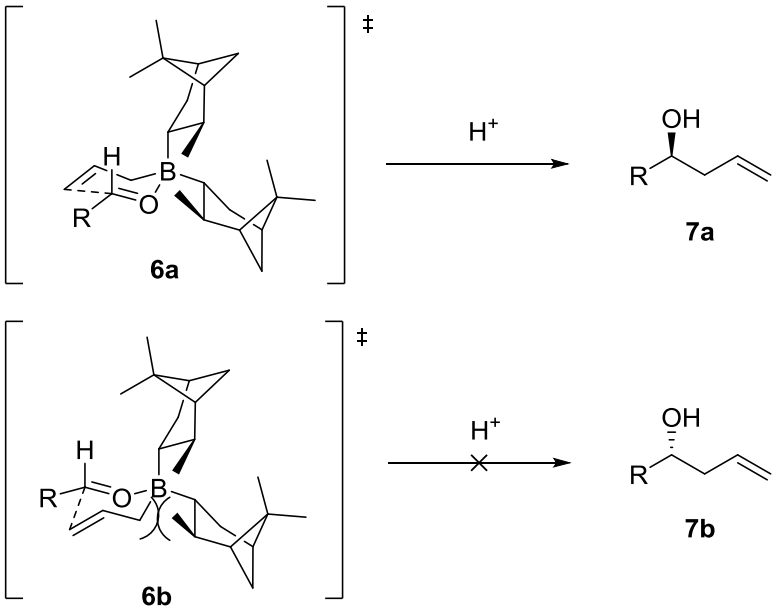
2.1.2 *Brown*- and *Roush-Hoffmann*-Allylation

Different to nucleophilic attacks on allylic and crotylic compounds *Brown*-allylation is used to produce homoallylic compounds through attack of *C*1 at the electrophilic carbon (Scheme 2). In a second step such homoallylic compounds are usually transformed to "Aldol-like-products".[19]



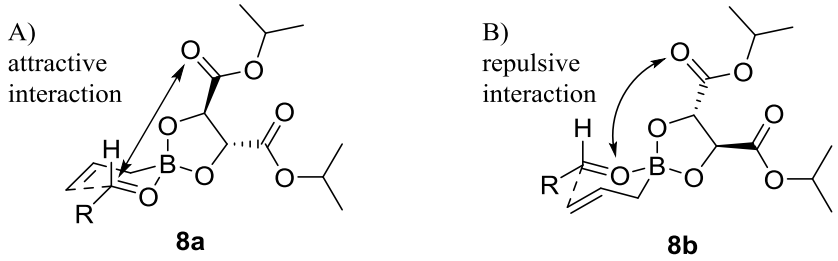
Scheme 2: General reaction mechanism of Brown allylation.

This reaction was developed to overcome problems that occurred when simple allyl magnesium halides or allyl lithium reagents were used to allylate aldehydes or ketones. Not only selectivity problems could be avoided via allyl boranes, also stereoselectivity could be controlled via pinene as ligand. The stereoselectivity can be explained through the Zimmermann-Traxler model (Scheme 3).



Scheme 3: *Zimmermann-Traxler* model of allyl((-)Ipc)$_2$borane reacting with an aldehyde.

Roush and Hoffmann developed a very similar reaction with an allylboronic ester in 1985.[20] In this reaction, stereoselectivity is controlled via attraction-repulsion energies between oxygen and hydrogen in the transition state (Scheme 4).[21]



Scheme 4: Model caclulations for the transition state in *Roush-Hoffmann* allylations.

The *Brown*-allylation as well as the *Roush-Hoffmann*-allylation are capable to produce *anti*- and *syn*-products out of *E*-stereosisomers as well as *Z*-stereoisomers. *E*-Isomers are faster converted to the *syn*-products because of minor steric hindrances.

2.1.3 *Hosomi-Sakurai* Reaction

Similar to allyl magnesium halides or allyl lithium reagents allyl silanes and allyl stannanes can be used for allylation of aldehydes or ketones. In the case of allyl silanes, strong Lewis acids like titanium tetrachloride are essential to enable such an electrophilic allyl shift.[22] This type of reaction is possible for two reasons. Firstly, Lewis acid dependent activation of the electrophilic carbon which is followed

by the rate determining step, the nucleophilic attack by the allyl carbon. The second reason is the β-silicon stabilization effect. This effect enables the formation of an unstable carbocation intermediate. Silicon donates into an empty p-orbital which leads to a shared silicon orbital between the two carbons (Figure 1). Hence, the positive charge is stabilized over 3 atoms.

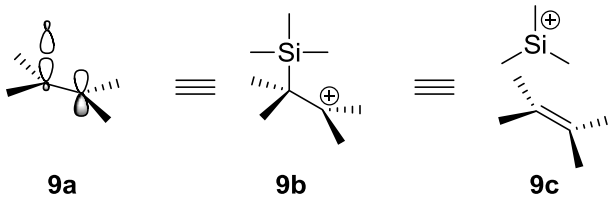


Figure 1: β-silicon effect or silicon hyperconjungation in the Hosomi-Sakurai reaction.

In general, the mechanism is accepted to occur through an open transition state. It is observed that in reactions of aldehydes with either *E* or *Z* isomers and aldehydes in both cases the thermodynamically more stable product (*syn*) is formed.

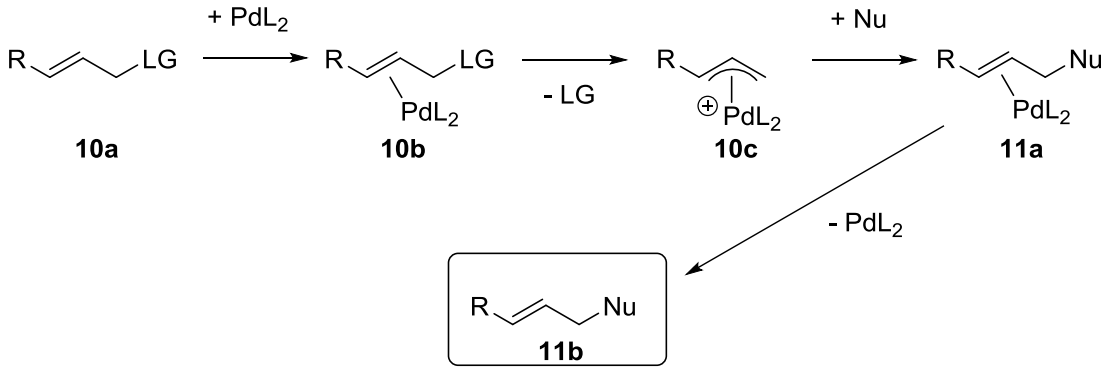
2.2 Palladium-Catalyzed Allylations

Besides the *Tsuji-Trost* reaction, allylic substrates and palladium-catalysis play a synergistic role in deprotection of various molecules. Usually, palladium-catalysis is used for deprotection of allylated acids, alcohols, or amines on a wide substrate scope.[23] As *C-C* bond formation in most cases leads to the thermodynamic product, a *C-C* bond cleavage plays a minor role, especially in the case of allylating aromatic compounds.

2.2.1 The *Tsuji-Trost* Reaction

The exchange of a leaving group in allylic position through a nucleophile was first reported from *Tsuji et al*. in 1965.[24] Jiro Tsuji was inspired by the work of *Smidt et al.* in which allyl palladium chloride complexes were reacted with water. At this time *Smidt et al.* proposed the attack of a hydroxide anion onto the allyl species.[25] It was concluded from Tsuji that other nucleophiles like carbanions should also undergo this reaction and lead to a *C-C* bond forming reaction. He managed the allylation of ethylmalonate and enamines without any ligands at room temperature. One problem at that point was the stoichiometric use of a η^3-allylpalladium(II) chloride dimer. This obstacle was overcome within the next few years.[26] In 1973 *Trost et al.* introduced ligands to this reaction. Barry M. Trost was also the first to define soft nucleophiles (pKa < 25) as the coupling partner in this Pd-catalyzed reaction.[27] A few years later, he confirmed that soft nucleophiles can be coupled with η^3-C_3H_5 – species.[17] Soon after, he realized that this reaction can be deployed to generate enantiomeric products.[28] For the next few years, this reaction was applied a dozen of times for otherwise difficult to synthesize molecules.[29] Especially in total synthesis the asymmetric allylic alkylation reaction became a popular transformation. A huge number of natural products could be synthesized more efficientlly via *C-C*

bond formation with *β*-diketones or -diesters as nucleophiles, *C*-*O* bond formation with primary alcohols or carboxylates or *C*-*N* bond formation with amines and amides.[29] All of these reactions can be simplified to one reaction scheme (**Fehler! Verweisquelle konnte nicht gefunden werden.**), wherein the leaving group is usually an acetate, carbonate or halide leaving group.

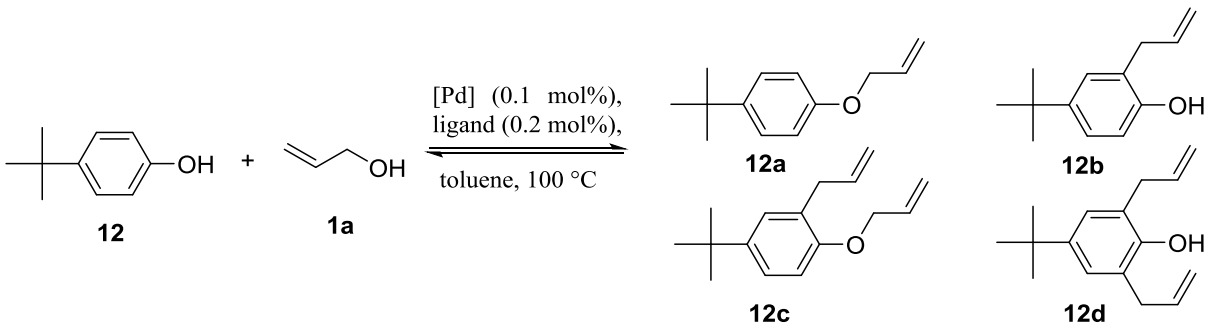


Scheme 5: Reaction mechanism of the *Tsuji-Trost* reaction.

Reactions that follow the *Tsuji-Trost* pattern (substitution of a leaving group in allylic position with a soft nucleophile) have been improved since the late 90's. Different groups specialized or modified these reaction conditions to more applicable substrates.[30] The next few chapters will concentrate on the efficiency of allylation reactions of electron rich aryls.

2.2.2 Work of *Bouwman et al.*

C-allylation is not the only desirable goal for Pd-catalyzed reactions with phenols but also *O*-allylation plays an important role in scientific research. Such allylic phenyl ethers are used as monomers for polymerization to phenolic resins in industry. [31] Additionally, by understanding *O*-allylation processes, mistakes in *C*-allylation reactions can be avoided. Therefore, the work of *Bouwman et al.* was used for insight into this process. In their work a focus was set on bidentate ligands, justified in their first screening with triphenylphosphine (PPh_3) as the only monodentate ligand tested. In that first screening, the other bidentate phosphines only differ in CH_2-chain lengths. Although conversions were very limited to 6 h at 100 °C, *O*-allylation selectivity was achieved by the use of dppm, dppe and dppp. Dppb on the other hand had a huge tendency to convert the *O*-allylated phenol (1 h reaction time) to a mixture of *O*- and *C*-allylated side-products. They also monitored that a 1:4 ratio of precatalyst palladium acetate [$Pd(OAc)_2$] to phosphine ligand has the highest activity compared to an 1:2 and 1:1 ratio. Best *O*-allylating results were achieved with dppp. Further, it was concluded that geminal di-alkylated ligands should kinetically stabilize the intermediate zerovalent palladium complexes.



12 1a 12a 12b 12c 12d

Scheme 6: General reaction scheme for reaction of 4-*tert*-butylphenol with allyl alcohol, catalyzed by different Pd-diphosphine complexes.

In an additional experiment, this assumption could be clarified. Conversion increased to more than 50 % in 22 h in all cases and led to same selectivity results as in the case of dppp. A significant improvement could be monitored using diallylether as the allylating source (80 % conversion). In the next step, several other ligands (Figure 2) could be adapted to the catalytic system via the use of $Pd(dba)_2$ as the pre-catalyst.

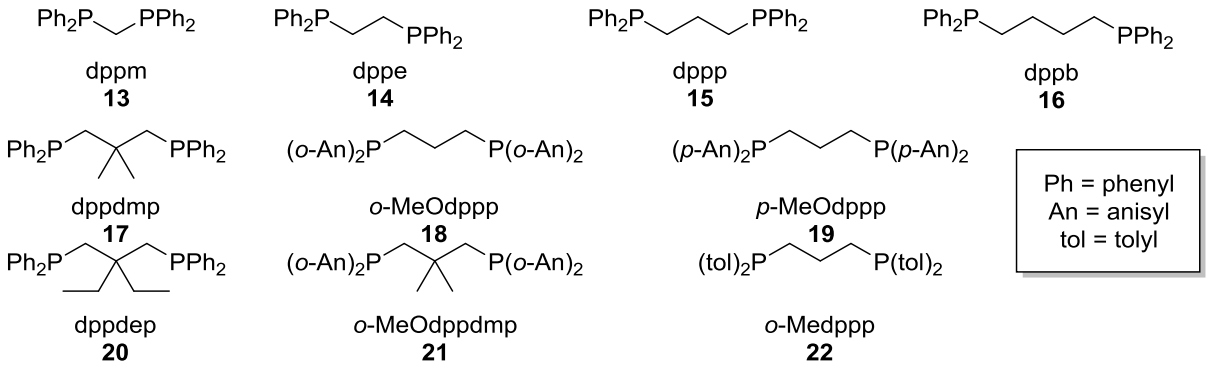


Figure 2: Overview of bidentate ligands used in the work of *Bouwman et al.*[32]

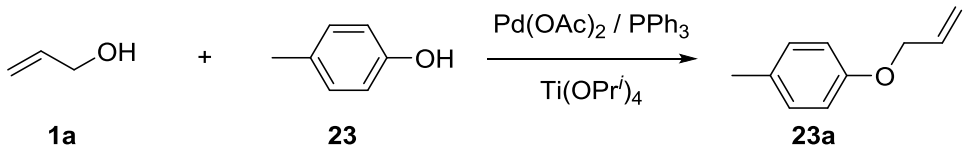
So far, the selectivity could be improved with other ligands but not the conversion. One trend was slightly perceptible. If $Pd(dba)_2$ is used as the pre-catalyst and conversion is improved (50 % and higher), side products occur more often (entry 1 and 6 in Table 1). It was also concluded that the increase of steric bulk around the Pd center could not be the sole reason for low activity of catalyst with *o*-anisyl ligands, since *o*-tolyl groups cause similar steric hindrance. Additionally, electron poor ligands like triphenylphosphite $P(OPh)_3$ have shown to diminish conversion to a minimum. The application of this Pd-catalyzed system with other nucleophiles such as primary amines, alcohols and aniline did not lead to comparable results or improvements. Although, this catalytic system had its limitations a lot of investigation and progress was made on *O*-allylation via ruthenium catalysis (Chapter 2.3.1).[32]

Table 1: Reaction of 12 with 1a catalyzed by different Pd-diphosphine complexes starting from $Pd(dba)_2$.

entry	ligand	conversion of phenole after 22 h (%)	selectivity after 22 h (%)	
			12a	**12b-12d**
1	dppdmp	49	96	4
2	*o*-MeOdppp	10	100	0
3	*o*-MeOdppdmp	12	100	0
4	2 P(*o*-An)$_3$	17	100	0
5	*p*-MeOdppp	38	100	0
6	*o*-Medppp	72	71	29
7	2 P(OPh)$_3$	11	100	0

2.2.3 Work of *Miura et al.*

O-Allylation was also in the focus of Miura's work which was published in 1997. Similar to the work of *Bouwman et al.*, the activation of the allyl alcohol played an important role in the catalytic cycle. In a previous paper,[33] addition of titanium alkoxides and LiCl enabled a nucleophilic substitution of allyl alcohols with zink enolates. With the use of phenols as nucleophiles a satisfying method to generate alkyl aryl ethers was found.



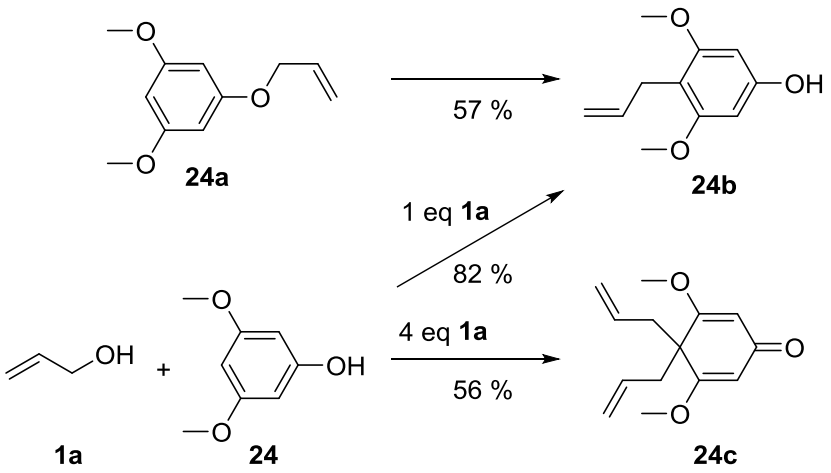
Scheme 7: General reaction scheme of allyl alcohol with *p*-cresol.

An optimal ratio of 0.25/0.1/0.25 or 0.01/0.04/0.25 of $Pd(OAc)_2/PPh_3/Ti(O\text{-}iPr)_4$ with addition of 4Å MS produced 93 % of the desired allyl aryl ether within 1 h at 50 °C (Table 2). This catalytic system also enabled the formation of ethers with phenols which had either electron withdrawing or electron donating groups.

Table 2: Reaction condition screening for *O*-allylation of *p*-cresol.

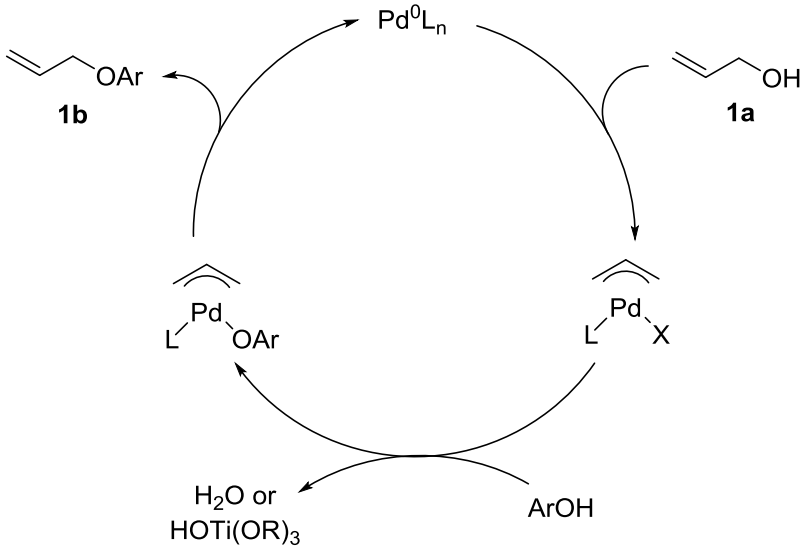
Entry	$Pd(OAc)_2$:PPh_3:$Ti(OPr^i)_4$	time (h)	yield of **23a** (%)
1	0.025:0.1:0	20	34
2	0.025:0.1:0	7	26
3[a]	0.025:0.1:0.25	1	93
4	0:0.2:0.25	1	0
5[b]	0.025:0.1:0.25	20	91
6	0.01:0.04:0.25	1	61
7[a]	0.01:0.04:0.25	1	93
8	0.01:0.1:0.25	1	90

[a] Addition of 200 mg MS 4Å. [b] Reaction at r.t.



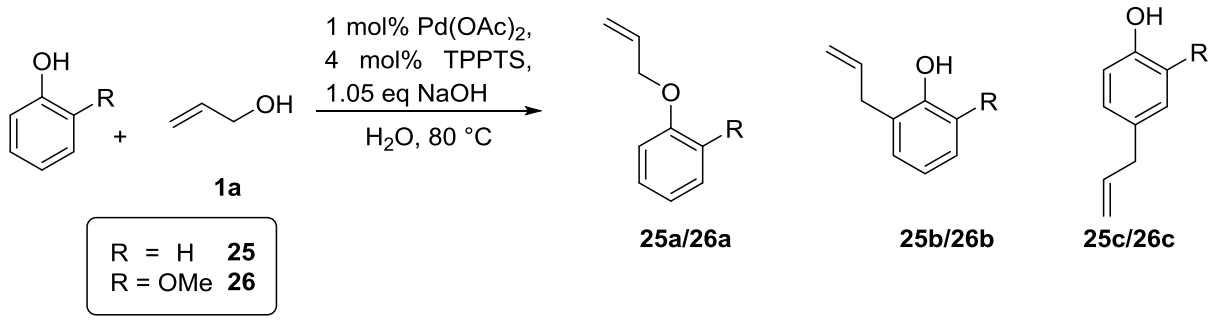
Scheme 8: Allylation reactions with 3,5-dimethoxy phenol.

More sterically demanding groups on phenols like 2,6-di-*tert*-butyl phenol could not be allylated. One unexpected product was formed when 3,5-dimethoxyphenol was used as aryl reagent. **24b** or **24c** could be formed selectively by either 1 or 4 eq allyl alcohol (**Fehler! Verweisquelle konnte nicht gefunden werden.**8). This *C*-allylated product was proven to be the isomerization product of the allyl ether. Other allyl alcohols were also tested which gave the desired products in very good yields. The fact that **24** and **24a** formed the same product indicated a π-allylpalladium intermediate which was essential for the proposal of the following mechanism (**Fehler! Verweisquelle konnte nicht gefunden werden.**9).[34]



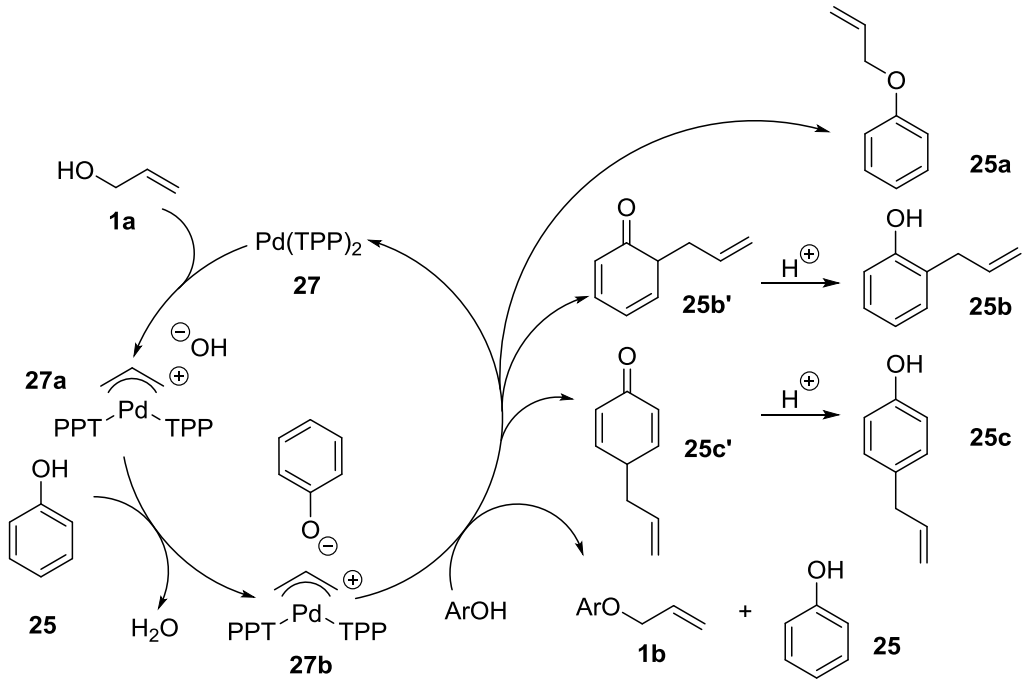
Scheme 9: Proposed mechanism for allylation of alcohols with Pd and $Ti(OR)_4$.

