



Palladium–diphosphine complexes as catalysts for allylations with allyl alcohol

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ABSTRACT

Several palladium complexes with bidentate phosphine ligands were tested for their activity in the O-allylation of phenols with allyl alcohol. The use of C₃-bridged bidentate phosphine ligands results in very high selectivity for O-allylation. The reactions do not require stoichiometric amounts of additives to control the chemoselectivity. Especially, catalysts with *gem*-dialkyl substituted C₃-bridged bidentate phosphine ligands perform very well, resulting in a (equilibrium) conversion of ~50% of phenol with a selectivity of 99% for O-allylation. The use of diallyl ether as the allylating agent results in a significant increase in phenol conversion while maintaining high selectivity for O-allylation. Apart from Pd(OAc)₂ as catalyst precursor, Pd(dba)₂ was also employed, making it possible to use other types of phosphine or phosphite ligands. With the palladium catalytic system not only phenol, but also aliphatic alcohols can be allylated, as well as aromatic and aliphatic amines.

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1. Introduction

In the context of the development of an environmentally benign catalytic route to epoxy resins, O-allylation of phenols is a highly desirable reaction [1]. Allyl phenyl ethers can be epoxidized to obtain glycidyl ethers, which are currently produced in the epoxy resin industry via the conventional epichlorohydrin route with the co-production of stoichiometric amounts of chloride-containing waste. Allylation reactions of phenols are mostly performed with allylating agents such as allyl chloride or allyl acetate and stoichiometric amounts of base are added to induce selectivity for O-allylation [2,3]. Numerous allylation reactions, generally known as the Tsuji–Trost reaction, using palladium catalysts have been reported [4–6]. Regarding atom efficiency, it