2.2.4 Work of *Kuntz et al.*

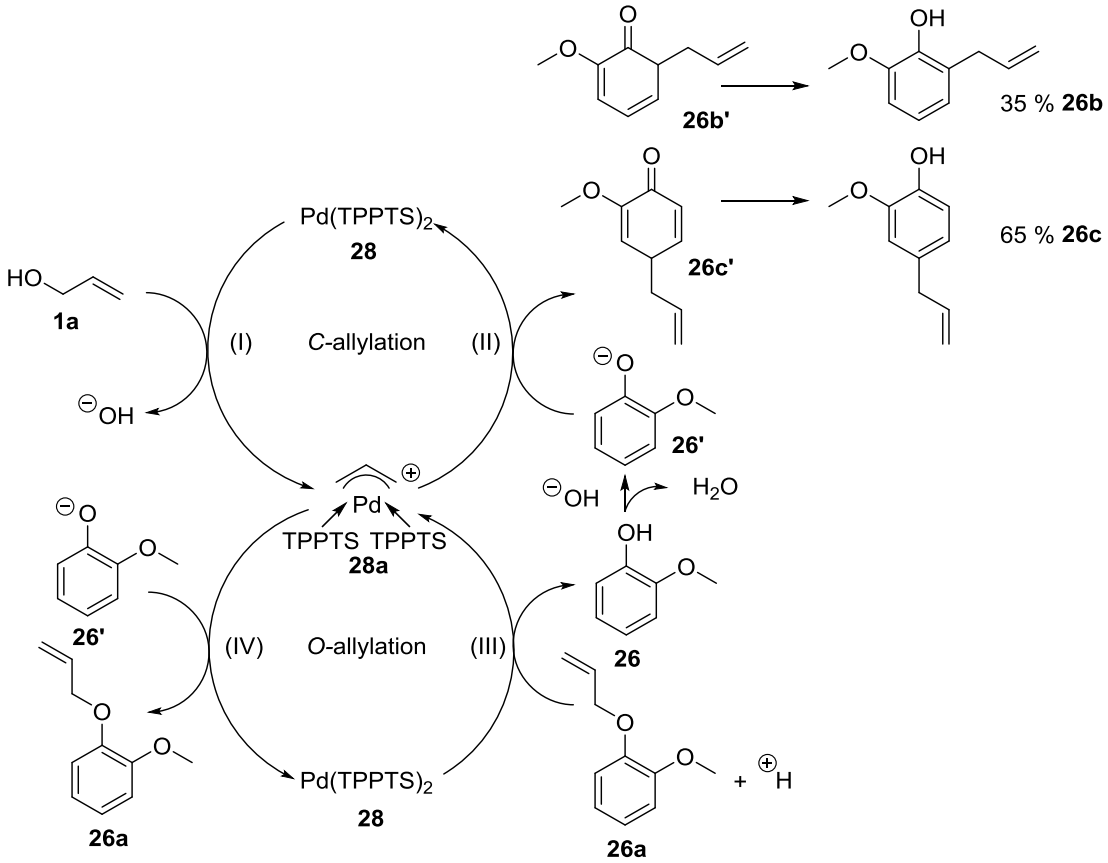


Scheme 10: General reaction conditions for allylation of phenol derivatives in water.

The group of Kuntz made a huge progress in the *C*-allylation of phenols, in 2005. They enabled *C*-allylation in water with the water soluble ligand triphenylphosphine tris-(sulfonate) (TPPTS). Additional advantages were the use of prop-2-en-1-ol (allyl alcohol) as allylic source and the immiscibility of the generated products in water. Essential for the *C*-selective allylation was the addition of sodium hydroxide as base. Without base only *O*-allylated product was formed after 1 h at 80 °C. Guaiacol as a more electron rich substrate was also tested with the established catalytic system. Once more, the importance of additional base was shown in a NaOH/guaiacol ratio screening. In that screening, 1.05 eq of base was necessary to favor *C*-selectivity. Pd(0)TPPTS and Pd(II)TPPTS exhibited the same reactivity and selectivity in these screenings. A kinetic study, which compared *C*-allylation to conversion, indicated that allylphenylethers could be converted into *C*-allylated products. This hypothesis was supported by the results in the following screening, in which NaOH turned out to be essential for *C*-allylation.



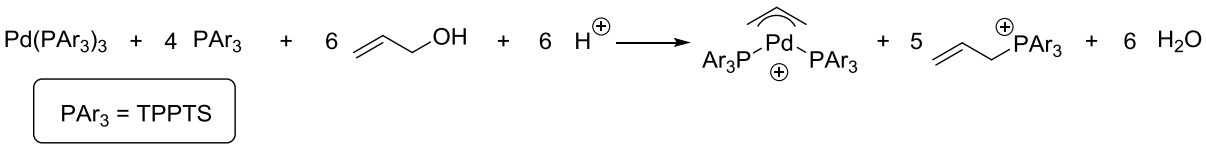
Scheme 11: Allylation of phenol in organic phase with PPh_3 (TPP) as organo-soluble ligand.



Scheme 12: Proposed reaction mechansim for guaiacol in aqueous solution.

With additional kinetic and NMR studies, two mechanisms (one in water and one in organic solvents) could be proposed for this catalytic system (Scheme 11+Scheme 12).[35] In a second paper, *Kuntz et al.* provided essential results in the study of this catalytic system in various stability versus pH and

temperature experiments. It was demonstrated that the reaction of allyl alcohol with $Pd(OAc)_2$ and an excess of TPPTS quantitatively forms (η^3-C_3H_5)$Pd(TPPTS)_2$ and OH^- (Scheme 11). In case of an excess of allyl alcohol, allylTPPTS salt is generated and further decomposed to propene and TPPTS oxide. By these means, pH dependent experiments at pH 3, 7 and 9 were performed. The proton dependent enhanced formation of (η^3-C_3H_5)$Pd(TPPTS)_2$ (**28a**) was demonstrated by addition of perchloric acid. At pH 3 and 7 the initial phases are comparably fast. After 5 min the reaction rate at pH 3 decreases not as fast as the reaction rate at pH 7. The consumption of protons at pH 9 and the formation of **26b** and **26c** slows down to a rate of one proton consumed per 2 h. A general mechanism (comparable to Scheme 11) in aqueous solution and a reaction equation (Scheme 13) were proposed from the gathered information.[36]



Scheme 13: Formation of the allyl Pd complex in aqueous solution at low pH-values.

2.2.5 Work of *Tamaru et al.*

In a preceeding research *Tamaru et al.* focused on selective allylation of indoles in *C3* position.[37] Based on the results from allylation of indoles and pyrroles with direct activation of allyl alcohol via $Pd{\cdot}BEt_3$ catalysis, naphthols and benzene polyols were considered as suitable substrates for direct *C*-allylation. 1-Naphthol and 2-naphthol showed different reactivities in this catalytic system. 2-Naphthol (**29**) was allylated in *C*2 position with a yield of 95 %, whereas 1-naphthol only gave a mixture of 22/17 mono (*ortho*-position) and di (*ortho*- and *para*-position) allylated product. By blocking of the *para* position with an acetate and activation of the *ortho* position via a methyl group in *meta* position selective *ortho* allylation could be achieved for 1-naphthol.

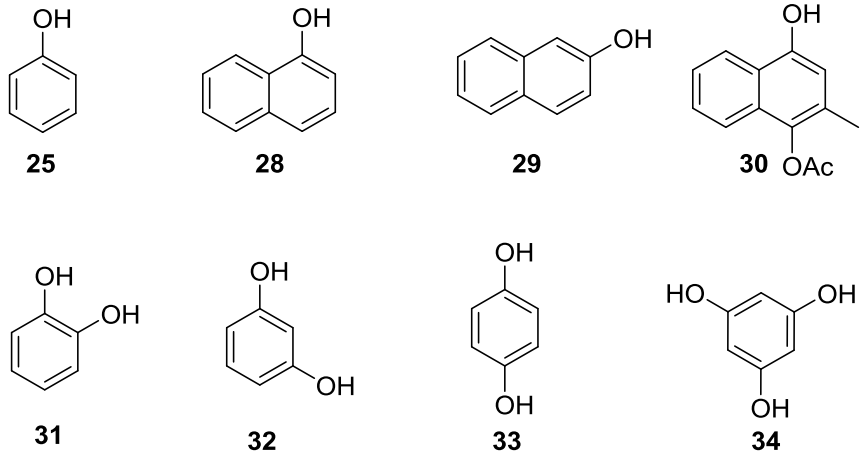
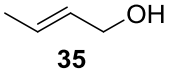
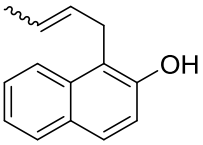
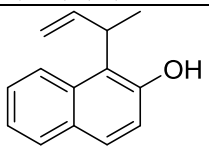
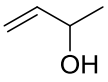
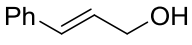
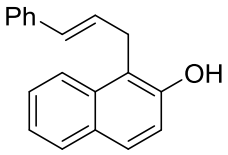
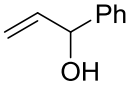
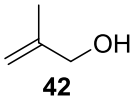
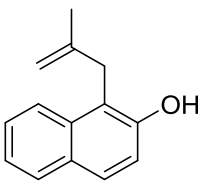


Figure 3: Phenol and naphthol derivatives that were reacted with 1.2 eq allyl alcohol, 5 mol% $Pd(PPh_3)_4$ and 2.0 eq BEt_3 at r.t. in THF.

The use of toluene instead of THF as solvent showed remarkable results. It shortened reaction time to 2 instead of 48 h in the case of 2-naphthol but also produced diallylated 2-naphthol in *ortho*-position by loss of aromaticity. This solvent effect also influenced the results that were achieved with 1-naphthol. In the case of 1-naphthol, neither acceleration of the reaction nor selectivity enhancement were monitored but the yield of both products was improved. This solvent acceleration effect facilitated the use of other allylic alcohols for that catalytic system (Table 3). In further investigations of benzene polyols **31**-**34**, toluene evolved as the solvent of choice. The next catalytic development was based on the use of phenol derivatives. Astonishingly, only resorcin was converted to the desired mono *C*-allylated product. In the other cases, only *O*-allylation (phenol) or no conversions (catechol and hydroquinone) were monitored. Allylation of resorcin with *trans*-cinnamyl alcohol on *C6* led to an allylated product. Instead a lot of side products like *C*2-allylated resorcin, diallylated resorcin and polyallylated resorcin were observed. This fact led to an experiment generating a pentaallylated resorcin in nearly quantitative yield. Additionally, perallylation was achieved on pholoroglucinol (**34**) in the same way with minor yields. The use of THF as solvent was necessary for this substrate due to poor solubility in toluene. [38]

Table 3: Allylation results of the Pd·BEt_3 catalytic system with various allylic alcohols and 2-naphthol.

entry	allyl alcohol	product, yield (*E*:*Z*) (%)	
1	 **35**	 **36** 52 (8:1)	 **37** 16
2	 **38**	**36** 52 (7:1)	**37** 16
3	 **39**	 **40** 98	
4	 **41**	**40** 96	
5[a]	 **42**	 **42** 97	

2.3 Ruthenium-Catalyzed allylation

2.3.1 Work of *Bouwman et al.*

As mentioned in Chapter 2.2.2, the work of *Bouwman et al.* focused on catalytic methods to obtain *O*-allylated phenolic products via allyl alcohol or diallyl ether as allyl donor. With the use of cationic Ru(II) complexes as catalysts either *O*- or *C*-allylated products could be generated with good selectivities. Cationic ruthenium catalysts were obtained via addition of AgOTs. As typical reaction conditions 0.1 mol % catalyst loading at 100 °C in toluene were used. It was pointed out that *C*-allylated products occured due to a consecutive reaction of *O*-allylated phenols. A time dependent product distribution with **50** as catalyst revealed the formation of **12b** and **12c** as side products. Consequently, a time dependent bidentate ligand screening was carried out to analyze *O*- and *C*-allylated product ratios.

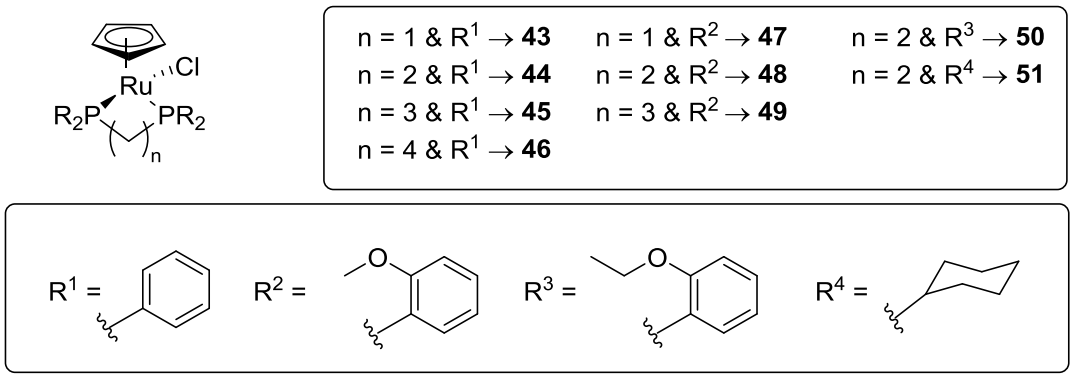


Figure 4: Pre-catalysts that have been used in the work of *Bouwman et al.*[39]

Although desired *O*-allylation with good selectivity of 92/8 *O*-allyl/*ortho*-allyl product was found for **50** and diallyl ether as allylating agent, other side products (**12b** and **12c**) emerged already after 3 h. In case of this catalyst, a conversion of 80 % in 30 min was achieved. All other ligands were unable to convert 4-*tert*-butylphenol (**12**) that fast and only *o*-MeOdppp showed a better selectivity towards *O*-allylation but with a conversion below 10 % in 1 h. Despite the low *O*-allylation selectivity, other catalysts have found to be more selective towards *C*-allylation. *o*-MeOdppm (**49**) turned out to be the most potent ligand for *C*-allylation. In 3 h around 40 % of starting material was converted to 90 % mono *C*-allylated product. Similar to *o*-MeOdppm, dppm was also able to mono *C*-allylate in quite the same selectivity but with only poor conversion of starting material. Increasing chain lengths of ligands led to increasing conversions but at a ligand bridge length of 4 CH_2 as for PPh_3 allyl alcohol was isomerized to propanal. The use of diallyl ether was also an option to increase conversion of **12** despite the change of ligand. Thus, the effect of allyl ethers and their mechanistic understanding towards *C*-

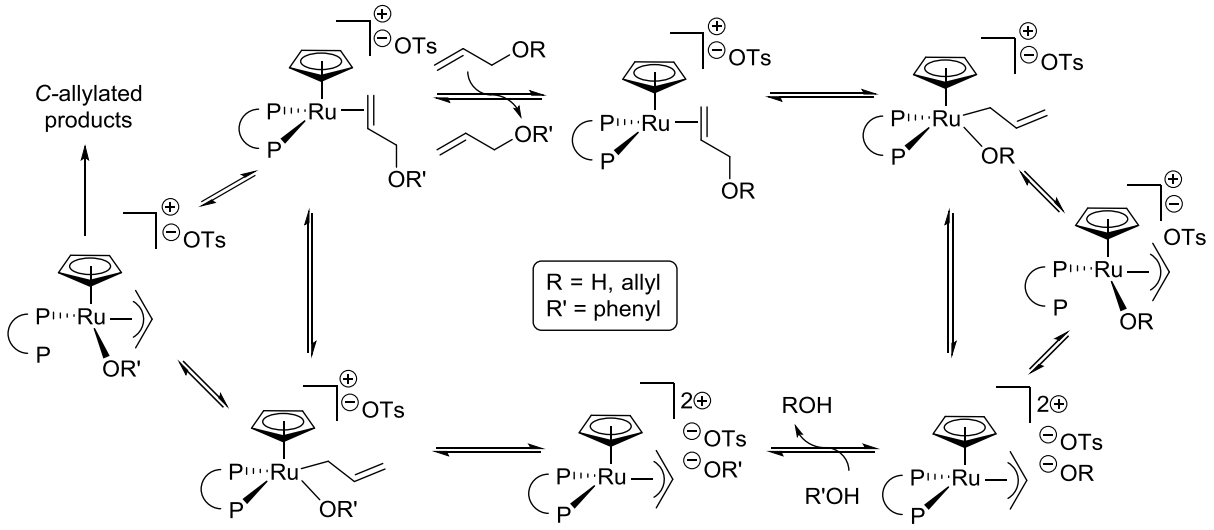
allylated phenols was studied. Allyl 4-*tert*-butyl phenyl ether was chosen as starting material. Due to lack of activity with this starting material, additives were tested (Table 4).

Table 4: Additive screening with allyl-4-*tert*-butylphenol and 49 as catalyst.

entry	additives	conversion of **12** [%]	selectivity [%]			
			12a	**12b**	**12c**	**12d**
1	-	0	0	0	0	0
2[a]	H_2O	99	20	55	3	22
3[b]	*p*-cresol	92	40	54	2	4
4[c]	HOTs	86	33	40	3	24
5	camphorsulfonic acid	49	28	44	21	7

[a] Added after 18 h. [b] Conversions are total of *tert*-butylphenol and *p*-cresol derived products. [c] HOTs = *p*-tolenesulfonic acid.

For each used additive activity could be monitored. The stronger acids HOTs and camphorsulfonic acid were less reactive and less selective. H_2O and *p*-cresol were more reactive and more selective compared to the allylation with the same ligand and 4-*tert*-butylphenol as starting material. It was hypothesized that added *p*-cresol or likewise the generated hydrolysis product 4-*tert*-butylphenol would function as an acidic co-catalyst which would have an enormous effect on selectivity. Additionally, catalytic amounts of strong acid did increase reactivity to a TOF of 6200 h^{-1} and selectivity towards *C*-allylation. Hence, catalytic addition of HOTs was studied on bidentate ligands **43**-**46**. Although catalytic reactivity was enhanced, *C*-allylation selectivity was only observed for dppe and dppp as ligands. On the other hand, *O*-allylation is favored using dppm or dppb as ligands for this catalytic system. Intriguingly, the isomerization of allyl alcohol to propanal is stopped by addition of acid with dppb as ligand.



Scheme 14: Proposed catalytic cycle for allylation of 12a.

This ligand and acid screening was extended to allylphenylether. Once again, dppe and dppp showed good activity and selectivity to the *C*-allylated products, whereas dppm and dppb failed. Hence, a reaction mechanism for *O*- and *C*-allylation was proposed, which includes the activation via acid

(Scheme 14). In their following work *Bouwman et al.* discovered that *O*-allylation can be favored if the bidentate ligand is derivatized with *geminal* dialkyl groups (Table 5). Although selectivity is increased, conversion is decreased through those *geminal* dialkyl groups. Furthermore, a consistent pictureof ligand characteristics was obtained through these experiments.

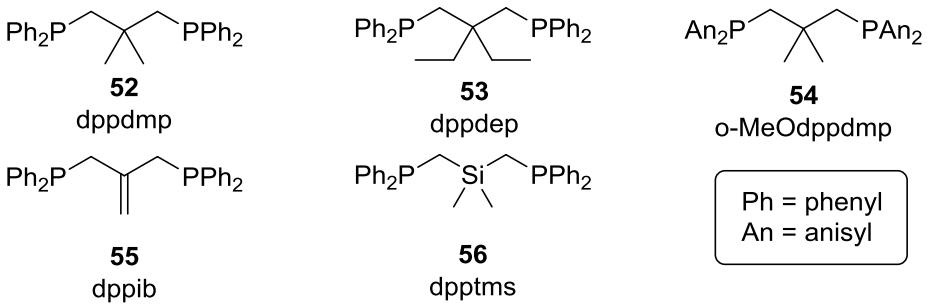


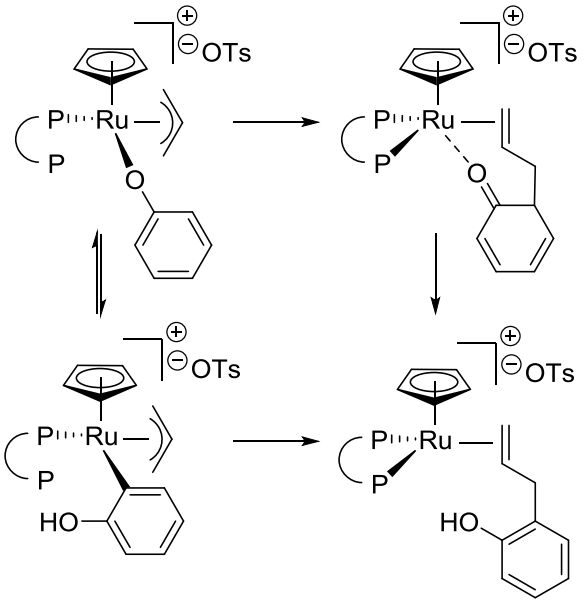
Figure 5: Tested geminal alkylated ligands.

Restricted coordination space at the Ru-center is a crucial parameter to prevent *C*-allylation. From NMR and X-ray analysis, a significant stereoelectronic change based on backbone substitution was not observed. Stability of the produced pre-catalyst by implication of resistance to oxidation was decisive. This fact also strengthens the theory that *O*-allylation can take place with less space available compared to *C*-allylation, which would need a decoordination of the ligand. In a subsequent paper, *Bouwman et al.* presented that *O*-allylation can take place at lower temperatures (60 °C) with $[RuCp(PPh_3)_2](OTs)$ as catalyst with the addition of acid.

Table 5: Ligand effects on a $[RuCp(PP)]^+$ complex system with 4-*tert*-butylphenol and allyl alcohol.

entry	ligand	conversion [%]		selectivity [%]			
		1 h	6 h	1h		6 h	
				12a	**12b-d**	**12a**	**12b-d**
1	dppdmp	7	63	> 99	0	82	18
2	dppdep	4	31	> 99	0	88	12
3	o-MeOdppdmp	0	17	-	-	99	1
4	dppib	4	46	> 99	0	63	37
5	dpptms	2	41	> 99	0	84	16

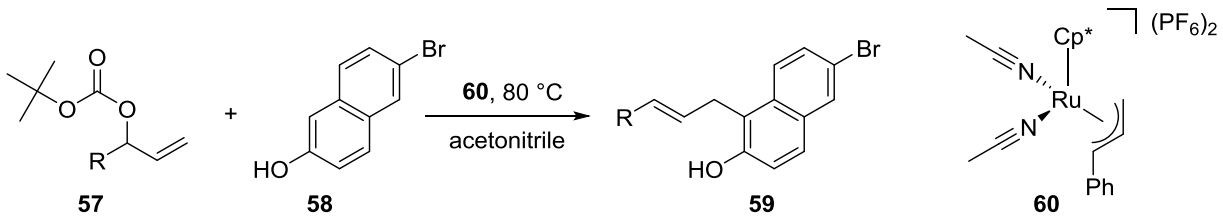
It was proven that the addition of acid was necessary to avoid isomerization of allyl alcohol to propanal. Herein, 20 eq of HOTs were necessary to achieve optimal results in inhibiting propanal formation. This new additive was tested with several other ligands in which all of them were selective for *O*-allylation. At last, this catalytic system was tried out on other nucleophiles, but only electron rich phenols and thiophenol itself could be allylated selectively in good conversions. Finally, mechanistic implications led to a quite similar reaction mechanism as in Scheme 14. [39-41]



Scheme 15: Proposed *C*-allylation of phenol either via a *Friedel-Crafts* like reaction or *ortho* metallation.

2.3.2 Work of *Pregosin et al*.

Similar to the work of *Tamaru et al.*, Paul S. Pregosin and his group researched on allylation of indoles at *C*3-position. In their work, Ru-catalysis was used to achieve such a *C*-*C* bond formation. Compared to [38] no additives were needed to activate the allylic alcohol at 23 °C. Due to the concentration dependent studies achieved in [42] a Hammett study of 5-substituted indoles was performed. It was shown that EWGs decrease reactivity to a greater extent than EDGs increase reactivity. They also reported a *C*-allylation of 2-naphthol (**29**) and phenol (**25**) at 80 °C in acetonitrile with their Ru-catalyst (Scheme 16) on which they concentrated in a subsequent paper.[43]



Scheme 16: Reaction conditions of the selective *C*-allylation on naphthols via allyl-*tert*-butylcarbonat.

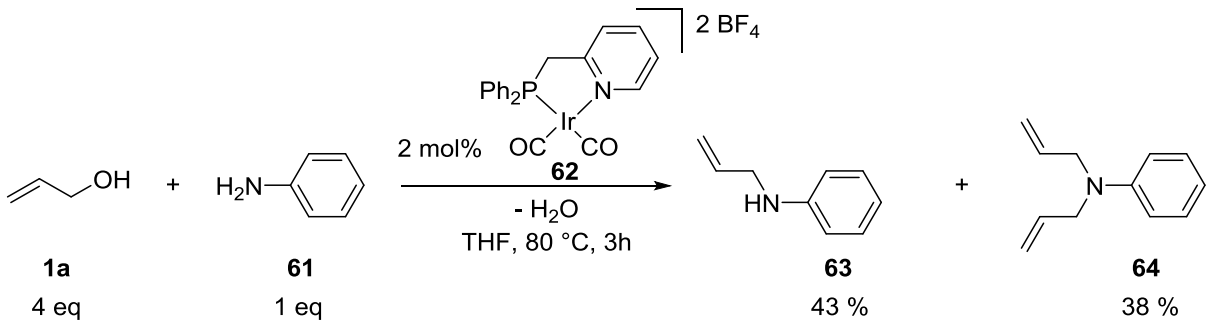
Additional experiments similar to the work of *Bouwman et al.* with acid as co-catalyst did prove them right in their proposed mechanism for *C*-allylation of indoles. The understanding of the proposed

mechanism led to the following paper in which phenyl allylic alcohols were used to allylate phenol derivatives. In general, the Ru(IV) (**60**) was a potent catalyst for this reaction. Remarkably, the main product was always *para*-allylated if phenol derivatives were used. For 6-bromonaphthalenol (**58**) only one product could be detected, which in nearly every case was produced faster than allyl phenol derivatives. One problem of this catalytic system was the use of allyl alcohol itself. This substrate could not be used to allylate phenol and the reaction time with **58** increased to 2 h. Interestingly, electron rich phenyl allylic alcohols reacted either very slowly or generated conversions below 15 %.

2.4 Other Transition Metal Catalyzed Allylations

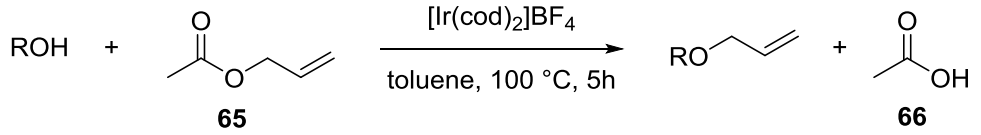
2.4.1 Iridium-Catalyzed Allylations

A general method for activation of allylic alcohols which persists in most of the previous works also finds its place in the work of *Akita et al*. The new concept of activating the OH group of allylic alcohol via nucleophilic interactions with CO in **62** was performed. It was concluded that the Lewis acidic character of **62** additionally promotes the *OC*-O bond formation as well as the subsequent C(allyl)-O bond. Crystallographic analysis strengthened the mechanistic hypothesis. Nevertheless only aniline was tested as a potential nucleophile. Only a mixture of mono and di *N*-allylated products could be observed.[44]



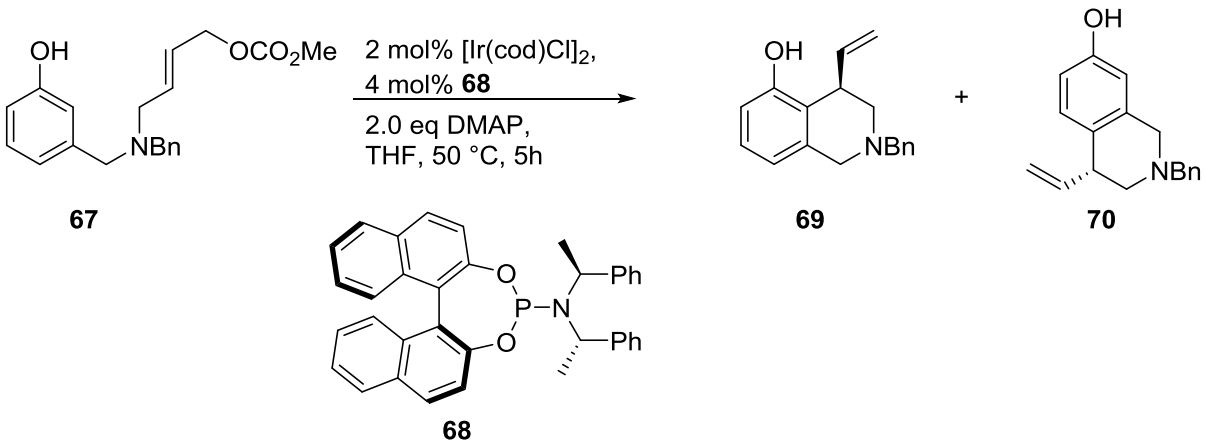
Scheme 17: Allylation of anilin with allyl alcohol and 63.

Different to the previous catalyst (**62**) the cationic $[Ir(cod)_2]BF_4$ catalyst was used in Ishii's group to produce allyl ethers from allyl acetate and long chain alcohols. An excess of 10 eq allyl acetate at 100 °C in toluene showed the best results. Changes in the catalytic system like the use of $[IrCl(cod)]_2$, $[IrCl(CO)(PPh_3)_2]$ or $[Rh(cod)_2]BF_4$ as pre-catalysts produced esters or were unable to produce any product.



Scheme 18: General reaction conditions for etherification with allyl acetate.

Several other nucleophiles like phenols, anilines, carboxylic acids, and thiols were tested. In general, good yields and conversions were achieved for all substrates. Aromatic compounds turned out to require longer reaction times compared to acids and primary alcohols. Aniline was the only aromatic compound which could be di-allylated in 5 hours. This reactivity can be followed in the reaction of 4-aminophenole, where a mixture of di-*N*-allylated product and per-allylated product can be monitored. In general, product mixtures occur if more than one position can be allylated. In the case of *p*-cresol 8 % of *o*-allyl *p*-cresol was detected.[45] In *Tsukada et al.*'s case a very selective *C*-allylation was achieved with $[Ir(cod)(CH_3CN)_2]PF_6$ and $[Rh(nbd)(CH_3CN)_2]PF_6$ as catalysts. Even though both catalysts had a high selectivity to *para*-allylation, this selectivity decreased if one position was substituted with a methyl group. Nevertheless, yields, reaction temperature (0 °C) and *C*-allylation selectivity were outstanding compared to other comparable catalytic systems. The low reaction temperature was a result of the use of allyl 4-methylbenzene sulfonate, concluding $^{-}$OTs to be a good leaving group even at those temperatures.[46]

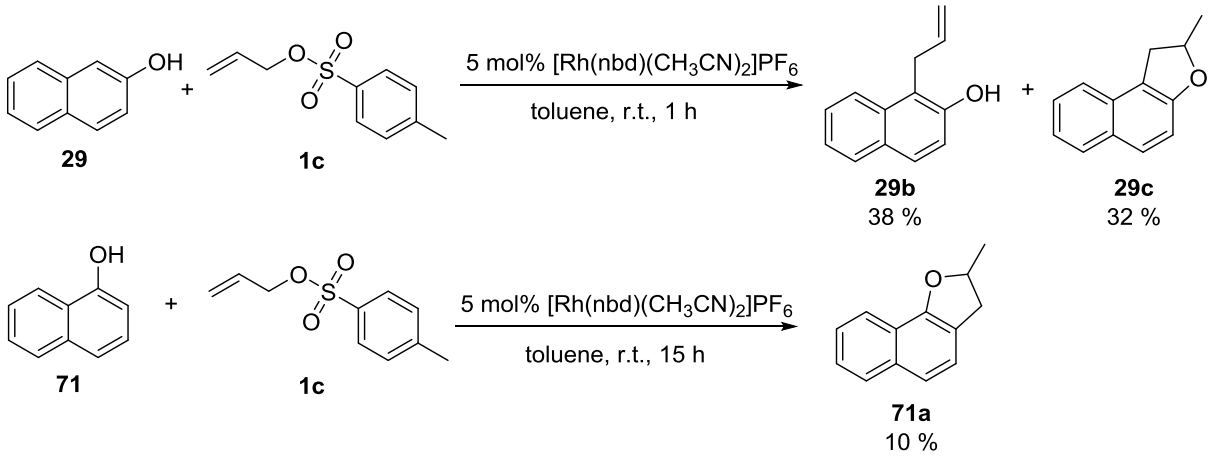


Scheme 19: *You et al*'s work on tethered allylation of phenols.

A comparable *C*-allylation with Ir-catalysis was achieved in You's group. They enabled enantioselective intramolecular *C*-allylation via cyclization of allyl carbonates at room temperature. Although the reaction time could be shortened to 5 h and conversions were in most cases very good, an inevitable use of 2 eq of base (DMAP) was necessary. Reaction conditions were tested in different solvents and with different bases. Except for acetonitrile which gave a 1:1 mixture of **70** to **71**, all other solvents preferentially produced **70**.[47] Adaption of this system was successfully for substrates with derivatization on the aromatic ring.

2.4.2 Rhodium-Catalyzed Allylations

As already mentioned in the previous chapter (2.4.1) Tsukada and his group were able to *C*-allylate phenols at low temperatures. In the case of their Rh-catalyst *C*-allylation was achieved even with anisole, mesitylen, 1,3-benzodioxole and their electron rich derivatives. Superior to phenol substrates only *para*-allylated anisoles and 1,3-benzodioxoles were produced.



Scheme 20: Reaction conditions for allylation of naphthols at increased temperatures.

Surprisingly, ⁻OMesyl did not work out as a good leaving group for this catalytic system. Compared to the Ir-catalyst that has been used, higher *para*-selectivities for phenols as substrates were found but lower yields were achieved with the Rh catalyst. Interestingly, if 2-naphthol was used as substrate 38 % of **29b** and 32 % of **29c** were yielded (Scheme 20). If 1-naphthol was used, only 10 % of **71a** were generated after a 15-times longer reaction time.

In contrast to Tsukadas work Frank Glorius and his group obtained a catalytic system with Rh(III) to allylate different arenes, especially benzamides.[48] Allylmethylcarbonate was used as main allylating agent and reaction temperatures could be lowered to 35 °C via addition of PivOH. Due to the slight excess of PivOH and $AgSbF_6$, and chlorbenzene as solvent the thermodynamically less favored product (allylated product) was obtained in good ratios and yields. By increasing reaction temperature other EWG could be applied to this catalytic system. Additionally, different allylcarbonates were tested to efficiently alkylate a broad range of substrates in the represented positions (Figure 6).

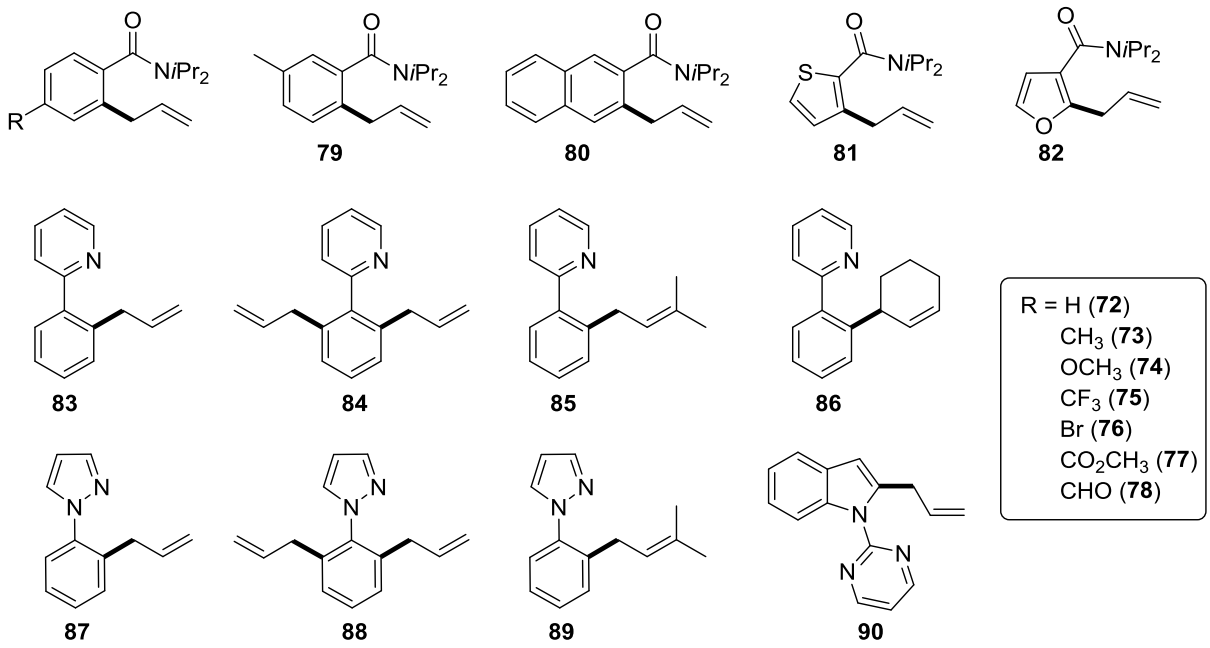
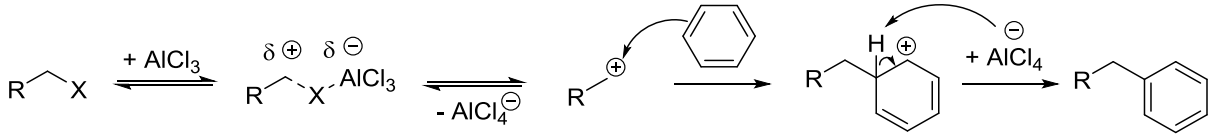


Figure 6: Substrate scope of *Glorius et al.*'s catalytic system.

Finally a kinetic isotope effect of 5.4 was examined that indicated a *C-H* bond breaking in the rate determining step and a mechanism with concerted metallation and deprotonation.[49,50]

2.5 *Friedel-Crafts* Alkylation

Considering the huge amount of opportunities that were enabled via this reaction method to alkylate benzene derivatives for more than 125 years and the fact that various preceding authors stated their *C*-allylation methods as *Friedel-Crafts*-like reaction,[38,42,46] a short discussion of this reaction will be given.



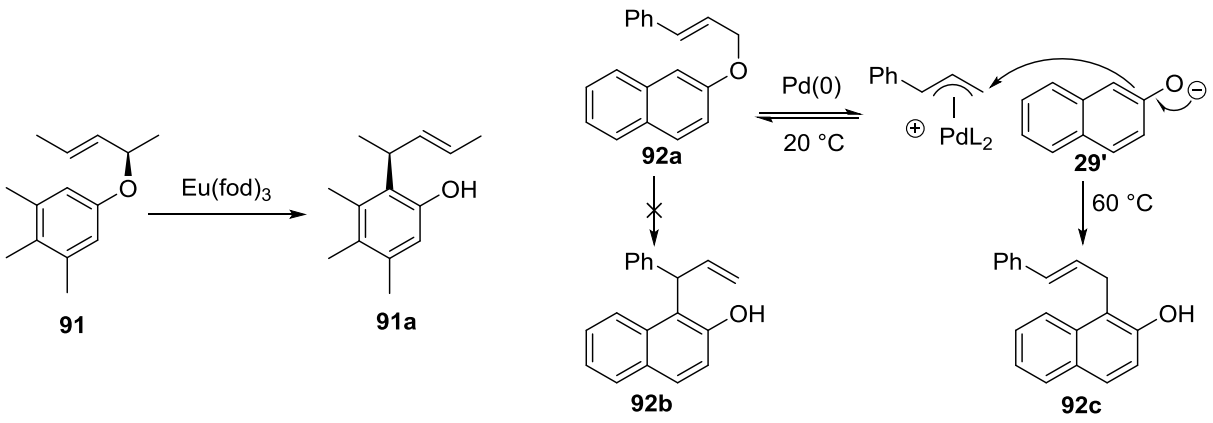
Scheme 21: Reaction mechanism for the *Friedel-Crafts* alkylation.

In a classical *Friedel-Crafts* alkylation Lewis acids ($FeCl_3$, $AlCl_3$, $HgSO_4$, etc.) serve as catalysts but usually have to be added in stoichiometric amounts due to the trapping by coordination to the product.

The carbon next to the halide is activated via the coordination of the Lewis acid to the halide. An electron rich arene then attacks the more positive carbon which leads to a carbocation and temporary loss of aromaticity. Aromaticity is then regained via an attack of the halide anion at the tertiary hydrogen. Usually, alkylation proceeds until all electron-rich positions are alkylated due to the fact that alkylation electronically enriches aromatic molecules. Hence, arenes are used in an excess. This disadvantage is nowadays solved via different catalytic systems. Several groups reported asymmetric addition of aromatic compounds since the mid 1980's. There are many *Friedel-Crafts* procedures to produce such asymmetric products with a huge variety of substrates.[51] Nonetheless, only a few groups concentrated on allylating aromatic compounds like phenols.

2.5.1 Molybdenum-Catalyzed *Friedel-Crafts* Allylation

Among numerous alkylation reactions that refer to Friedel-Crafts reactions the work of *Kocovsky et al.* was the most intriguing, considering the ability of mono-alkylation of phenol and anisole derivatives.[52,53] A predominant derivatization in *para* position was achieved with a rather simply synthesized Mo(II) catalyst. Highlighting the accomplishment of this work, several electron rich heteroarenes and benzenes were successfully allylated. Additionally, a broad scope of allylating reagents like crotyl, cyclopentenes and cyclohexenes could be used with the Mo(II) catalyst without loss of stereochemistry on the allyl reagents at room temperature. More interestingly, a comparison with the catalytic system established by *Sinou et al.* [54] and *Trost et al.* [55] was made to determine a possible mechanism. Although, *O*-allylated by-products were rarely observed in the work of *Kocovsky et al.* a Claisen-rearrangement was taken into consideration. Therefore only Trost's $Eu(fod)_3$ catalyst was proven to undergo a Claisen-rearrangement (Scheme 22). In the case of Sinou's Pd(0) catalytic system the formed product (**92c**) could be traced back to the naphtholate intermediate which must function rather as a leaving group than as a partner in a pericyclic-like-reaction.



Scheme 22: Trost's Eu catalyzed Claisen-rearrangement and Sinou's Pd catalyzed *C*-nucleophilic attack.

Similar to Sinou's work Kocovsky's group produced enantiopure allyl phenyl and allyl naphthyl ether. These allyl ethers were reacted with $[Mo(CO)_4Br_2]_2$ and led to *C*-allylated racemic products. Nonetheless, this reaction was much slower than the direct *C*-allylation of phenol and naphthol derivatives. In conclusion, an intermolecular process was considered as a plausible transformation rather than an intramolecular process and *para*-selectivity was explained due to orbital interactions between the allylic cation and the substrate (Figure 7).

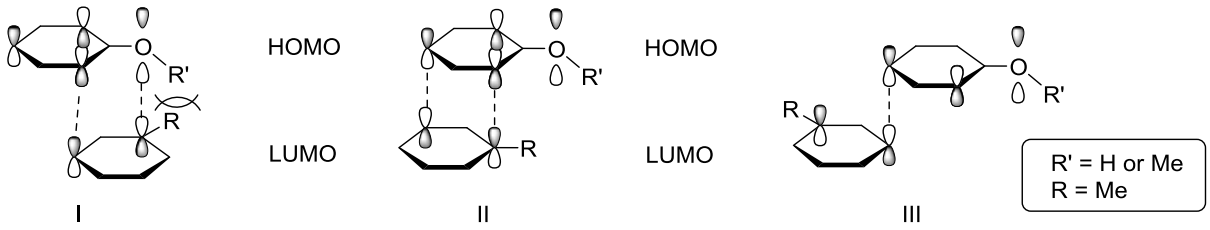
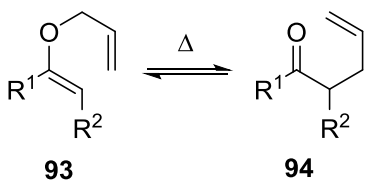


Figure 7: Considered HOMO – LUMO interactions between allylating agent and arene.

In addition to the Mo(II) catalyzed Friedel-Crafts-like reaction other Lewis acidic transition metals also have been reported to allylate phenols in good yields.[56] In that special case a free OH group on the arene was necessary to coordinate the used metal ($In(OTf)_3$ or $Zn(OTf)_2$). Additionally more chromane compared to the work of *Kocovsky et al.* was produced depending on the used catalyst and *ortho*- to *para*-selectivity leveled off in a 1:1 mixture.

2.6 *Claisen* Rearrangement

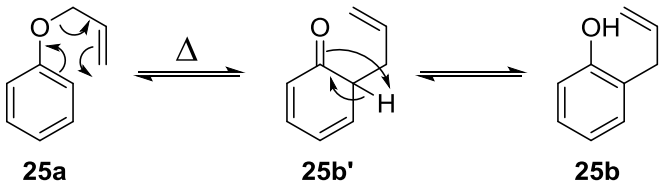
The [3,3]-sigmatropic shift of allyl vinylic ethers to *γ,δ*-unsaturated ketones (**Fehler! Verweisquelle konnte nicht gefunden werden.**), also known as *Claisen* rearrangement, was the first pericyclic reactions before several others have been established.[57-59] Notably, allylphenylethers undergo such a reaction to form the *ortho* allylated phenol. Therefore, an understanding of this reaction could help to distinguish between other already mentioned reactions. It is known that allylphenylethers undergo such a rearrangement by a temporary loss of aromaticity (if existent). Aromaticity is then regained through a rearrangement of the *ortho* positioned hydrogen (Scheme 24).[60]



Scheme 23: Thermally induced [3,3]-sigmatropic shift of allyl vinylic ethers.

The main reason for this [3,3]-sigmatropic shift is the formation of the thermodynamically favored product. Additionally, this reaction is observed at high temperatures (≥ 150 °C) to overcome the high activation barrier.[36] It is therefore a convenient reaction for simple molecules, but should not be

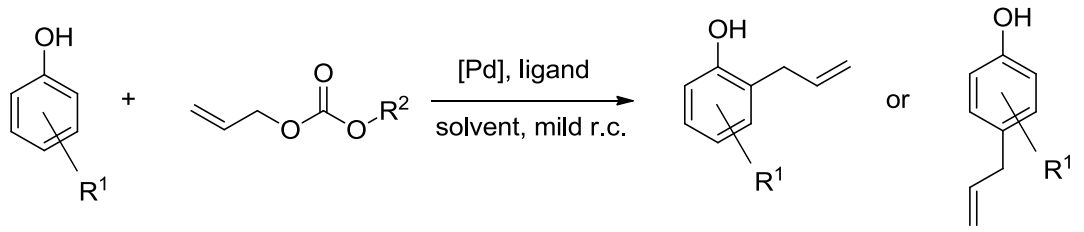
planned for more complex molecules which would not withstand these harsh reaction conditions. Serious efforts were also made on the topic of catalyzed *Claisen*-rearrangement and improvement of reaction conditions. Most often transition metals were used therefore,[61,62] but organocatalysis was also successfully adapted.[63]



Scheme 24: Aromatic *Claisen* rearrangement of allylated phenol.

3. Goals and Ambition

The original aim of this diploma thesis derived from an achievement in the Ph. D. thesis of Hilmar Schröder. The *Tsuji-Trost* reaction was successfully optimized on sulfur nucleophiles with Pd as catalyzing metal. Several bidentate ligands were tested until a broad range of substrates could be allylated efficiently. Hence, an expansion of such a catalytic method would be very favorable. Well established are Pd-catalyzed allylations of soft nucleophiles, like 1,3 diketones, enolates and amines. Especially, *C*-*C* bond forming types are of high interest. Therefore, direct *C*-allylation of phenols would ease their accessibility. This kind of reaction was already monitored by H. Schröder as a side reaction. Palladium was chosen as leading metal, due to already existing protocols for *C*-allylation of classical *Tsuji-Trost* substrates and naphthol derivatives at high temperatures.[17,64] Taking into account that an intensive literature search already exposed several groups who worked on this topic, an optimization to present protocols would be desirable. In general, simple reaction conditions, low reaction temperatures, a simple catalyst handling, high selectivity and broad substrate scope should be achieved with a new catalytic system. For that reason, allyl carbonates were suitable allyl donors which would not need a base as additive. Phenol itself is an inexpensive and accessible substrate that could be allylated efficiently only in a few papers.[36,52] Additionally, *in situ* generation of the catalyst would simplify the reaction conditions. The circumvention of additives and the possibility to use several substrates and solvents should also be accomplished.



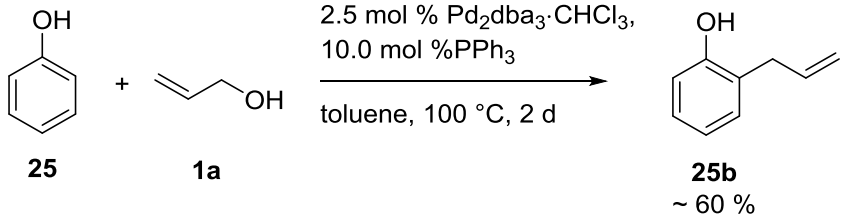
Scheme 25: General reaction overview of the Pd-catalyzed allylation of phenols.

Due to low conversions,[36] poor selectivities,[36,65] need of additives,[38,40] high temperatures,[32,64] substrate inapplicabilities,[38,43] and complex catalysts[43,52] most of the established systems are far from perfection. Hence results a wide margin of reaction conditions to overcome the disadvantages of other comparable catalytic systems. To sum up, a Pd-based system should be established to catalyze the direct *C*-allylation of phenol and phenol derivatives with allyl carbonates as allyl donors. Reaction temperature, conversion, and selectivity (*ortho*:*para*) should lead to comparable if not enhanced results to other known systems (Chapter 2.2.4 - 2.5.1). Such an optimized reaction should be applicable for total-synthetic pathways, comparable to the successfully adopted catalytic asymmetric allylic alkylation,[66,67] and/or big scale reactions.

4. Discussion of Results

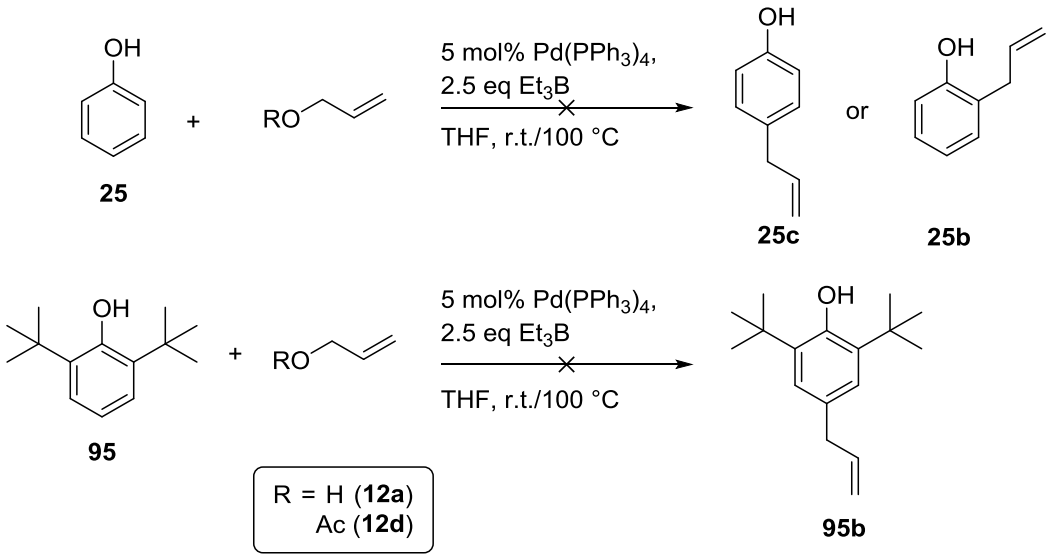
4.1 First steps to a running system and comparison of *in situ* and *ex situ* formed $Pd(PPh_3)_4$

For a first assessment of suitable reaction conditions the work of *Tamaru et al.* [37] and *Yamamoto et al.* [64] were considered as simple starting conditions. Allyl methyl carbonate had to be synthetized from allyl alcohol and methyl methylchloroformiate. $Pd(PPh_3)_4$ was generated from palladium dichloride and triphenyl phosphine in DMSO at 140 °C according to the work of Abegaz.[68] The product was crystallized from DMSO after 4.0 eq hydrazine monohydrate were added at 140 °C. The bright yellow crystals were collected by filtration under inert conditions and washed with ethanol (dry) and n-hexane (dry) to yield 92 % product. In the case of allyl methyl carbonate only 63 % of colorless liquid could be yielded, due to losses during the workup. Allyl methyl carbonate turned out to be more water soluble than comparable carbonates. Therefore, some of allyl methyl carbonate was lost during extraction with water.



Scheme 26: Achieved *o*-allylation with allyl alcohol as substrate and *in situ* generated catalyst.

The first surprising *C*-allylation results were already achieved with allyl alcohol and phenol. Toluene was used as solvent according to comparable literature procedures.[37,64] 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$ and 10 mol% triphenylphosphine were used to generate the catalyst *in situ*. The reaction was run at 100 °C under inert conditions. Around 25 % of *ortho*-allylated phenol could already be monitored after 3 h. This increased to roughly 60 % after 2 d. Such high temperatures and long reaction times were necessary to increase leaving group properties of the hydroxy group. Decreased reaction temperature led to complete inactivity of allyl alcohol as substrate. Despite the fact that phenol could not be successfully allylated with reaction conditions (rc) used in *Tamaru et al*'s work, an attempt was made with those reaction conditions at r.t. and at 100 °C. As expected, phenol and even 2,6-di-*tert*-butylphenol showed no conversion even after 3 d.



Scheme 27: Allylating reactions with *Tamaru et al.* established reaction conditions.

Allyl methyl carbonate and phenol were reacted at different temperatures in toluene with various pre-catalysts to get an overview of reaction conditions that are required for a minimum of activity and at the same time comparison of *in situ* and *ex situ* generated $Pd(PPh_3)_4$. Interestingly, only *O*-allylated products occurred even at 100 °C (compared to allyl alcohol at 100 °C). *In situ* generated catalyst was as potent as *ex situ* formed catalyst in terms of reaction time and product distribution. Thus, *in situ* synthesized catalysts were used henceforth, due to their simpler handling.

4.2 Reaction Condition Scanning and Ligand Screening

After reactivity of the catalytic system was proven via systematic screening, experiments to optimize ligand properties were carried out. To simplify these experiments, Tolman properties were chosen to select representative ligands for these experiments (Figure 8). Reaction conditions were tested simultaneously to the ligand screening to clarify if *C*-allylation could be achieved below 100 °C. Surprisingly, only reactions with tributyl phosphine as ligand and allylmethylcarbonate as allylating reagent enabled *C*-allylation at 100 and 80 °C. Thus, small ligands with a high electron donating character favor *C*-allylation. Results achieved with other ligands confirmed this tendency (Table 7-11).

Table 6: Tested reacion conditions with *in situ* generated catalysts.

Entry	phenol [eq.]	allyl carbonate [eq.]	pre-catalyst [0.02 eq.]	ligand [eq.]	temperature [°C]
rc 1	1.0	1.2	$Pd_2dba_3{\cdot}CHCl_3$	0.08	20
rc 2	1.0	1.2	$Pd_2dba_3{\cdot}CHCl_3$	0.08	80
rc 3	1.0	1.2	$Pd_2dba_3{\cdot}CHCl_3$	0.16	80
rc 4	1.0	1.2	$Pd_2dba_3{\cdot}CHCl_3$	0.08	100
rc 5	1.0	1.2	$(C_3H_5PdCl)_2$	0.08	80
rc 6	1.0	1.2	$(C_3H_5PdCl)_2$	0.16	80

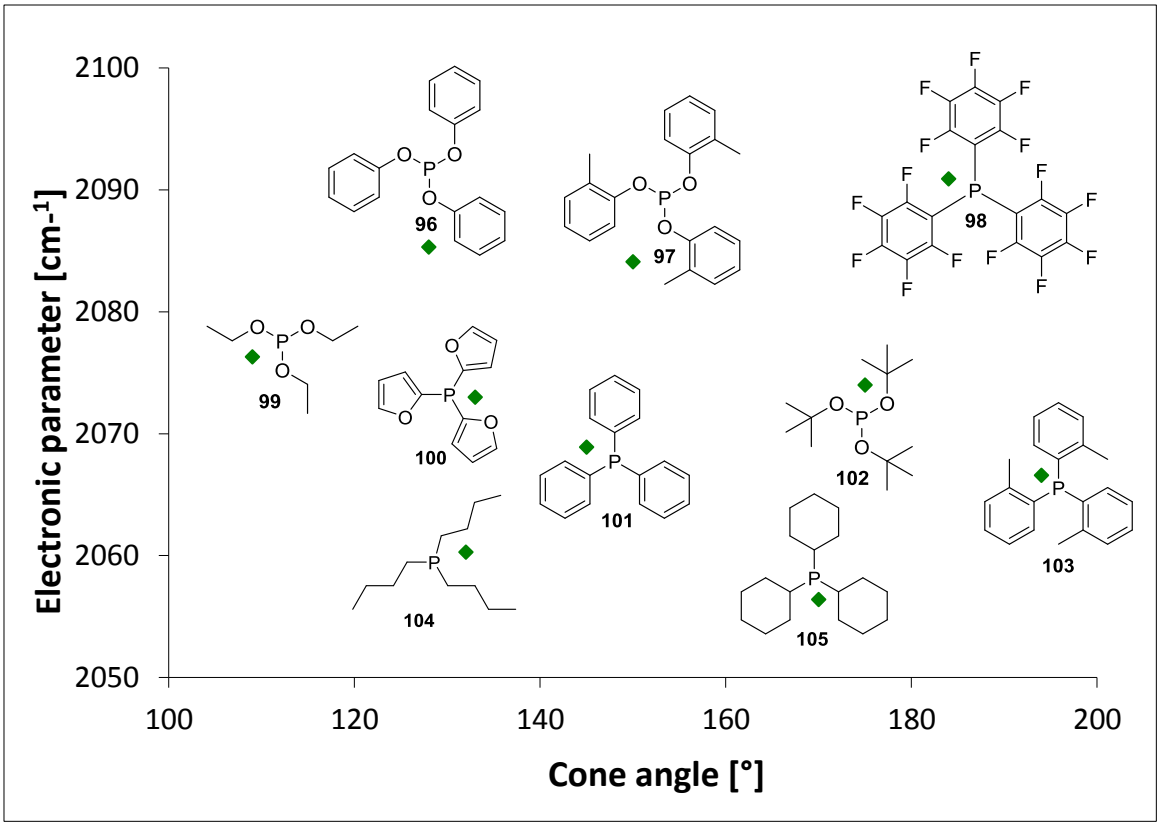


Figure 8: Overview of the monodentate ligand properties.

On the contrary, the perfluorinated ligand **98** was neither able to *O*-allylate at 80 °C nor *C*-allylate at the tested reaction conditions. In addition, Pd-black formation did occur with this ligand already after 1 h at temperatures around 80 °C and higher. Comparable electron withdrawing ligands (phosphites) exhibited same Pd-black formation over a longer time period (more than 1 h). Other ligands turned out to be quite good for *O*-allylation even at 20 °C, confirming that electron rich ligands are even more potent for *O*-allylation. The rather good *O*-allylations with this catalytic system are in comparison to the work of *Bouwman et al.* quite surprising. Advantages of *Bouwman et al*'s catalytic system are the use of allyl alcohol and a low catalyst loading (0.1 mol%). This low catalyst loading and the as previously mentioned poor hydroxyl leaving group would therefore probably need higher temperatures (100 °C) to enable good conversions. Nonetheless, this catalytic system ($Pd_2dba_3 \cdot CHCl_3$ as pre-catalyst and several ligands at 20 °C) was better in producing allylphenylether than the system established by *Miura et al.*, which needed 50 °C and was not able to produce more than 93 % allyl-4-methylphenylether. The only advantage of Miura's $Ti(Oi\text{-}Pr)_4$ supported system is the direct use of allyl alcohol.

Table 7: Combined screening of ligands and rc with results after 24 h.

$P(OPh)_3$	phenole [%]	O-Allyl [%]	**$P(OTol)_3$**	phenole [%]	*O*-Allyl [%]
rc 1	13	87	rc 1	5	95
rc 2	14	86	rc 2[i]	2	96
rc 3	30	70	rc 3[i]	19	80
rc 4	40	60	rc 4[i]	15	71

Table 8: Combined screening of ligands and rc with results after 24 h.

$P(C_6F_5)_3$	phenole [%]	*O*-allyl [%]	**$P(OEt)_3$**	phenole [%]	*O*-allyl [%]
rc 1	81	19	rc 1	22	78
rc 2	100	-	rc 2	13	87
rc 3	100	-	rc 3	5	95
rc 4	100	-	rc 4	5	95

Table 9: Combined screening of ligands and rc with results after 24 h.

PPh_3	phenole [%]	*O*-allyl [%]	**PFu_3**	phenole [%]	*O*-allyl [%]
rc 1	-	>99	rc 1	30	70
rc 2	2	98	rc 4	18	82
rc 3	3	97			
rc 4	-	>99			
rc 5	2	98			
rc 6	4	96			

Table 10: Combined screening of ligands and rc with results after 24 h.

$PTol_3$	phenole [%]	*O*-allyl [%]	**PCy_3**	phenole [%]	*O*-allyl [%]
rc 1	14	86	rc 1	-	>99
rc 2	12	88	rc 2	2	98
rc 3	4	96	rc 3	2	98
rc 4	40	60	rc 4	-	>99

Table 11: Combined screening of ligand and rc with first *C*-allylation results after 24 h.

P^nBu_3	phenole [%]	*O*-allyl [%]	*o*-allyl [%]	*p*-allyl [%]	di-allyl [%]	tri-allyl [%]
rc 1	50	50	-	-	-	-
rc 2	6	94	-	-	-	-
rc 3	65	11	18	-	4	-
rc 4	37	6	39	2	16	-
rc 5	54	3	39	-	4	-
rc 6	82	12	6	-	-	-

In some cases, an increase in ligand concentration did enhance *O*-allylation, and more important in the case of **104** did it also enable *C*-allylation with rc 3. This outcome could not be validated with (η^3-$C_3H_5PdCl)_2$ as pre-catalyst. Nevertheless, rc 5 turned out to be the mildest reaction condition in which *C*-allylation was achieved with phenol. The activation of the catalyst via (η^3-$C_3H_5PdCl)_2$ underlies the fact that a η^3-allyl palladium species is already present and does not need to be generated from allyl

[i] Allyl-*o*-tolyl ether was also observed.

methyl carbonate. This corroborates the presumption of a rate determining step in dissociation of the LG. Moreover, similar reactions (*Tamaru et al.*) surpass this step via activation of such a LG (BEt_3 promoted activation of allyl alcohol) and enable *C*-allylation at room temperature.[38]

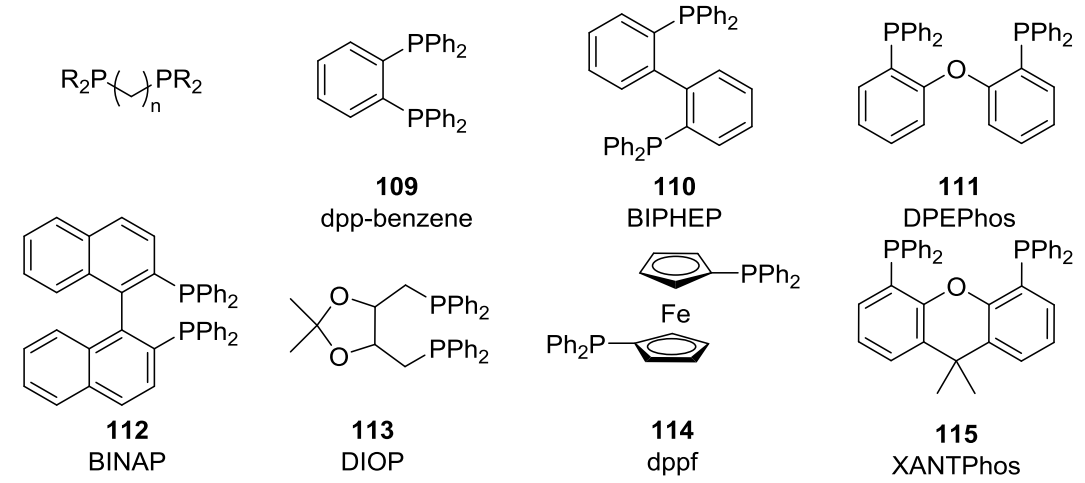
Table 12: Results with PMe_3 as ligand.

PMe_3	phenole [%]	*O*-allyl [%]
1h	99	1
1d	23	77
3d	23	77

Owing to the results in monodentate ligand screening, it was considered that electron donating and small phosphine ligands enhance the formation of *C*-*C* bonding. Presumably, the use of trimethyl phosphine should lead to better results. This was not confirmed due to high volatility of PMe_3 (b.p.: 40 °C), which exited the active catalyst and led only to allylphenylether formation.

4.3 Bidentate Ligand Screening

Additionally to Tolman properties the bite angle β [°] of bidentate phosphine ligands plays major role. It was shown in various experiments that bite angles in most cases effect conversions, activities and selectivities in similar ways that Tolman properties do.[69] Several bidentate ligands differing in bite angle and structure were tested with rc 5.



Scheme 28: Tested bidentate ligands with rc 5.

As a result of this screening, bite angle of around 102 ° seemed to be ideal for *C*-allylation. DPEPhos enabled conversion of 40 % to the mono *ortho* allylated phenol in 1 d. Other ligands with similar bite angles also enabled *C*-allylation but with either less conversion or less selectivity. One exception is dppe (**14**). This ligand is known for general stabilization of many transition metal complexes, similar to 5-metallacycles this five membered ring seems to ensure higher stability.[69]

Table 13: Bidentate ligand screening with achieved results after 24 h.

Ligand	Bite angle [°]	*O*-allyl [%]	*o*-allyl [%]	di and tri allyl [%]
dppm	72	87	0	0
dppe	85	40	14	7
dppp	91	78	0	0
dppb	98	13	25	28
dcypb[i]	-	0	24	62
dpp-pentane[i]	-	98	0	0
dpp-hexane[i]	-	89	0	0
dpp-benzene	83	91	0	0
dppf	99	38	12	10
BIPHEP	92	92	0	0
DIOP	90-120	92	0	0
BINAP	85	88	0	0
DPEPhos	102	5	42	17
XANTPhos	111	72	0	0

In this screening bite angles play a more important role than chemical characteristics or electronic parameters. This can be clearly seen by comparison of Xantphos and DPEPhos or the chain lengths of bidentate ligands like dppe, dppp and dppb. Unfortunately, not all bite angles are literature known (dcypb, dpp-pentane, dpp-hexane), but reactivities of some ligands allow rough estimations of bite angles. The gained achievements encouraged to use DPEPhos and $P(n\text{-}Bu)_3$ in subsequent optimization screenings.

4.4 Solvent Screening

After reaction temperature, as well as pre-catalyst and ligands were determined, solvent properties for this reaction needed to be settled. A wide range of solvents was tested. Unfortunately, no improvements were monitored. Worse than assumed, change in solvent properties proved nearly all of the examined solvents as *O*-allylation favoring solvents. Only DME and DMF could sustain a minimum of *C*-allylation selectivity. DMF with DPEPhos promoted slight generation of the product and DME led to better results with tributylphosphine compared to DPEPhos.

[i] No literature known bite angles.

Table 14: Results for solvent screening.

		phenole [%]	O-allyl [%]	*o*-Allyl [%]	di-Allyl [%]	tri-Allyl [%]
Toluene	PBu_3	37	6	39	16	-
	DPEPhos	33	6	40	20	1
Acetonitrile	PBu_3	39	61	-	-	-
	DPEPhos	27	72	-	-	-
DMF	PBu_3	24	76	-	-	-
	DPEPhos	61	34	3	1	-
Chloroform[i]	PBu_3	2	98	-	-	-
	DPEPhos	87	13	-	-	-
DME	PBu_3	77	2	17	2	2
	DPEPhos	41	58	-	1	-
THF[i]	PBu_3	100	-	-	-	-
	DPEPhos	34	76	-	-	-
Dioxane	PBu_3	18	82	-	-	-
	DPEPhos	19	81	-	-	-
Isopropanol	PBu_3	99	-	1	-	-
	DPEPhos	36	64	-	-	-
DCE	PBu_3	89	-	11	-	-
	DPEPhos	9	91	-	-	-
DMSO	DPEPhos	28	72	-	-	-

In the case of THF with tributylphosphine, even *O*-allylation was inhibited at 60 °C. An increase in temperature to 80 °C with $CHCl_3$ and THF as solvents was surprising, because the reaction in THF stayed inactive, wherease the reaction in chloroform resulted in 11 % product after 1 d. However, these temperatures led to extreme solvent loss, although *Schlenk*-tubes were used. In the end, toluene turned out to be the solvent of choice, indicating that other groups performed such solvent screens without referring to them.[32,37,46]

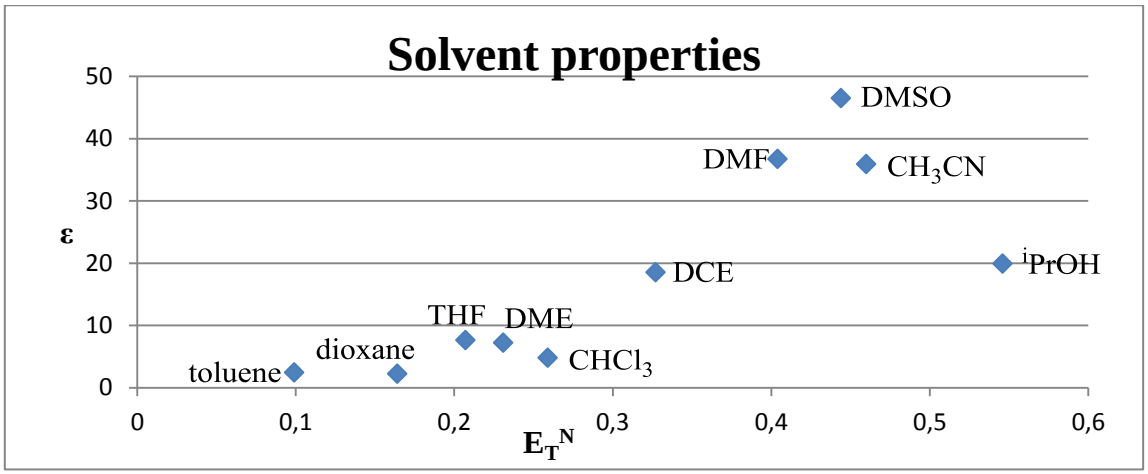


Figure 9: Overview of solvent properties with tested solvents.

[i] Reaction temperature was set to 60 °C.

4.5 Cationic Catalyst Screening

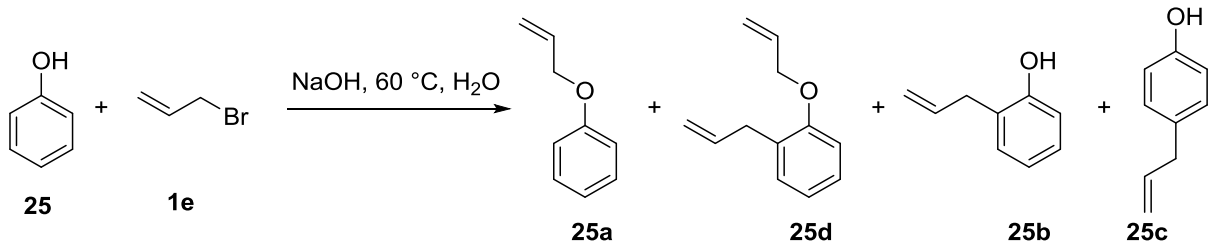
Despite the fact that classical *Tsuji-Trost* reactions use (η^3-$C_3H_5PdCl)_2$ or Pd(0) pre-catalysts, the question still arises, if the active catalyst derives from a Pd(0) or Pd(II) species. Reactions with *in situ* generated Pd(II) from silver salts were reported to enable this formation. The outcome of these experiments would further give insight into the reaction mechanism or even increase conversion and/or selectivity. Therefore, BF_4^- and PF_6^- salts were used. *In situ* generation of cationic catalysts can be achieved just by mixing the chemicals in solvent together.[70] However, no improvements concerning the conversion to the desired product were observed. Additionally, no clear statement could be made towards preferences for either one or the other ligands with either the one or the other cat- or anion. This screening revealed that the mechanism does not follow a simple *Friedel-Crafts* alkylation, which would preferably work better with Lewis-acidic catalysts. Contrary to the proposed *Friedel-Crafts* like reaction did electron rich ligands enable *C*-alkylation, which weakens the Lewis-acidic character of Pd.

Table 15: Results for a cationic pre-catalyst screening with rc 5 after 1d.

additive	ligand	phenole [%]	*O*-allyl [%]	*o*-allyl [%]	*p*-allyl [%]	di-allyl [%]
NH_4BF_4	PBu_3	49	39	1	-	1
	DPEPhos	16	84	-	-	-
NH_4PF_6	PBu_3	51	39	6	-	4
	DPEPhos	10	90	-	-	-
$AgBF_4$	PBu_3	40	54	4	-	2
	DPEPhos	100	-	-	-	-
$AgPF_6$	PBu_3	100	-	-	-	-
	DPEPhos	64	21	15	-	-

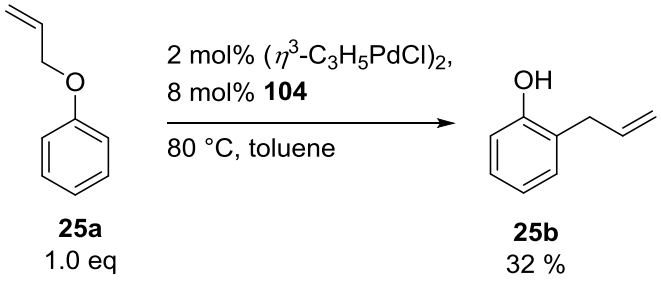
4.6 Allylphenylether Conversion

Insight into this reaction and overview of a possible reaction pathway became necessary at this point as the formation of allylphenylether was monitored each time *C*-allylation was achieved. The possibility that *O*-allylation occurs first and rearrangements lead to *C*-allylation was taken into consideration. The use of allylphenylether as reagent should consequently clarify this proposal. The first attempt to synthesize allylphenylether failed due to inefficient separation from the *ortho* allylated allylphenylether.



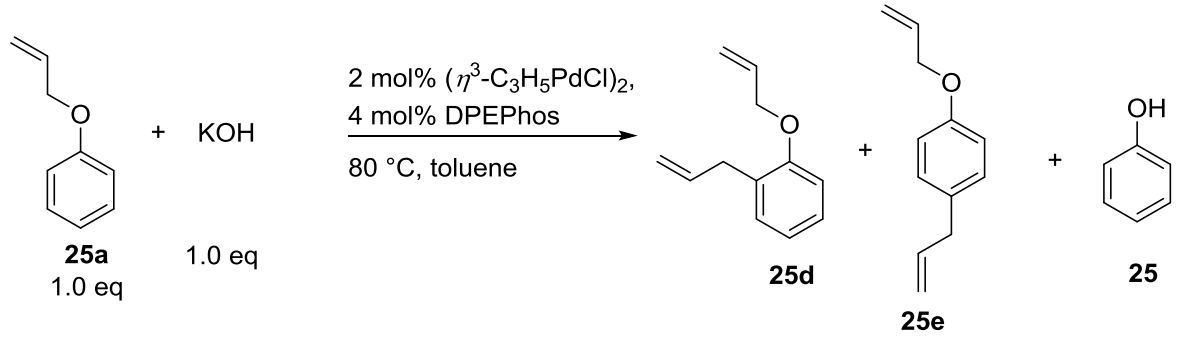
Scheme 29: Observed products in water after 1 d reaction time.

The reaction depicted in Scheme 30 produced a significant amount of by-products such as *ortho*- and *para*-allylphenol and allylphenylallylether. This observation turned out to diminish the success of *Kuntz et al*. catalytic system, which used NaOH as base in H_2O to improve the reactivity of their catalytic system significantly. Nonetheless, allylphenylether needed to be synthesized. This was achieved with similar reaction conditions as in the preceding reaction. K_2CO_3 was used as base and acetone as solvent. After purification, allylphenylether was used as substrate. Classical reaction conditions were used with both ligands. Surprisingly, only tributylphosphine was able to convert allylphenylether into *C*-allylated products. Selectivity and conversion were comparable to the results achieved with allylmethylcarbonate, phenol and tributylphosphine as ligand. Remarkably DPEPhos showed no activity with this substrate, indicating that either allylphenylether was a by-product produced via a different pathway with DPEPhos or the necessity of a base to induce *C*-allylation.



Scheme 30: Transformation of allylphenylether with PBu_3 as ligand.

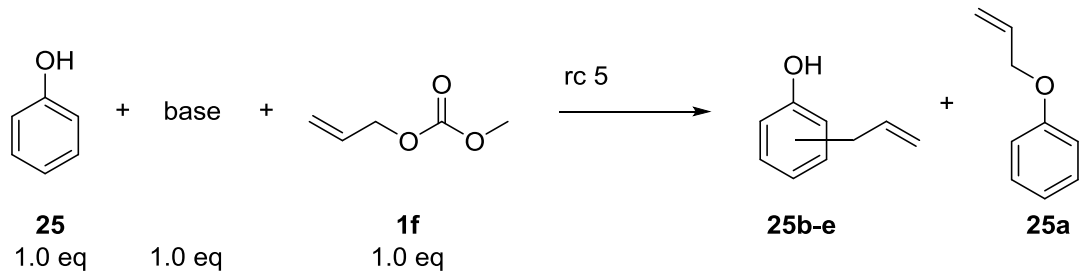
However, the effectiveness of tributylphosphine was confirmed. The reaction with both ligands was repeated three times to exclude activity of any unknown parameters. The reactivity of tributylphosphine and the results with DPEPhos could be reproduced in each case. Addition of base to allylphenylether to replace the formed alcoholate in case of allylphenylcarbonate as allylating reagent enabled *C*-allylation with DPEPhos. Nevertheless, simple mono-allylation was not achieved with DPEPhos as ligand.



Scheme 31: Reaction conditions which enabled *C*-allylation with allylphenlether as substrate.

4.7 Base Screening

While experiments with allylphenylether produced some interesting results, the previous screenings did not enhance the reactivity of the catalytic system.



Scheme 32: General reaction conditions for base screening.

At that point, bases were considered to increase reactivity of the catalytic system. Different to the work of *Kuntz et al.*, the added base should primarily deprotonate phenol (usually done by methanolate from allylmethylcarbonate) and shield the phenolate nucleophile with a counterion (f.i.: alkali metals). Sterically demanding and non-nucleophilic bases were used additionally to the alkali bases that have been used in the work of *Kuntz et al.* Serendipitously, the addition of some bases did increase reactivity, but a general pattern for either solubility enhancement or counterion size could not be observed. NaOH promoted conversion to 54 % *ortho*-allyl phenol within 1 h, but only in the case of DPEPhos as ligand. Tributylphosphine as ligand and NaOH as base led to no improvements. Vice versa did the use of KOH, KO^{t}Bu and Cs_2CO_3 as base improve *C*-allylation only with **111**. The use of KO^{t}Bu with 18-crown-6 ether even minimized *C*-allylation to roughly 10 % and enhanced the formation of Pd-black. In general, more side-products (especially di-*ortho*-allylphenol) were produced with DPEPhos as ligand.

The non-nucleophilic bases (2,6-di-*tert*-butylpyridine and DIPEA) turned out to favor *O*-allylation instead of *C*-allylation. Misleading results were achieved with 1,8-diazabicycloundec-7-ene (DBU) and PBu_3. After 1 d 94 % *ortho*-allylphenol was monitored via GC-MS. This surprise led to a DBU-

concentration screening which should examine if addition of DBU was catalytically or stoichiometrically necessary and if reaction conditions could be improved. However, neither addition nor subtraction of DBU led to better results. If anything, worse results were achieved with increasing DBU-concentration. Concentrations of lower than 1.0 eq DBU led to inferior *C*-allylation results and concentrations of higher than 1.0 eq DBU led to only allylphenylether. Surprisingly, detection of the formed products was more difficult when more DBU was used, indicating that during the work up free alcohols like phenol were deprotonated and adsorbed on the silica pad. Work up with extraction of the products from 1 M aqueous HCl supported the proposal that in the first reaction phenol was immobilized on the silica pad. Consequently, a few drops of the reaction mixtures were extracted with ethyl acetate from 1 M HCl to avoid discrimination during the work up.

A repetition of the reaction with DBU revealed the minor activity of the catalytic system and a side-reaction with DBU. Even though, the reaction was repeated several times and with minor changes in reaction conditions no improvements of the reaction could be observed. An expansion of the base screening with tetramethylnaphtalene-1,8-diamine (TMND), diazabicyclononene (DBN) and P_1-t-Bu showed even less activity and selectivity.

4.8 Catalyst Activity Screening

Several papers from Buchwald,[71] Hayashi[72] and Wei[73] opened the discussion if and how the active Pd-species can be generated. Buchwald's approach concentrated on modified pre-catalysts accelerating the initiation phase of the catalytic cycle. The easier accessible and more convenient method was the approach of *Wei et al*. concentrating on the activation step of Pd(0)-catalyzed systems. Different screenings rendered reaction conditions for optimal activation/yields. Hence, activation of the allylic alkylation like it was executed for phenols in this work could pose a problem and needed to be tested. Similar reaction conditions were used for the subsequent screening to investigate the initiation phase and effectiveness of the catalytic system.

Table 16: Selected additives for generation of a Pd^0 pre-catalyst.

	TBAOAc	**DBU**	**H_2O**
a	-	-	0.15 µL
b	-	-	-
c	2.2 mg	-	0.15 µL
d	3.1 mg	-	-
e	-	1.2 µL	0.15 µL
f	-	1.2 µL	-

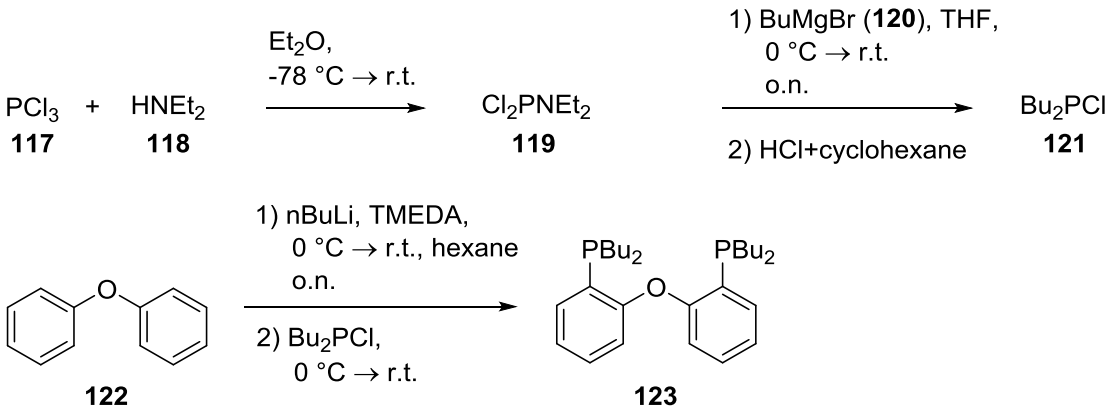
The tested reaction conditions were not able to keep up with the established $(\eta^3\text{-}C_3H_5PdCl)_2$ system. Little amounts of desired product (2-1 %) were detected after 2 d. In general, 65 to 90 % allylphenylether were produced without significant change during the whole reaction time.

Table 17: Results for activity Pd^0 based screenings.

reaction conditions	time	phenol	*O*-allyl	*ortho*	sideproducts
a	1h	31	69	0	0
	1d	36	64	0	0
	2d	31	62	2	5
b	1h	32	68	0	0
	1d	35	65	0	0
	2d	34	62	1	3
c	1h	30	70	0	0
	1d	34	66	0	0
	2d	36	61	0	3
d	1h	13	87	0	0
	1d	20	80	0	0
	2d	35	62	0	3
e	1h	27	73	0	0
	1d	32	68	0	0
	2d	32	63	1	4
f	1h	9	91	0	0
	1d	13	87	0	0
	2d	13	87	0	0

4.9 Ligand Synthesis

Experiments have shown that a bite angle of 102 °, electron rich and sterically less demanding groups are favorable for *C*-allylation of phenol. The information from mono and bidentate ligand screening suggested to test a new ligand **123**, which features the combined characteristics. The synthetic route depicted in Scheme 33 was devised to synthesize ligand **123**. Other routes for n-alkyl phosphines used highly pyrophoric biphosphines as starting materials. The synthesis route was adapted from similar ligands (all literature known) starting from phosphorous trichloride (**117**).



Scheme 33: Intended forward synthetic route to the new ligand.

The first step was prepared according to *Charette et al.*[74] Freshly distilled PCl_3 was dissolved in diethyl ether (dry) in a 500 mL three-necked round bottom flask under inert conditions and cooled to -78 °C via a CO_2(s) acetone cooling bath. Diethylamine was dissolved in diethyl ether (dry) in a 250 mL dropping funnel. The diethylamine solution was added slowly to the PCl_3 solution at -78 °C. Appearing hydrochloric fumes were redirected with nitrogen counterflow into a saturated sodium bicarbonate solution. The white suspension was allowed to warm to r.t. after complete addition of diethylamine. This reaction mixture was stirred over night. The resulting white precipitate was filter off through a pad of dry Celite in a fritted funnel and washed with diethylether (dry). A subsequent concentration of the filtrate under reduced pressure with a N_2 (l) cooling trap and vacuum distillation (45 °C / 1.2 mbar) yielded 42 % **119** as a colorless liquid. An increased yield may be achieved with additional diethylamine to compensate the inactivated diethylamine hydrochloride.

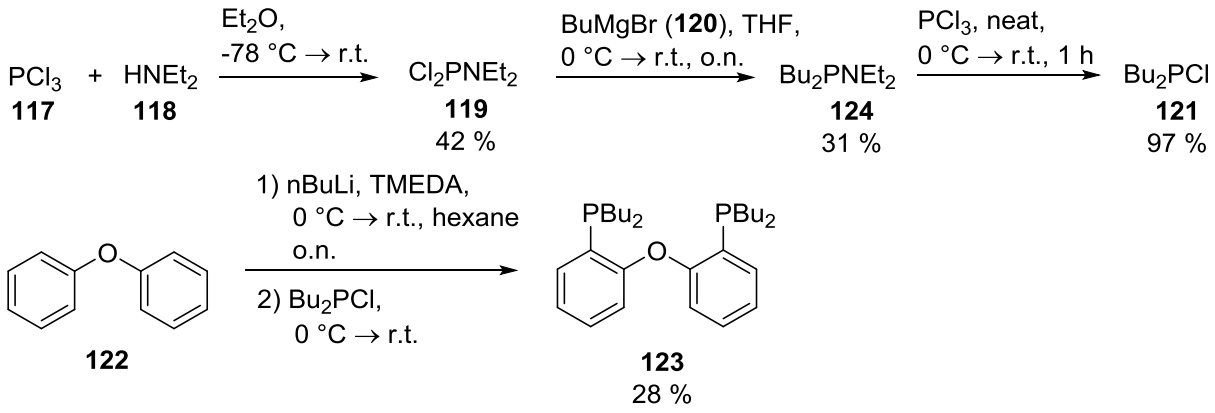
The first attempt to synthesize dibutylchlorophosphine according to *Charette et al.* was inefficient and unsuccessful, due to water and possible air contamination via *ex situ* generated dry hydrochloric diethyl ether solution. A 2.8 M n-butylmagnesiumbromide in diethylether solution was generated and titrated according to the procedure in Chapter 6.2.2.9. In a 1 L three-necked round bottom flask *N*,*N*-diethyl-phosphoramidous dichloride was dissolved in dry THF and cooled to 0 °C via an ice-bath. The *Grignard*-reagent was added dropwise at 0 °C in a time period of 30 min, stirred for 1 h at 0 °C, then filtered through a pad of Celite in a fritted funnel. Inert HCl (generated via addition of H_2SO_4 to $CaCl_2$ under inert conditions) was discharged into diethyl ether (dry) via a drying tube. Titration of this solution was not achieved. Each drawing of the solution led to degassing of the diethyl ether. The hydrochloric diethylether solution was added slowly to the dibutyl(diethylamino)phosphine filtrate at 0 °C. The precipitate was filtered again via a pad of Celite in a fritted funnel and washed with diethylether (dry). Only *P*,*P*-dibutyl-*N*,*N*-diethylphosphinic amide could be detected after concentration of the filtrate via reduced pressure indicating that the alkylation with n-butylmagnesiumbromide worked. Generation of the hydrochloric diethylether solution posed the main problem in the first attempt towards dibutylchlorophosphine. A second attempt using a bigger drying tube apparatus with the previous procedure and a subsequent vacuum distillation (54 °C / 2.5 mbar) yielded 8 % desired product (**121**).

The last step in the ligand synthesis incorporated a lithiation of diphenylether with consecutive addition of the alkyl chlorophosphine. In an 80 mL Schlenk tube diphenylether and tetramethylethylendiamine (TMEDA) were dissolved in n-pentane (dry). n-Butyllithium was titrated with diphenylacetic acid (Ø 50 mg) in 5 mLTHF (dry). This was performed three times in evacuated *Schlenk* tubes. After titration 2 eq n-butyllithium were added slowly to the cooled (0 °C) diphenylether solution. A few drops of the slightly yellow suspension were extracted with ethyl acetate from D_2O to indicate complete lithiation of diphenylether (16 h) via GC-MS. 2 eq Bu_2PCl were added at 0 °C to the reaction mixture. The now whitish suspension was stirred for 3 h at r.t.. The reaction was quenched

degassed H_2O, extracted with diethyl ether (abs.) and washed with degassed brine. The organic layer was dried over anhydrous $MgSO_4$, filtered, washed with diethyl ether under inert conditions and concentrated under reduced pressure. GC-MS of the crude product indicated a nearly quantitative amount of tributyl phosphine. This can be explained via inappropriate titration with diphenylacetic acid in THF (dry) of the n-BuLi reagent. Due to water contamination of the THF (the last 20 mL of the bottle) more n-BuLi was needed to achieve persistence of the yellow color during the titration. Consequently, more n-butyllithium was present in solution and reacted with the added chlorophosphine (**121**).

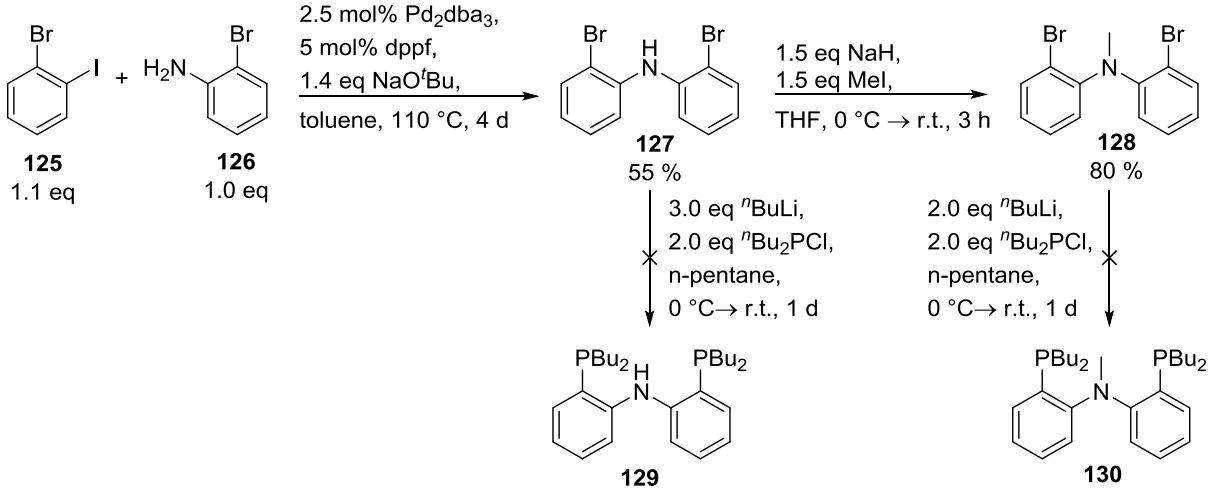
Slight modifications have been made in a second synthesis of the ligand starting from phosphorous trichloride. Amidation was proceeded according to literature. The second step was performed as previously described but the intermediate 1,1-dibutyl-*N*,*N*-diethylphosphinamine was purified this time via vacuum distillation (56 °C / 0.52 mbar). Chlorination of this compound was the next crucial step. This time 1 eq phosphorous trichloride was added slowly to neat 1,1-dibutyl-*N*,*N*-diethylphosphinamine at 0 °C. A following vacuum distillation yielded 97 % dibutylchlorophosphine.

The last step was performed according to chapter 6.2.2.14. Titration of the organolithium reagent was performed three times with freshly absolutised THF (1 mL each) and 90 mg diphenylacetic acid. In this second attempt, amount of surplus n-butyllithium was reacted with phenyl aldehyde which was then extracted with ethyl acetate from H_2O. After indication of complete conversion similar to the procedure described previously, dibutylchlorophosphine was added at 0 ° to the reaction mixture. The reaction was quenched with degassed H_2O extracted with diethylether (dry) and washed with degassed brine. The crude product was dried with anhydrous $MgSO_4$, washed with diethyl ether (dry) and concentrated under reduced pressure. Inert column chromatography was difficult, due to the same R_f values on TLC with mono phosphonated diphenyl ether but the final ligand could be purified as indicated via ^{1}H, ^{13}C and ^{31}P NMR.



Scheme 34: Final established route towards the desired ligand 123.

An attempt for a modified ligand (**129** and **130**) was assumed, due to the upcoming benefits of pincer ligands in catalysis. The proposed synthesis (Scheme 34) was successfully used up to the last steps. The first step in ligand synthesis involved activation of the catalyst. This was achieved via stirring the pre-catalyst and the ligand (dppf) in toluene for 10 min. at r.t. in a *Schlenk*-tube. The orange reaction mixture was heated up to 100 °C after base was added. The substrates were added at 100 °C and then heated up to 110 °C. Conversion of the starting material was monitored via GC-MS. More than 85 % of product **127** could not be detected even after 4 d. The crude product was washed with water and extracted with diethylether. Purification of the product was achieved via column chromatography with cyclohexane as eluent after drying over sodium sulphate, filtering and concentrating under reduced pressure of the crude product.



Scheme 35: Synthetic steps for pincer-like ligands 129 and 130.

Due to impure starting material (2-bromaniline) only 55 % clean product were yielded after the first step. Half of the product was used for methylation. 1.5 eq NaH (60 w% in mineral oil) was added to a cooled solution of **127** in THF (dry). After stirring for 30 min at 0 °C 1.5 eq MeI were added slowly. The white suspension was allowed to warm to r.t. and stirred for 3 h. After washing with water and extraction with diethyl ether 80 % of product could be isolated via 2 steps by crystallization from cooled cyclohexane (6-10 °C). The last step included the same reaction conditions as for ligand **123**. One exception was the use of 3 eq n-BuLi for **129**. Both reaction mixtures turned orange after n-BuLi was added at 0 °C. The crude product of **129** was washed with slightly degassed conc. hydrochloric acid and extracted with diethylether (dry) according to a literature procedure.[75] Washing with conc. HCl probably protonated the amine function and kept the product in aqueous phase. In this state, the ligand was easily degraded after 1 d. The other ligand was washed with degassed water and extracted with diethylether (dry) to avoid the preceding problems with ligand **129**. The crude product was concentrated under reduced pressure. Inert column chromatography with n-pentane as eluent was unsuccessful. A rather pure product could be isolated but indicated only mono phosphination.

4.10 Second Generation Ligand Screening

This screening involved four ligands bearing a similar bite angle to DPEPhos of roughly 102 °. Unfortunately, the bite angles of the ligands are not literature known, but the added bond lengths from one to the next phosphor in each ligand are comparable. Flexibility of the ligands was also desired as Xantphos appeared to be inactive for *C*-allylation, but consists of the same bond lengths (Chapter 4.3). Ligands **131**, **132** and **133** were contributed by Felix Anderl. DPEPBu was synthesized according to chapter 4.10 and 6.2.2.14.

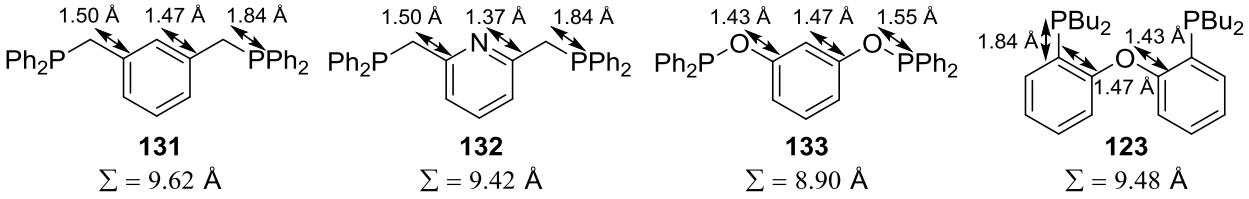
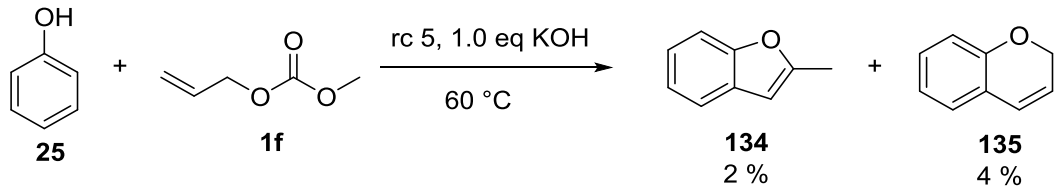


Figure 10: Bondlength comparison of the tested ligands.

These ligands were tested with rc 5. As expected, ligand **123** turned out to be quite potent. 12 % *ortho*-allylated phenol was already monitored after 1 h. Over-allyation occurred due to the high activity of the resulting catalyst. 2,6 Diallyl phenol was produced in high amounts in a quite short time range compared to PBu_3 or DPEPhos. Other poly-allylated side-products in amounts of 4-11 % were monitored too. *Para*-allylated phenol was observed after 1 d indicating that this reaction may be more selective if fast enough to convert all of the allyl methyl carbonate.

Ligands **132** and **133** on the other hand were adequate *O*-allylating ligands. Even though **133** should be less electron rich, phenol was converted faster with this ligand. **131** was completely inactive for any reaction.

Subsequently, some of the preceding screenings have been repeated with ligand **123** without too many improved results. Experiments at 60 °C showed that 80 °C were necessary to *C*-allylate phenol with this catalytic system. Surprisingly, 2 % 2-methylbenzofuran and 4 % 2*H*-chromene were produced with KOH as additive after 2 d at 60 °C. Less allylphenylether was produced when base was added in that screening. The importance of adding allylmethylcarbonate and phenol via a stock solution to the catalyst mixture was demonstrated. If phenol or allyl methyl carbonate were added before heating to 80 °C, complete loss of activity or decreased *C*-allylation was observed. This effect was also monitored by Buchwald for his amination, in which the catalyst had to be activated first before adding substrates.[71]



Scheme 36: Observed products with DPEPBu as ligand at 60 °C.

An increase in catalyst loading (0.1 eq (η^3-$C_3H_5PdCl)_2$) with **123** (0.2 eq) did increase conversion rate but selectivity problems sustained. With increased activity 33 % **25b** and 24 % diallylated phenol were already produced after 1 h.

4.11 Leaving Group Screening

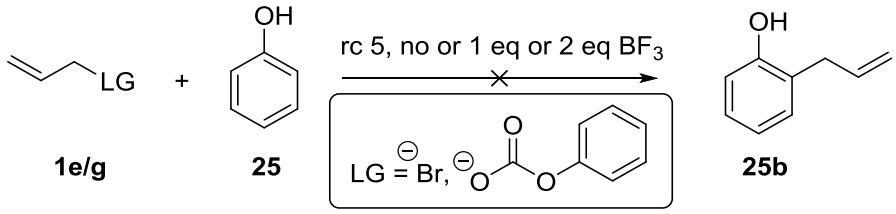
The aspect of increasing LG-character in the allyl-molecule to facilitate catalytic activity seems to be a fundamental motif in Pd-catalyzed allylating reactions. The work of *Tsukada et al.* determined that allyl-4-methylbenzenesulfonate was necessary to reduce reaction temperature in their catalytic system with Rh and Ir.[46] The very good LG-character of ⁻OTs is known for several reactions. Other LGs (methyl carbonate, acetate, iodide, bromide) that are also known to be quite potent did not react at all with Tsukadas catalysts. This result led to experiments with different allylating reagents. Allyl-4-methylbenzenesulfonate needed to be synthesized to examine if it was a useful reactant for this catalytic reaction. This reagent was synthesized via a known literature procedure [76] to give 87 % product. Allyl alcohol and allyl acetate were added to that screening due to their easy and cheap accessibility.

According to the classical LG properties, allyl-4-methylbenzenesulfonate should show better results than allylacetate which in turn should show better results than allyl alcohol. An extrapolation of expected results for this catalytic system could not be rendered. *C*-allylation was achieved with allyl alcohol (3 % *ortho* allyl phenol) and allylOTs (6 % *ortho* and 6 % *para*). Allyl acetate only produced allylphenylether (~50 %). A problem with *C*-allylation, in addition to the poor conversion was the extended reaction time (2 d in both cases). An interesting side-product was observed with allylOTs as reagent. After a long inactive phase of more than 1 d allylated toluene (6% *ortho* and 6% *para*) could be observed via GC-MS. The lost *ortho* to *para* selectivity with allylOTs tends to strengthen the *Friedel-Crafts* Pd-catalyzed proposal. Astonishingly, *O*-allylated product could not be observed during the whole reaction time, although ⁻OTs should be a worse nucleophile (pKa ~ -2) than the phenolate-anion (pKa = 10).

This is in contrast to the work of *Amatore et al*. in which a good leaving group was proven to be a poor nucleophile for a backward reaction (attack at the η^3-C_3H_5). They proved that the reaction of allylic carboxylates (allyl-LG, LG: acetate, chloroacetate, trifluoroacetate, substituted benzoates, carbonates) with Pd^0 ligated by mono or bidentate ligands is a reversible multistep reaction. They also

concluded that a cationic (η^3-C_3H_5)Pd(II)(P-P)$^+$ complex with LG^- as the counter anion may be formed in organic media. This was independently proven by *Schoenebeck et al.* for Suzuki-Miyaura reactions.[77] Consequently, the oxidative addition step was determined as the slowest step for less good LGs (acetate, benzoate), but was faster than the complexation step for better LGs (carbonate, trifluoroacetate). Amatore emphasized the complex characteristics of several LGs and their active role in catalytic processes. Additionally, the steric properties of allylic carbonates were examined. The equilibrium constant decreases when steric hindrances increase and a high equilibrium constant determines a better LG.[78]

Encouraged by their work, allyl phenyl carbonate and allylbromide were tested. Herein, allylbromide turned out as inactive. Experiments with allylphenylcarbonate should exhibit if the naked phenolate anion could be more easily allylated. A stronger mesomeric effect was proposed for a naked phenolate anion. In the rc5 pathway, a similar way to the phenolate anion was achieved with the produced methanolate anion which should easily deprotonate phenol due to the pKa differences (pKa (phenol) = 9.99 and pKa (methanol) = 15.54). A comparison of the two ways to expose one as the more efficient was performed. Inspired by the work of *Knochel et al.* [79] the addition of frustrated lewis acids (BF_3) may block the attack of the naked phenolate anion (**25'**) at the harder electrophile Pd(0). For the screening with allylphenylcarbonate no addition as well as addition of 1 eq and 2 eq $BF_3 \cdot Et_2O$ with DPEPhos was tested to get an overview of reactivity.



Scheme 37: LG-screening with allylbromide and allylphenylcarbonate

When $BF_3 \cdot Et_2O$ was added to the reaction mixture the only observed side-products were *ortho* and *para* allylated toluene. A comparable reaction but without catalysis to allylate toluene with trimethylallylsilane and hypervalent organo iodine compounds was already reported.[80] Nevertheless, *C*-allylation was not achieved with allylphenylcarbonate. The poor LG-properties of the phenolate anion (**25'**) with DPEPhos are consistent with previous experiments.

4.12 Substrate Screening

A broad range of aromatic compounds was tested to evaluate the catalytic system for other molecules. It is known that electron rich arenes can be more easily alkylated. Phenol itself was in most cases hard

to allylate.[37,50] An improved reactivity could be expected for various substrates with EDGs. Additionally, selectivity may be improved for *ortho* and/or *para* substituted phenol derivatives.

DPEPhos and PBu_3 led to similar product ratios for cresols. Best results were achieved with *o*-cresol (36 % *o*-allylated *o*-cresol). Side-products were achieved in less than 10 % (allylcresylether, *p*-allyl-*o*-cresol and diallyl *o*-cresol) for *o*-cresol. The other cresols were either less active (*p*-cresol: 4 % *C*-allylation) or very unselective (*m*-cresol: 15 % + 21 % *C*-allylated products). Anisole turned out to be inactive for *C*-allylation. The mesomeric state of deprotonated phenol (Scheme 39) may enable a nucleophilic attack on the η^3-$C_3H_5PdL_2$ intermediate. *C*-allylation was also not observed for aniline. Only mono and di *N*-allylation could be monitored.

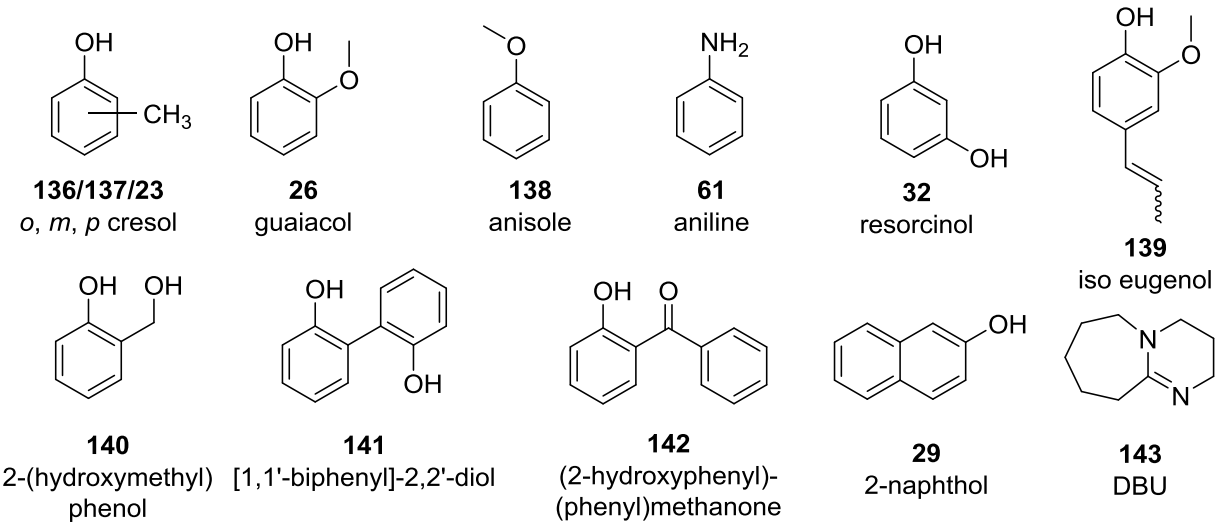


Figure 11: Substartes which were considered for allylation with rc5.

A lot of other substrates turned out to be rather unselective (**137**, **32**, **140**) or unreactive (**138**, **141**, **142**). Unreactive or only *O*-allylated substrates can be attributed to their electron withdrawing character or possible chelating effect (**140**, **141**, **142**). The exception was guaiacol in which 20 % were *o*-allylated within 1 d. Outstanding was the successful *C*-allylation of 2-naphthol. Reports on successful allylation of 2-naphthol were already mentioned in previous chapters (Chapter 2.2.5 and 2.3.2), indicating that 2-naphthol is more reactive and easier to allylate. **143** was tested as substrate, due to the rather selective side-reaction that was observed with DBU as added base for phenol allylation. Work up of GC-MS probes with MeOH as eluent disclosed the polar components that have been formed after a few hours of reaction time.

Table 18: Substrate specific results for allylation after 24 h.

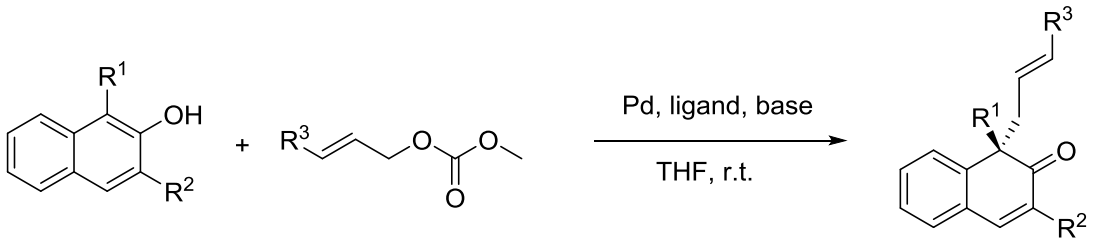
substrate	ligand	educt [%]	*O*-allyl [%]	*C*-allyl [%]	di-allyl [%]
136	PBu_3	54	9	36	2
	DPEPhos	54	6	38	2
137	PBu_3	57	28	11	-
	DPEPhos	59	1	36[i]	4
138	PBu_3	54	39	5	2
	DPEPhos	63	34	3	-
26	**123**	79	2	18	1
138	PBu_3	100	-	-	-
61	PBu_3	12	88[ii]	-	-
32	**123**	55	20	25[iii]	-
139	**123**	70	30	-	-
140[iv]	**123**	-	67	-	-
141	**123**	90	10	-	-
142	**123**	87	13	-	-
29	PBu_3	-	-	≥ 99	-

A bigger scale reaction was run to isolate sufficient amounts of by-product to elucidate its structure, as such a reaction or formed product has not been observed in literature. GC-MS indicated a double allylated DBU as main product. Three other DBU-derivatives were present, but molecular weight was bigger and more difficult to analyze via fragment masses than the main product. DBU itself could not be observed during the whole reaction time. The reaction was stopped after 2 d with rc5. Toluene was removed under reduced pressure. ^{1}H and ^{13}C-NMR strengthened the proposed double allylated DBU as main product. Further, ^{13}C-NMR revealed that the amidinic carbon in all formed products had reacted in some way. A lot of TLCs were made to estimate the polarity and column behavior. A main spot could be spotted with $KMnO_4$ at R_f 0.21 (DCM/MeOH/NH_4OH 5+4+1). This high polarity turned out to be a bigger problem. After column chromatography with a gradient of 20+4+1 to 5+4+1 only impure products could be collected. These products emerged as more impure than the starting raw material. A second attempt to synthesize the formed product was made, but purification problems remained. A reaction with 2,4,6-trinitro phenol should enable crystallization of polar amines.[81] 2,4,6-trinitro phenol was dissolved in warm ethanol (60 °C) and poured into a flask in which crude product was dissolved in ethanol at r.t. A biphasic system evolved in which a dark brown phase built the heavier phase. The yellow pikrinic acid phase built one impure brownish crystall after ethanol was evaporated. Purification of this crystal is still ongoing.

[i] A mixture of 2- and 6- allyl *p*-cresol (15/21 %) was observed.
[ii] A mixture of mono- and di-*N*-allylanilin (64/24 %) was observed.
[iii] A mixture of 2- and 6- allyl resorcinol (6/19 %) was observed.
[iv] 33 % of unidentified side-product was observed.

4.13 Mechanistic Conclusions

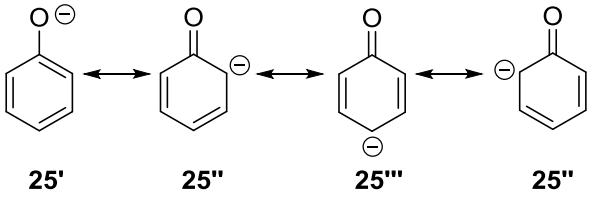
Derived from the preceeding results, mechanistic conclusions can be made with implication of the studied publications. The first step in the catalytic cycle may be a crucial step if poor leaving groups are used. This crucial step was solved from different groups via addition of NaOH in aqueous media[36] or BEt_3,[38] phosphoric acids,[82] or via self-assembling ligands [83] in organic media to enable allylations with $^-$OH as LG even at r.t.. Other groups were able to allylate naphthol derivatives with allylmethylcarbonate. In *You et al*'s case addition of 1 eq base was necessary to enantioselectivly allylate and dearomatize 1,3 derivatized naphthols at r.t..[84] Regardless from these results, *C*-allylation of phenol was not achieved at temperatures lower than 80°C with allylmethylcarbonate as LG in this thesis. A pathway to the active η^3-$C_3H_5PdL_2$ catalyst (Scheme 5) that has been reported from several groups can be assumed as consistent.



Scheme 38: Standard reaction scheme of *You et al*'s allylic dearomatication.

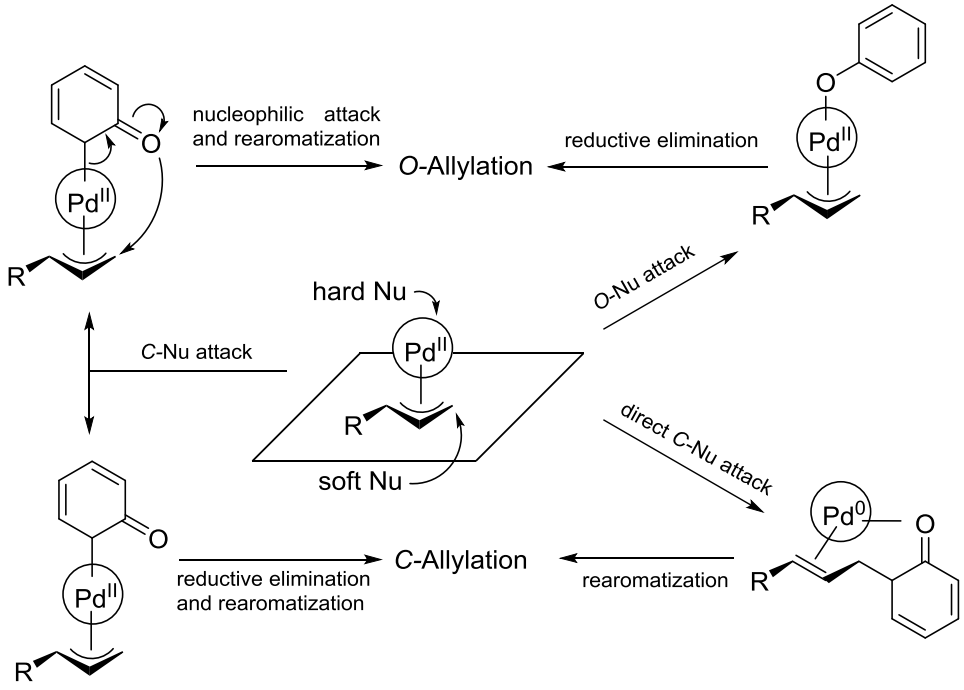
More difficult is the proposal of a direct *C*-allylative step in catalytic cycles that includes arenes. Only a few scientists dared to propose such catalytic cycles. The first to publish was Kuntz in 2006 (Scheme 11). *Bouwman et al.* implicated two possible ways. Either an *ortho* metallation or a *Friedel-Crafts* like reaction pathway were suggested for *C*-allylation (Scheme 15). *Pregosin et al*. also assumed the *Friedel-Crafts* like reaction pathway to be the most favorable one.[43] Ru was the central atom in *Pregosin et al*'s and *Bouwman et al*'s work and mechanistic proposal. This metal may undergo a slightly different pathway compared to Pd as the Ru(III) catalyst can change from the trigonal dipyramidal to the square pyramidal configuration.

More important is the catalytic cycle proposed from *Kuntz et al*. in organic media. An equilibrium state for the phenolat anion was not underlined but can be expected especially in apolar solvents. This is in accordance with the solvent screening, wherein the most apolar solvent (toluene) turned out to emphasize *C*-allylation. In protic or polar solvents stabilization of the phenolat anion **25'** can be easily achieved. The catalytic pathway via a phenolat intermediate can be explained by the inactivity of anisole. So do the excess anions around the catalytic center in cationic catalyst screening which disable a diffusion of the phenolat anion towards the catalyst. Additionally, surplus presence of $^-$OH did accelerate the reaction (Chapter 4.7). This underlines the necessity of a phenolat anion.



Scheme 39: Mesomeric equlibration state of a phenolat anion.

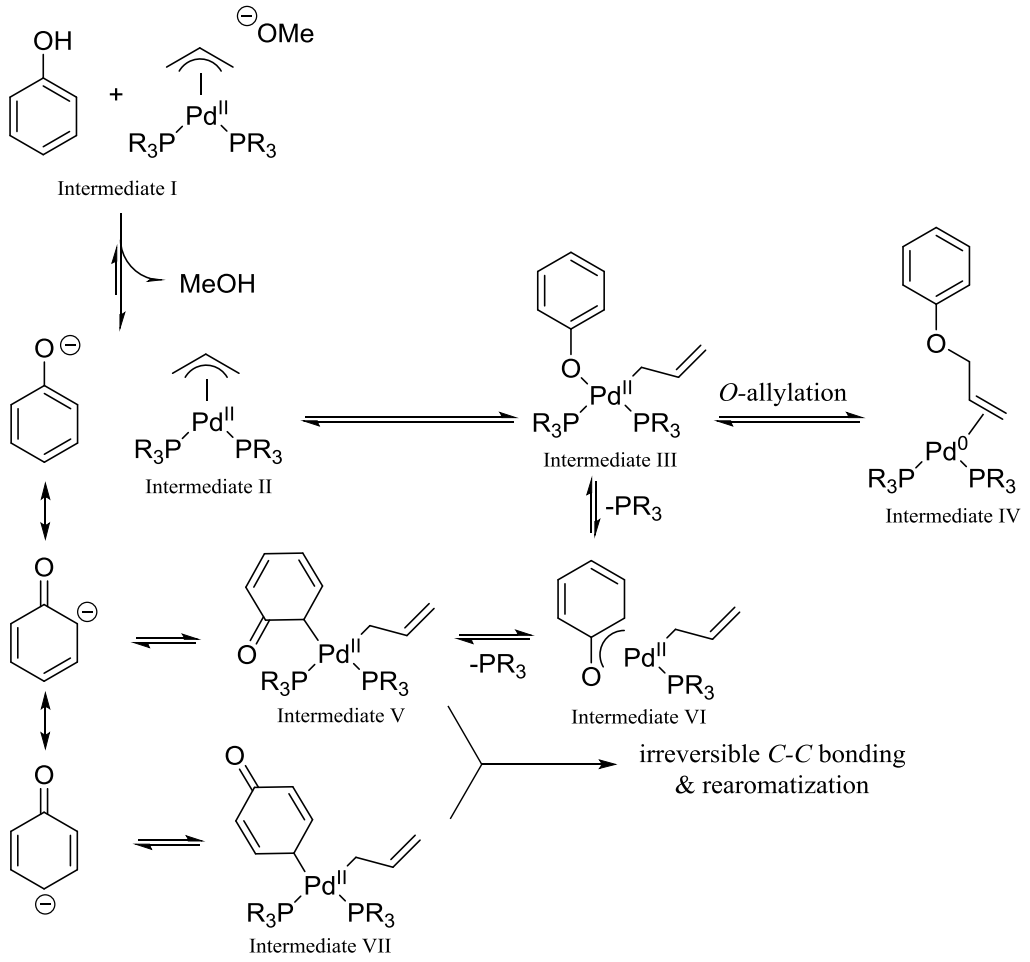
Regarding the work of *Gong et al*. hard nucleophiles should attack the more Lewis acidic molecule/atom. The electron donating properties of PBu_3 may only reduce the Lewis acidity of Pd to a lesser extent. This may be enough to facilitate the attack of the softer nucleophile onto Pd.



Scheme 40: Possible reaction pathways to *O*- and *C*-allylation.

Refocusing on ligands which enabled *C*-allylation, the properties of PBu_3 and DPEPhos turned out to be of high importance. The question arised how the properties of ligands affect the reaction in detail. In case of monodentate ligands, electron richness and a small cone angle were necessary. It is known that electron rich ligands ease oxidative additions in several transition metal catalyzed reactions. This implicates the faster formation of the η^3-$C_3H_5PdL_2$ catalyst from allylmethylcarbonate and a Pd-pre-catalyst as well as the results achieved with allylphenylether as substrate. Apparently, electron rich ligands facilitate the oxidative addition of allylphenylether onto Pd(0) and small ligands enable the *C*-nucleophilic attack in *ortho* position. According to that proposal, electron rich and sterically demanding ligands should either lead to allylphenylether and to *p*-allylphenol. This was not observed

in the case of tricyclohexylphosphine (only allylphenylether was formed). A catalytic cycle depending on the reversible oxidative addition/reductive elimination of allylphenylether and the mesomeric effect of the phenolate anion is therefore more likely to be the key step in *C*-allylation than a direct attack of any *C*-nucleophile (Scheme 41). The only direct attack can be assumed from the *C*-nuclophilic enolate in *ortho* position as it is the softer nucleophile. This is in correspondence with the barely observed *para*-allyl-phenol. If an attack of the *C*-nucleophiles would be preferred a ratio of 2:1 *ortho*:*para* should be monitored. This was not observed. One additional explanation to enhanced *ortho* selectivity may be the stabilization of the phenolate anion via η^3-phenolate intermediate (Scheme 41, Intermediate VI) indicating the dissoziation of one ligand to sustain a quadratic planar 16 e^- complex.



Scheme 41: Proposed mechanism for *O*- and *C*-allylation with PBu_3 as ligand.

The formation of methanol is in favor due to the higher pK_a of MeOH compared to phenol. Use of allyl-4-methyl-benzensulfonic acid did not lead to the desired reaction as a result of unachieved deprotonation.

An accurate explanation for bidentate ligand properties represents a challenge. Aside from the unusual bite angle, electronic properties should correlate with PPh_3 for nearly all tested bidentate ligands.

Interesting was the comparison of bidentate ligands which had similar bite angles. Other bidentate ligands which showed some activity for *C*-allylation lacked either selectivity (dcypb) or reactivity (dppf). On closer inspection of DPEPhos, the structural features of this ligand may correspond to a pincer-like ligand. Unfortunately, other pincer-ligands (Figure 10) did have no effect on improving *C*-selectivity. Intriguing was the observation of a literature known octahedral Pd(II) complex. This ligand, a tris(2,4,6-trimethoxyphenyl)phosphine, was proven to coordinate with a lone pair of the excisting *ortho* positioned methoxy groups.[85] A possible conformational state of DPEPhos, comparable to the work of *Dunbar et al.*, can be assumed (Figure 12). These intermediates also represent Pd(II) complexes comparable to *Dunbar et al*..

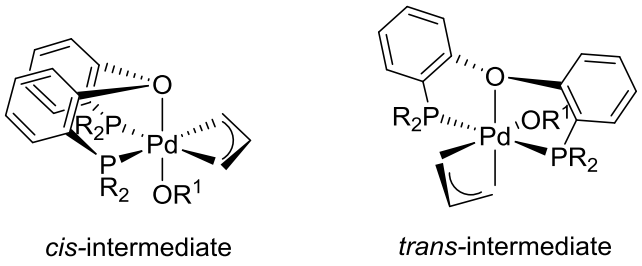


Figure 12: Proposed octahedral intermediates for DPEPhos.

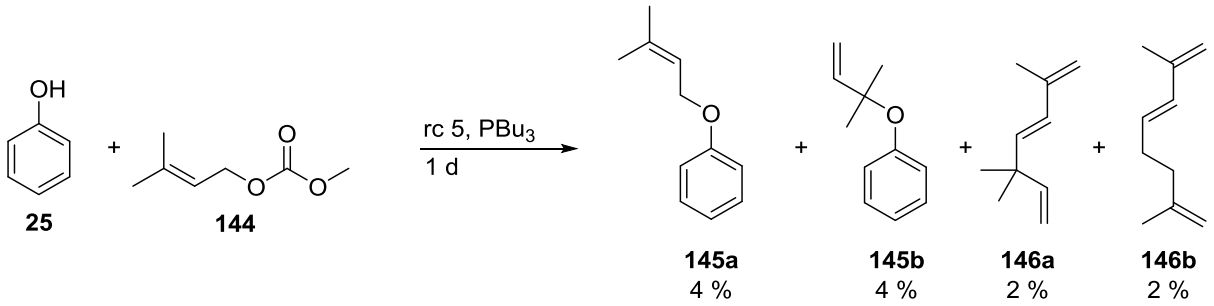
Nevertheless, such a octahedral intermediate in Pd-complexes is rather unusual and was only observed at low temperatures (-70 °C) even with other ligands.[86] It may be more likely that the flexibility of DPEPhos plays a part in contributing to *C*-allylation comparable to Scheme 41. This is assured via the proposed mechanism of *Bouwman et al*. wherein the dissociation of one phosphine end of the bidentate ligand enables coordination of the phenolat (Scheme 15). This theory is strengthened as in the case of Pd, small cone angle ligands made room for *ortho* allylation and dissociation of one phosphine end may produce the needed space for *ortho*-allylation.

The reaction with allyphenlyether as substrate revealed the necessity of base for the oxidative reaction step with DPEPhos as ligand. Thus, the use of bases ($^{-}$OMe, KOH) eased conversion and the oxidative addition of allylphenyl ether.

4.14 Sidereactions

Another side reaction was assumed to occur during the intentioned reaction apart from the observed side reaction with DBU. In an allylating reaction with methylprenylcarbonate a mixture of two dimeric isoprene-like products could be monitored. Methylprenylcarbonate was synthesized according to the synthesis of allylmethylcarbonate (Chapter 4.1 and 6.2.2.3). The poor yield (18%) can thus be explained due to concentration and evaporation of surplus pyridine in high vacuo. The reaction with

this reagent did not lead to *C*-allylation at all. Even *O*-allylation was observed in trace amounts (Scheme 42). A similar dimerization of butadiene and ethene was reported from *Wilke et al.* in 1966. Several transition metals were tested with alkenes in which Pd formed linear alkene dimers. Ni produced cyclic alkene dimers, Cr and Co polymerized allyl functionalities. In the case of Pd, dimerization was accelerated via excess addition of trialkylphosphines, comparable to PBu_3 used in this work.[87]



Scheme 42: Observed products in the reaction with methyl-prenylcarbonate (144).

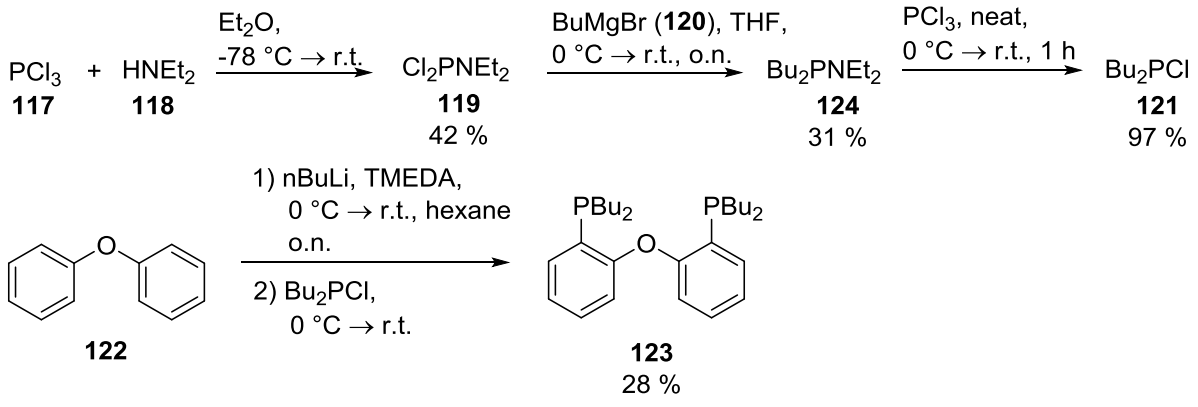
A very related and informative subject was reported from *Brookhart et al.* comparable to the work of Wilke alkylphosphine ligands were necessary to dimerize olefins and especially acrylates.[88] Such dimerizations were observed even at very low temperatures (-90 °C). Hence, dimerization of η^3-C_3H_5 via a $(\eta^3\text{-}C_3H_5)_2Pd^{II}$ intermediate can be expected in reactions where the formed allylphenol equivalents do not match the used allylmethylcarbonate equivalents and unreacted or regained phenol.

5. Summary and Outlook

5.1 Summary and Conclusion

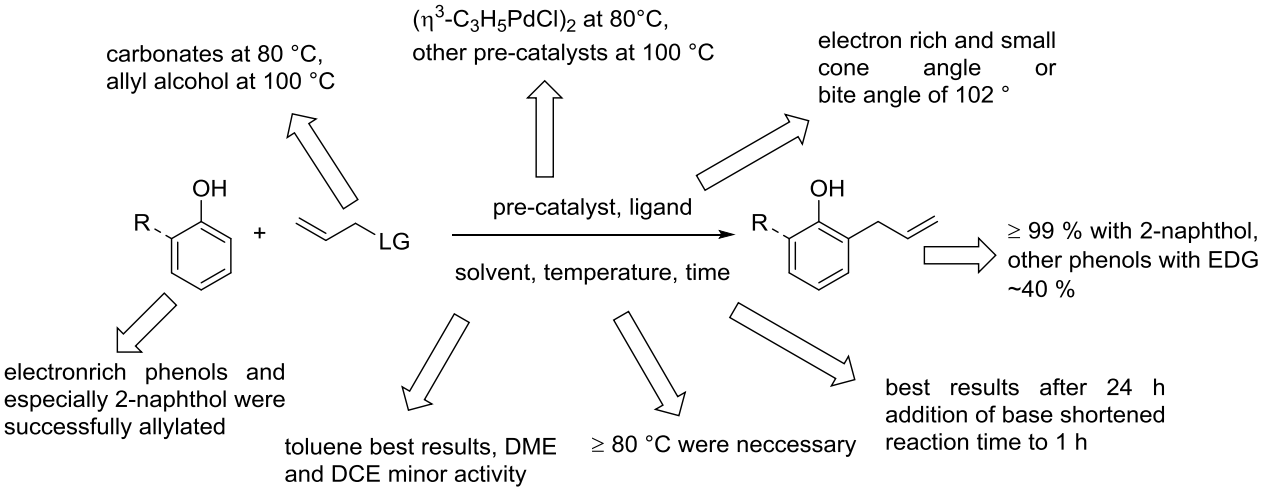
The set goal of this thesis was the creation of a catalytic system for either *ortho* or *para* allylation of phenolic molecules. This catalytic system should at least imply some improvements compared to other published catalytic systems.[32,36,38,43,64] Exclusion of additives, milder reaction conditions, simplified catalyst activation, broad substrate specificity and improved selectivity belonged to the goals. Such a catalytic system could be of synthetic value as it would provide a simplified access to terminal olefins on phenols which can be used for further coupling. This coupling can include polymerization wherein allylphenols are used as monomers or linkage of tyrosines in enzymes or natural products with spacers via thiol-ene or cross metathesis.

Rather harsh reaction conditions of 100 °C were necessary at the beginning of this work to facilitate *C*-allylation of phenol with different pre-catalysts. These reaction conditions could be minimized to 80 °C with [η^3-C_3H_5PdCl] and appropriate ligands in toluene. Essential for improved results was the preceeding formation of active catalyst and the consequent addition of stock solution to the heated catalyst solution. Several screenings to underline the importance of ligand features exposed PBu_3 and DPEPhos as the most potent ligands for *C*-allylation. Electron rich and small cone angle ligands as well as ligands with a bite angle of around 102 ° enabled *C*-allylation at 80 °C. Addition of $^-BF_4$ and $^-PF_6$ salts as well as a solvent screening did not lead to any improvements during this work, whereas addition of some bases did increase reactivity. Each use of base was linked with disadvantages. In the case of DBU selectivity towards 2-allylphenol could be improved but the occurring sidereaction with DBU itself decreased the overall conversion of phenol. The shortened reaction time and produced amount of *C*-allylated phenol was significantly improved with alkaline bases but overallylation was also facilitated with these bases. Reaction temperature could not be reduced even with the addition of base.



Scheme 43: Reaction pathway to ligand 123.

Ligand **123** was synthesized, which combined the beneficial properties of mono and bidentate ligands. The new ligand **123** reduced the reaction time to a quarter (6 h) of the primary reaction time (24 h). The remaining problem was the overallylation of phenol which leveled off in 42 % desired product and 29 % 2,6-diallylphenol. A consequent substrate screening revealed 2-naphthol as ideal substrate. 1-allyl-2-naphthol could be observed after 1 h at 80 °C in ≥ 99 %. Additionally, guaiacol, *o*-cresole and *m*-cresole could be *C*-allylated in comparable results to phenol. Increasing the reaction temperature to 100 °C enabled the use of allyl alcohol as reagent for this kind of reaction.



Scheme 44: Overall achieved results during the work on Pd-catalyzed allylation of phenols.

In conclusion, a Pd-catalyzed system with simple catalyst activation (Chapter 6.2.1.1) which enabled rather selective *ortho*-allylation (mono and di *ortho*-allylation) with improved features was developed. The possibility of phenol *C*-allylation can be highlighted as no additives were necessary compared to other works. A detailed reaction mechanism has been proposed which reflects the achieved results.

5.2 Outlook and Future Work

Although some achievements have been made during this thesis, a lot of improvements still need to be made to either increase selectivity and conversion or decrease reaction temperature. Other improvements could include the use of allyl alcohol as substrate at milder reaction conditions or broadening the substrate scope.

One approach to improve the reaction should be the use of phenolat salts. This would lead directly to the phenolat anion, and the counter cation may also have an influence on the allylated position comparable to the *Kolbe-Schmitt* reaction.[89] Additionally, the formed NaCl or KCl from the η^3-$C_3H_5PdL_2Cl$ catalyst should not be able to interfere with the reaction.

Another topic that drew attention during this thesis was the side reaction with DBU. Intentional catalyzed reactions in which DBU was used as reagent have not been reported so far and thus, a purification and identification of the generated product would be of high interest for further investigations.

6. Experimental

6.1 General Aspects, Materials and Methods

6.1.1 General

If not otherwise denoted standard *Schlenk* technique was used for screenings and synthesis. Therefore evacuated glassware was heated with a heat gun and afterwards cooled with argon or nitrogen ventilation. Dry or absolute solvents were obtained via different methods denoted in 6.1.3. Reaction conversions were either monitored via GC-MS or TLC (6.1.3.2 and 6.1.3.3). For screening via GC-MS, 5 drops of each reaction mixture were distributed between ethyl acetate and aqueous 5 M HCl (1 mL). The organic layer was filtered through a silica gel and magnesium sulfate filled Pasteur pipette. All other GC-MS probes were just dried via magnesium sulfate filled Pasteur pipettes.

6.1.2 Materials

6.1.2.1 Chemicals

All chemicals for synthesis were purchased from Sigma Aldrich, Merck, Alfa Aesar, Carl Roth, Acros Organics, Fluka, Strem Chemicals, VWR Chemicals, and ABCR Chemicals and were not purified any further, unless noticed in the experimental procedures.

6.1.2.2 Solvents

3 Å and 4 Å molecular sieves (MS) were first dried in a 500 mL round bottom flask at 115 °C in a compartment drier for 1 d and thereafter at 150 °C with mantled heating and oil pump vacuum for 1 d. The molecular sieves were then cooled to r.t. with argon ventilation.

Cyclohexane: Cyclohexane with a minimum amount of 99.99 % was purchased in 5 L metal cans from VWR (23224.362).

Tetrahydrofuran (THF) dry: Tetrahydrofuran was dried via heating under reflux over Na under argon atmosphere. Benzophenone was used to indicate dryness via formation of the ketyl-radical (deep blue). After distillation THF was stored under argon with 4 Å MS in a 1 L darkened conical shoulder bottle.

Ethyl Acetate: Ethyl acetate with a minimum amount of 99.99 % was purchased in 2.5 L darkened glass bottles from VWR (23224.362).

Dichloromethane (DCM): Dichloromethane with a minimum amount of 99.99 % was purchased in 2.5 L darkened glass bottles from VWR (23366.327).

Dichloromethane (DCM) dry: Dichloromethane was first dried over phosphor pentoxide, then refluxed over calcium hydride and distilled into a 1 L darkened conical shoulder bottle. Thereafter DCM was stored under argon with 4 Å MS.

Diethyl ether: Diethyl ether from VWR with an minimum amount of 99 % was distilled to remove the stabilizer 2,6-bis(1,1-dimethylethyl)-4-methylphenol (BHT).

Pyridine dry: Dry pyridine was purchased from Sigma Aldrich (270970, anhydrous, 99.8 %, under argon atmosphere).

1,2-Dimethoxyethane (DME) dry: Dry DME was purchased from Sigma Aldrich (38568, puriss., dried over 4 Å MS, ≥ 99.5 %, stored under argon).

Saturated aqueous sodium bicarbonate: $NaHCO_3$ was added to distilled water under stirring until $NaHCO_3$ precipitated.

i-Propanol dry: HPLC grade i-propanol was dried over 4 Å MS under nitrogen.

N,N-Dimethyl formamide (DMF) dry: Dry DMF was purchased from Acros Organics (326870010, $H_2O \leq 0.005$ %, stored under argon with 3 Å MS).

Trichloromethane dry: Dry trichloromethane was purchased from Sigma Aldrich (472476, anhydrous, ≥ 99 %, with amylene as stabilizer, stored under argon with 4 Å MS).

Dimethylsulfoxide (DMSO) dry: Dry DMSO was purchased from Acros Organics (610420010, stored under 4 Å MS and argon).

Toluene dry: Dry toluene was generated via a drying alox column apparatus (stored under argon with 4 Å MS).

n-Pentane dry: Dry n-pentane was generated via a drying alox column apparatus (stored under 3 Å MS and argon).

N-Methyl-2-pyrrolidione (NMP) dry: Commercial NMP was stirred with CaH_2 (6 g/L) for 6 h, decanted and distilled under vacuum (stored under argon with 4 Å MS).

1,4-Dioxane dry: Dry 1,4-dioxane was purchased from Sigma Aldrich (296309, $H_2O \leq 0.005$ %, stored under argon with 4 Å MS).

1,2-Dichloroethane (DCE) dry: Dry DCE was purchased from Sigma Aldrich (anhydrous, ≥ 99.8 %, stored under argon with 4 Å MS).

Acetonitrile dry: Acetonitrile was purchased from Sigma Aldrich (271004, stored over 3 Å molecular sieves and under argon).

Acetone: Was purchased from Brenntag without further purification (447014).

6.1.3 Methods

6.1.3.1 Flash Chromatography

Column chromatography was performed with 60 Å silica gel with a particle size between 35 – 70 µm from Acros Organics. Applied pressure and amount of silica gel (20 – 50 fold) depended on the separation problem.

6.1.3.2 Thin Layer Chromatography

TLC silica gel on aluminium foil (60 F_{254}) and TLC aluminium oxide (neutral) on aluminium foil (60 F_{254}) were used for reaction monitoring. Detections were carried out with UV-light (254 nm) or additionally with staining ($KMnO_4$-solution).

$KMnO_4$ stain: 0.3 g $KMnO_4$ and 20 g K_2CO_3 were dissolved in 300 mL H_2O under stirring. 5 mL aqueous NaOH (5 %) were added therafter.

6.1.3.3 NMR

NMR spectra were recorded on a Bruker Avance III FT NMR spectrometer (300.36 MHz for ^{1}H-NMR and 75.53 MHz for ^{13}C-NMR) using an autosampler. ^{31}P-NMRs were recorded on a 300 Mercury Varian (121.58 MHz). Solvent peaks were used as internal standard. Chemical shifts (δ) are noted in parts per million (ppm) and coupling constants (*J*) are reported as absolute values in Hertz (Hz). Identified molecule fragments are correlated to the corresponding shifts (δ), coupling constants (*J*) and integrals given.

6.1.3.4 GC-MS

Analytical gas chromatography was performed on an Agilent Technologies 7890A equipped with a polar Agilent Technologies J&W HP 5MS capillary column (30 m × 0.25 mm × 0.25 µm film (5 % phenyl) methylpolysiloxane) in split mode with carrier gas (He 5.0). An Agilent Technologies 7683 autosampler was used for injection. Ethyl acetate and acetone were used to flush the needle before and after injection. Ionization was achieved via Electron Impact (EI, E = 70 eV). Masses were analyzed through Mass analyzer 5975C with inert MSD and triple axis detector. Retention time t_R, basis peak (BP) and molecular peak (relative intensity to the basis peak (BP)) are listed in the associated experiments. Intensities can only be seen as relative since no internal standard was used.

MK_STANDARD: 50 °C 1 min, ramp 1 40 °C/min linear to 300 °C, 5 min.

6.1.3.5 HR-MS

A Waters GCT premier micromass was used for high resolution mass spectrometry. An electron impact ionization (EI) with 70 eV was used as ionization source. Probes were either injected via direct inlet or via an Agilent Technologies GC 7890A with capillary column (DB-5MS, 30 m × 0.25 mm, film thickness: 0.25 µm). Heavier molecules (high molecular weight) were analyzed with a Micromass Tofspec 3E spectrometer with matrix assisted laser desorption ionization (MALDI), α-cyano-4-hydroxycinnamic acid as matrix and a time of flight mass analyzer (TOF).

6.1.3.6 IR-Spectroscopy

FT-IR-spectroscopy was performed on a Bruker Tensor 37 with a Standard Pike ATR cell. It is equipped with a room temperature DTGS detector, mid IR source (4000-400 cm^{-1}). Background spectrums were performed before every measurement. 16 scans were executed per analytical measurement in a range of 4000-600 cm^{-1}.

6.1.3.7 Melting Points

Not corrected melting points were determined with a Mel Temp melting point apparatus with integrated microscopical support from Electrothermal in open capillary tubes.

6.2 Experimental Procedures

6.2.1 General Allylation Reaction

6.2.1.1 Procedure A for *C*-allylation of Phenols

1.6 mg (4.4 µmol, 0.02 eq) allylpalladium(II) chloride dimer and 0.04 eq bidentate or 0.08 eq monodentate phosphine ligand were weighed into a Schlenk tube. 1 mL toluene (abs.) was added and the solution was heated to the specific temperature (100 °C to r.t.). After stirring for 5 min 1 mL of a stock solution (phenol (1.0 eq, 212.5 µmol) and allyl reagent (1.1 eq, 233.8 µmol) in toluene (abs.)) was added. Conversion was monitored at different time intervals (1 h, 1 d and 3 d) via GC-MS.

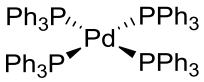
6.2.1.2 Procedure B for *C*-allylation of Phenols

1.6 mg (4.4 µmol, 0.02 eq) allylpalladium(II) chloride dimer and 0.04 eq bidentate or 0.08 eq monodentate phosphine ligand were weighed into a Schlenk tube. 2 mL toluene (abs.) was added and the solution was heated to the specific temperature (100 °C to r.t.). Thereafter the arene substrate

(1.0 eq, 212.5 µmol) was added. After stirring for 2 min allylic carbonate was added to the solution. Conversion was monitored at different time intervals (1 h, 1 d and 3 d) via GC-MS.

6.2.2 Experimental Procedures for Catalysts, Ligands and Substrates

6.2.2.1 Tetrakis(triphenylphosphine)palladium(0)



144

$C_{72}H_{60}P_4Pd$

[1155.59]

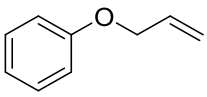
371 mg (2.09 mmol, 1.0 eq) palladium(II) chloride and 2724 mg (10.39 mmol, 5.0 eq) triphenylphosphine were dissolved in 30 ml DMSO (abs.) in a 100 mL two necked round bottom flask equipped with a pressure equilibrator. The orange suspension was heated to 140 °C. 403 µL (8.31 mmol, 4.0 eq) hydrazine monohydrate were added to the suspension in a period of 1 min. After 1 min of additional stirring at 140 °C, the brownish solution was cooled in a water bath (10 °C). The cooling bath was removed as soon as crystals appeared in the reaction mixture. After letting cool to r.t. the yellow crystals were collected by filtration in a fritted funnel and washed with absolute ethanol (2 × 5 mL) and absolute n-hexane (2 × 4 mL). The product was then dried in high vacuo.

Yield: 2.21 g (1.91 mmol, 92 %) shiny yellow crystals.

m.p.: 105 °C (decomposition), (96-105 °C lit.).[90]

IR (cm^{-1}): 3054 (C-H stretch, aromatic), 1475 (C-H bend, aromatic), 1431 (P-phenyl), 740 (C-H, aromatic), 691 (C=C-H aromatic).

6.2.2.2 Allylphenylether



25a

$C_9H_{10}O$

[134.18]

In a 25 mL two necked round bottom flask equipped with a dropping funnel 391 mg (4.16 mmol, 1.0 eq) phenol and 566 mg (4.10 mmol, 1.0 eq) potassium carbonate and 15 ml acetone were added. 357 µL (4.14 mmol, 1.0 eq) allyl bromide were added dropwise at r.t.. The reaction was then heated under reflux and stirred for 3 d. Potassium carbonate was filtered off and the filtrate concentrated in vacuo.

The crude product was purified via column chromatography with a gradient of cyclohexane/ ethyl acetate 95:5 to 10:1.

Yield: 308 mg (2.30 mmol, 56%) colorless liquid.

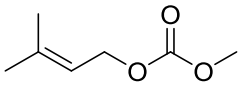
R_f: 0.67 (cyclohexane/ethyl acetate 10:1).

GC-MS (MK_STANDARD): t_R: 4.23 min; m/z: 134.1 (100 %, BP, MP), 77.0 (34.5 %) [M*-allyl-O].

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.32-7.18 (m, 2H, aromatic), 6.97-6.85 (m, 3H, aromatic), 6.12-5.95 (m, 1H, allylic), 5.45-5.35 (m, 1H, allylic), 5.30-5.22 (m, 1H, allylic), 4.55-4.45 (m, 2H, allylic).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 158.7 (C_q, O-C), 133.5 (CH, allylic), 129.6 (2 × CH, *meta* aromatic), 121.0 (CH, *para* aromatic), 117.7 (CH_2, olefinic), 114.9 (CH, *ortho* aromatic), 68.9 (CH_2, allylic).

6.2.2.3 Methyl (3-methylbut-2-en-1-yl) carbonate



145

$C_7H_{14}O_3$

[144.17]

In a 100 mL three necked round bottom flask 1.00 g (11.6 mmol, 1.0 eq) 3-methyl-but-2-en-1-ol and 1.87 mL (23.3 mmol, 2.0 eq) pyridine were dissolved in 10 mL dichloromethane (abs.). The solution was cooled to 0 °C and 1.80 mL (23.3 mmol, 2.0 eq) methyl chloroformate in 10 mL dichloromethane (abs.) were added slowly over a dropping funnel. The reaction was stirred overnight in the thawing ice bath and then washed with H_2O (3×120 mL) and saturated aqueous sodium bicarbonate (2×120 mL). The organic layer was dried over sodium sulfate, filtered and then concentrated under high vacuo.

Yield: 300 mg (2.08 mmol, 18 %) colorless liquid.

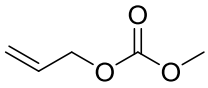
R_f: 0.29 (cyclohexane/ethyl acetate 10+1).

GC-MS (MK_STANDARD): t_R: 3.88 min; m/z: 144.1 (0.9 %, MP) [M], 85.0 (40.9 %) [M - Me-O-C*=O], 69.1 (100 %, BP) [*CH_2-CH=CH_2].

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.42-5.32 (m, 1H, allylic), 4.63 (d, $^3J_{HH}$ = 7.3 Hz, 2H, allylic), 3.77 (s, 1H, methyl), 1.74 (d, $^3J_{HH}$ = 7.3 Hz, 6H, 2 × allylic methyl).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 156.0 (C_q, OCO_2), 140.2 (C_q, olefinic), 118.2 (CH, allylic), 64.8 (CH_2, allylic), 54.8 (CH_3, OMe), 25.9 (CH_3, *E*), 18.2 (CH_3, *Z*).

6.2.2.4 Allyl methyl carbonate



1f

$C_5H_8O_3$

[116.12]

In a 1 L three necked round bottom flask 10 mL (0.146 mol, 1.0 eq) allyl aclohol and 56 mL (0.405 mol, 3.6 eq) triethylamine were dissolved in 200 mL dichloromethane (abs.). A solution of 31 mL (0.405 mol, 3.6 eq) methyl chloroformate in 20 ml dichloromethane was added slowly over a dropping funnel to the ice bath cooled solution. The reaction was stirred overnight at r.t.. The orange brownish solution was washed with H_2O (3×200 mL) and saturated aqueous sodium bicarbonate (2×200 mL). The organic layer was dried over sodium sulfate, filtered and then purified via vacuum distillation.

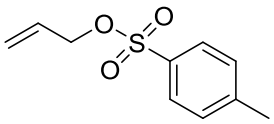
Yield: 3.89 g (33.6 mmol, 23 %) colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.00-5.84 (m, 1H, allylic), 5.40-5.20 (m, 2H, allylic), 4.67-4.53 (d, $^3J_{HH}$ = 2H, allylic), 3.78 (s, 3H, methyl).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 155.7 (C_q, OCO_2), 131.7 (CH, allylic), 118.9 (CH_2, olefinic), 68.9 (CH_2, allylic), 54.9 (CH_3, OMe).

GC-MS (MK_STANDARD): t_R: 3.59 min; m/z: 116.0 (1.8 %, MP) [M], 101.0 (4.5 %) [M* - Me], 57.0 (100 %, BP) [H_2C=CH-CH_2-O*].

6.2.2.5 Allyl 4-methylbenzenesulfonate



1c

$C_{10}H_{12}O_3S$

[212.26]

1.75 g (30.1 mmol, 1.0 eq) allyl alcohol and 6.09 g (31.9 mmol, 1.0 eq) *p*-toluene sulfonylchloride were dissolved in 40 mL diethyl ether (abs.) in a 250 mL two necked round bottom flask and cooled to – 18 °C via a sodium chloride ice bath. 3.91 g (97.8 mmol, 3.2 eq) sodium hydroxide were added and the reaction mixture was stirred overnight. The suspension was poured onto 150 mL iced water and extracted with diethyl ether (1 × 50 mL). The organic layer was washed with H_2O (2 × 50 mL), dried over sodium sulfate, filtered and concentrated via vacuo.

Yield: 5.58 g (26.3 mmol, 87 %) colorless liquid.

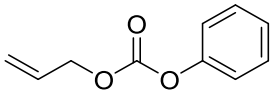
R_f: 0.29 (cyclohexane/ethyl acetate 10+1).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, $^3J_{HH}$ = 8.2 Hz, 1H, aromatic), 7.34 (d, $^3J_{HH}$ = 8.0 Hz, 1H, aromatic), 5.90-5.72 (m, 1H, allylic), 5.38-5.19 (m, 2H, allylic), 4.53 (d, $^3J_{HH}$ = 5.9 Hz, 2 H, allylic), 2.45 (s, 1H, aromatic methyl).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 144.9 (C_q, C – aromatic), 133.4 (C_q, S – aromatic), 130.4 (2 × CH, *meta* aromatic), 123.0 (2 × CH, *ortho* aromatic), 128.0 (CH, allylic), 120.4 (CH_2, olefinic), 70.9 (CH_2, allylic), 21.8 (CH_3, next to aryl).

GC-MS (MK_STANDARD): t_R: 3.59 min; m/z: 212.1 (3.6 %, MP) [M], 155.0 (33.6 %) [M* - allyl-O], 91.1 (100 %, BP) [benzene*].

6.2.2.6 Allyl phenyl carbonate



1g

$C_{10}H_{10}O_3$

[178.19]

In a 500 mL two necked round bottom flask 5 mL (73.18 mmol, 1.0 eq) allyl aclohol and 9 mL (109.73 mmol, 1.5 eq) triethylamine were dissolved in 100 mL dichloromethane (abs.). A solution of 14 mL (111.13 mmol, 1.5 eq) phenyl chloroformate in 20 ml dichloromethane was added slowly over a dropping funnel to the ice bath cooled solution. The reaction was stirred overnight at r.t.. The yellowish suspension was washed with H_2O (3×100 mL) and saturated aqueous sodium bicarbonate (2×100 mL). The organic layer was dried over sodium sulfate, filtered and then purified via vacuum distillation.

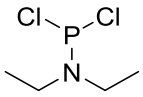
Yield: 10.7 g (60.05 mmol, 82 %) colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.50-7.40 (m, 2H, aromatic), 7.35-7.20 (m, 3H, aromatic), 6.15-5.98 (m, 1H, allylic), 5.55-5.35 (m, 2H, allylic), 4.83-4.76 (m, 2H, allylic).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 153.6 (C_q, carbonate), 151.2 (C_q, O-aromatic), 131.3 (CH, allylic), 129.6 (CH, *m*-aromatic), 126.2 (CH, *p*-aromatic), 121.1 (CH, *o*-aromatic), 119.6 (CH_2, olefin), 69.2 (CH_2, allylic).

GC-MS (MK_STANDARD): t_R: 5.08 min; m/z: 178.1 (5.5 %, MP) [M], 77.1 (91.8 %) [benzene*], 65.1 (100 %, BP).

6.2.2.7 *N,N*-Diethyl-phosphoramidous dichloride



119

$C_4H_{10}NPCl_2$

[174.01]

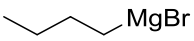
In a 500 mL three necked flask 76 mL (731.7 mmol, 1.0 eq) freshly distilled diethyl amine were dissolved in 200 mL THF (abs.) and cooled to -78 °C via a CO_2(s) acetone cooling bath. Then 64 mL (731.7 mmol, 1.0 eq) freshly distilled phosphorous trichloride in 60 mL THF (abs.) were added slowly via a dropping funnel over a period of 45 min at -75 °C. The white suspension was filtered through Celite via a fritted funnel after stirring for 16 h at r.t. and washed with absolute diethyl ether (5 × 40 mL) under inert conditions. The yellowish filtrate was concentrated in vacuo. The product was purified via vacuum distillation (45 °C / 1.2 mbar).

Yied: 53.16 g (305.5 mmol, 42 %) colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.43-3.25 (m, 4H, 2 × CH_2), 1.19 (t, $^3J_{HH}$ = 7.1 Hz, 6H, 2 × CH_3).

^{31}P-NMR (122 MHz, $CDCl_3$): δ = 162.4 (s).

6.2.2.8 n-Butylmagnesium bromide



120

C_4H_9MgBr

[161.32]

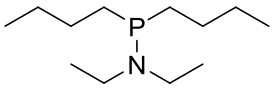
Magnesium turnings were weighed into a 500 mL three necked round bottom flask adapted with a dropping funnel, a reflux condenser and a gas valve. It was then evacuated and dried while stirring. Thereafter a tip of a spoon with iodine was added. After gaseous iodine had emerged 60 mL of diethyl ether (abs.) were added. 10 mL (92.98 mmol) n-butyl bromide were added slowly over a dropping funnel at r. t.. After decay of the exothermic reaction, the mixture was stirred for 3 h at 40 °C and overnight at r.t.. The magnesium left overs were filtered off via a fritted funnel and washed with additional diethyl ether (abs.). A titration of the filtrate according to procedure 6.2.2.9 was performed to obtain the concentration of the n-butylmagnesium bromide.

6.2.2.9 Titration of Grignard-reagent

2-5 mg *N*-phenyl-4-phenylazoaniline were dissolved in 2.0 mL stock solution (200.0 ml toluene (abs.) and 20.0 mL 2-butanol (abs.)) in a Schlenk flask. The calculated concentration of this stock solution

(c = 0.99 M) was used as reference for the titration of n-butyl magnesiumbromide. The n-butyl magnesiumbromide solution was added dropwise under inert conditions. The equivalence point was indicated by a color change from yellow-orange to brownish-red. This procedure was performed three times.

6.2.2.10 Dibutyl(diethylamino)phosphine



124

$C_{12}H_{28}NP$

[217.34]

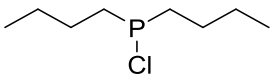
In a 1 L three necked round bottom flask equipped with a dropping funnel and a gas valve 9.01 g (103.6 mmol, 1.0 eq) *N*,*N*-diethyl-phosphoramidous dichloride were dissolved in 200 mL diethyl ether (abs.) and cooled to 0 °C. 37 mL of a 2.87 M n-butylmagnesium bromide solution were added over a period of 30 min. at 0 °C via a dropping funnel. The reaction was then stirred over night at r.t.. The suspension was filtered through a pad of dried Celite® in a fritted funnel and washed with absolute n-heptane (3 × 20 mL) and absolute diethyl ether (3 × 20 mL). The filtrate was concentrated via a liq. N_2 cooling trap and the product was purified via vacuum distillation (56 °C / 0.52 mbar).

Yield: 7.11 g (32.7 mmol, 31 %) colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.90 (m, 4H, 2 × CH_2 next to N), 1.55 (m, 2H, aliphatic), 1.37 (m, 8H, aliphatic), 1.18 (m, 2H, aliphatic), 1.00 (t, $^{3}J_{HH}$ = 7.1 Hz, 6H, 2 × CH_3), 0.89 (m, 6H, 2 × CH_3).

^{31}P-NMR (122 MHz, $CDCl_3$): δ = 53.9 (s).

6.2.2.11 Dibutylchlorophosphine



121

$C_8H_{18}PCl$

[180.66]

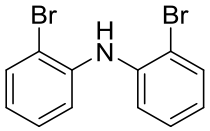
In a 10 mL round bottom flask equipped with a vacuum adapter 2.7 mL (30.83 mmol, 1.0 eq) phosphorous trichloride were cooled to 0 °C. 6.7 g (30.83 mmol, 1.0 eq) dibutyl(diethylamino)phosphine were added slowly at 0 °C via syringe. After stirring at 0 °C for 30 min the reaction was allowed to warm to r.t. and stirred for additional 90 min. The orange suspension was vacuum distilled (54 °C / 2.5 mbar).

Yield: 5.20 g (29.90 mmol, 97 %) colorless liquid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.84 (m, 4H, 2 × CH_2), 1.50 (m, 8H, 4 × CH_2), 0.93 (t, $^{3}J_{HH}$ = 7.2 Hz).

^{31}P-NMR (122 MHz, $CDCl_3$): δ = 113.6 (s).

6.2.2.12 Bis(2-bromophenyl)amine



127

$C_{12}H_9NBr_2$

[327.02]

In a 80 mL Schlenk tube 8.1 mg (8.8 µmol, 0.025 eq) Pd_2dba_3 and 9.8 mg (17.7 µmol, 0.050) dppf were dissolved in 12 mL toluene (abs.). After stirring for 5 min at r.t. 1099 mg (3.885 mmol, 1.1 eq) bromo-2-iodobenzene and 610 mg (3.535 mmol, 1.0 eq) 2-bromo-aniline were added. The reaction was then heated to 100 °C and 465 mg (4.8 mmol, 1.4 eq) NaO*t*Bu were added. Then the reaction mixture was stirred at reflux for 4 d. The crude product was concentrated in vacuo, distributed between H_2O (1 × 50 mL) and 50 mL diethyl ether. The organic layer was dried over sodium sulfate, filtered and concentrated in vacuo. The product was purified via column chromatography with cyclohexane.

Yield: 630 mg (1.93 mmol, 55 %) colorless to white prisms.

R_f: 0.37 (cyclohexane).

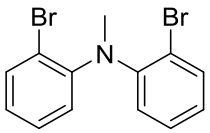
m. p.: 60 °C (61 °C lit.).[91]

GC-MS (MK_STANDARD): t_R: 7.37 min; m/z: 326.9 (30.9 %, MP) [M], 249.0 (3.6 %) [M* - Br], 167.1 (100%, BP) [M* - Ph-Br].

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.65-7.53 (m, 2H, *ortho* to Br), 7.34-7.16 (m, 4H, *meta* to Br), 6.90-6.80 (m, 2H, *para* to Br), 6.45 (s, 1H, NH).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 140.2 (C_q, N-C), 133.4 (CH, *ortho* to Br), 128.2 (CH, *para* to Br), 122.7 (CH, *para* to N-H), 118.1 (CH, *ortho* to N-H), 114.4 (C_q, Br-C).

6.2.2.13 2-Bromo-*N*-(2-bromophenyl)-*N*-methylaniline



128

$C_{13}H_{10}NBr_2$

[341.05]

In a 15 mL Schlenk tube 300 mg (0.917 mmol, 1.0 eq) bis(2-bromophenyl)amine were dissolved in 2 mL THF (abs.) and cooled to 0 °C. 55 mg (1.376 mmol, 1.5 eq) of a 60 w% sodium hydride dispersion in mineral oil were added slowly. After stirring for 30 min at 0 °C 85.5 µL (1.376 mmol, 1.5 eq) iodomethane were added at 0 °C. The reaction mixture is then stirred for another 3 h at r.t.. Then 10 mL H_2O were added and the reaction mixture was extracted with diethyl ether (5 × 5 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was recrystallized from cold cyclohexane.

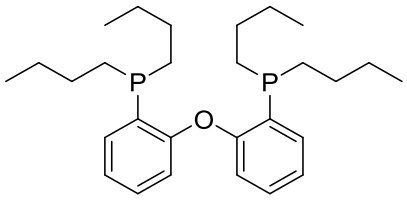
Yield: 250 mg (0.734 mmol, 80 %) white crystals.

m.p.: 98-105 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.56 (dd, $^3J_{HH}$ = 7.9 Hz, 2H, *ortho* to Br), 7.25 (m, 2H, *para* to Br), 6.97 (m, 4H, *meta* to Br), 3.23 (s, 3H, methyl).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 148.8 (C_q, N-C), 134.5 (CH, *ortho* to Br), 128.3 (CH, *para* to Br), 124.9 (CH, *para* to N), 124.99 (CH, *ortho* to N), 120.5 (C_q, *C*-Br), 41.5 (CH_3).

6.2.2.14 (Oxybis(2,1-phenylene))bis(dibutylphosphine)



123

$C_{28}H_{44}OP_2$

[458.61]

In an 80 mL *Schlenk* flask 621 µL (3.91 mmol, 1.0 eq) diphenylether and 1174 µL (7.83 mmol, 2.0 eq) tetramethylethylene diamine were dissolved in 16 mL n-pentane (abs.). After cooling to 0 °C 3.37 mL (7.83 mmol, 2.0 eq) of a 2.32 M n-butyl lithium in hexane solution were added slowly. The reaction mixture was allowed to warm to r.t. and stirred for 5 h then cooled again in an ice bath. 1.5 mL (7.83 mmol, 2.0 eq) dibutylchlorophosphine were added dropwise to the reaction mixture at 0 °C. The

reaction mixture was then stirred for 2 h at r.t.. The reaction was quenched with 10 mL degassed H_2O, extracted with diethyl ether (abs.) (2 × 10 mL) and washed with 10 mL degassed brine (1 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, washed with diethyl ether under inert conditions and concentrated under reduced pressure. The product was purified via inert column chromatography with n-pentane (abs.) as solvent.

Yield: 502 mg (1.09 mmol, 28 %) white viscous liquid.

R_f: 0.18 (pentane).

^{1}H-NMR (300 MHz, d^6-DMSO): δ = 7.46 (m, 2H, aromatic), 7.30 (m, 2H, aromatic), 7.14 (t, $^3J_{HH}$ = 7.3 Hz, 2H, aromatic), 6.65 (dd, $^3J_{HH}$ = 8.0, 2.5 Hz, 2H, aromatic), 1.78 (m, 8H, CH_2 next to P), 1.31 (m, 16H, CH_2 aliphatic), 0.81 (t, $^3J_{HH}$ = 6.7 Hz, CH_3).

APT-NMR (75.5 MHz, d^6-DMSO): δ = 159.1 (C_q, next to O), 132.4 (CH, *ortho* to P), 129.9 (CH, *para* to P), 129.3 (C_q, next to P), 123.5 (CH, *para* to O), 117.5 (CH, *ortho* to O), 27.7 (CH_2, aliphatic), 24.9 (CH_2, aliphatic), 23.7 (CH_2, aliphatic), 13.7 (CH_3, aliphatic).

^{31}P-NMR (122 MHz, $CDCl_3$): δ = -31.3 (s).

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8. Abbreviation List

8.1 Analytical methods

^{1}H-NMR	proton NMR
^{13}C-NMR	carbon NMR
^{31}P-NMR	phosphorous NMR
APT	Attached Proton Test
CH_{Ar}	aromatic proton
C_q	quarternary carbon
d	doublet
dd	doublet of doublet
decomp.	decomposition
dt	doublet of triplet
e.e.	enantiomeric excess
ESI	electrospray ionization
eV	electron volt
GC	gas chromatography
GC-MS	gas chromatography mass spectroscopy
HPLC-MS	high performance liquid chromatography mass spectroscopy
Hz	Hertz
ITC	isothermal titration calorimetry
J	signal multiplicity
m	multiplet
m/*z*	mass/charge-ratio
M^+	molecule peak
MHz	megahertz
mp	melting point
NMR	nuclear magnetic resonance
ppm	parts per million
q	quadruplet
R_f	retention factor
s	singlet
t	triplet
td	triplet of doublet
TLC	thin layer chromatography

t_R	retention time
UV	ultraviolet
δ	chemical shift

8.2 Chemical Abbreviations

Ac	acetyl
acac	acetyl acetonate
AcOH	acetic acid
AgOTs	silver *p*-toluenesulfonate
$AgSbF_6$	silver hexafluoroantimonate^V
AllylOTs	allyl *p*-toluenesulfonate
BINAP	*rac*-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Biphos	2,2'-bis(diphenylphosphanyl)-1,1'-biphenyl
Bn	benzyl
C	carbon
C-*C*	carbon-carbon
CAM	cerium ammonium molybdate
cod	1,5-cyclooctadiene
Cp	cyclopentadiene
Cp*	penta methyl cyclopentadiene
Cy	cyclohexyl
dba	dibenzylideneacetone
DBU	1,8-Diazabicycloundec-7-ene
DBN	1,5-Diazabicyclonon-5-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DIPEA	*N*,*N*-diisopropylethylamine
DMAP	*N*,*N*-dimethyl-4-amino pyridine
DME	1,2-dimethoxy ethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DMSO-d_6	deuterated dimethylsulfoxide
DIOP	2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
DPEPhos	bis(2-diphenylphosphinophenyl)ether
dpp-benzene	1,2-bis(diphenylphosphanyl)benzene

dppm	1,1-bis(diphenylphosphino)methane
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
dppb	1,4-bis(diphenylphosphino)butane
dcyb	1,4-bis(dicyclohexylphosphino)butane
dpp-pentane	1,5-bis(diphenylphosphino)pentane
dpp-hexane	1,6-bis(diphenylphosphino)hexane
dppf	1,1'-bis(diphenylphosphino)ferrocene
E	opposite (from entgegen, German)
EDG	electron donating group
eq	equivalent
Et	ethyl
Et_2O	diethyl ether
Et_3N	triethylamine
EtOAc	ethyl acetate
EtOH	ethanol
$Eu(fod)_3$	europium^{III}-tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate)
EWG	electron withdrawing group
Fu	2-furyl
η^3-C_3H_5	mesomeric allyl
HOMO	highest occupied molecular orbital
$In(OTf)_3$	indium(III) trifluorosulfonate
iPr	*iso*-propyl
iPrOH	*iso*-propanol
KO^tBu	potassium *tert*-butoxide
L	ligand
LG	leaving group
LUMO	lowest unoccupied molecular orbital
m	*meta*
Me	methyl
MeI	iodomethane
MeOH	methanol
N	nitrogen
nbd	bicyclo(2.2.1)hepta-2,5-dien (norbornadien)
n-BuLi	n-butyllithium
NMP	N-Methyl-2-pyrrolidone
Nu^-	nucleophile

O	oxygen
o	*ortho*
O-allyl	oxygen allylated
o -allyl	*ortho* allylted
$^{-}$OMe	methanolate
$^{-}$OMs	methylsulfonic anion
$^{-}$OTs	*p*-toluenesulfonic anion
P1-t-Bu	*N'''*-tert-butyl-*N,N,N',N',N'',N''*-hexamethylphosphorimidic triamide
p	*para*
p-allyl	*para* allylated
PBu_3	tri-n-butylphosphine
pH	logarithm of the reciprocal of the hydrogen ion activity
PivOH	pivlic acid
$P(OPh)_3$	triphenylphosphite
PPh_3	triphenylphosphine
P-tBu_3	tri(*tert*-butyl)phosphine
PTSA	*p*-toluenesulfonic acid
σ*	occupied sigma orbital
S_N1	nucleophilic substitution first order
S_N2	nucleophilic substitution second order
S_N2'	nucleophilic substitution second order at adjacent double bond
TBAOAc	tetrabutylammonium acetate
TBAOH	tetrabutylammonium hydroxide
tBu	tertiary butyl
TFA	trifluoroacetic acid
THF	tetrahydrofurane
TMEDA	*N,N,N,N*-tetramethyl ethyl-1,2-diamine
TMND	*N,N,N,N*-tetramethyl naphthalene-1,8-diamine
TPP	triphenylphosphine
TPPTS	3,3′,3″-Phosphanetriyltris(benzenesulfonic acid) trisodium salt
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
Z	together (from zusammen, German)
$Zn(OTf)_2$	$zink^{II}$ trifluorosulfonate

8.3 Others

(v:v)	volume/volume
(w:w)	weight/weight
°C	Celsius

Å	Ångström
β	Tolman angle
C_{Ar}-Br	aromatic carbon-bromine bond
cat.	catalytic
conc.	concentrated
d	day/-s
E	potential
e. g.	exempli gratia (lat.: for example)
EI	electron impact
eq	equivalents
et al.	*et alii* (lat.: and co-workers)
f. i.	for instance
g	gram
h	hour/-s
H^+	acidic
K_D	dissoziation constant
L	litre
lit.	literature
m	meter
M	molar (mol/L)
min	minute/-s
mL	milliliter
mm	millimeter
nm	nanometer
nM	nanomolar
pK_a	negative logarithmic acid dissociation constant
ppm	parts per million
quant.	quantitative
rac	racemic
rc	reaction condition
recryst.	recrystallized
r.t.	room temperature
sat.	saturated
TOF	turn over frequency
λ	wavelength
λ_{max}	absorption maximum
µL	microliter

μm	micrometer
μM	micromolar

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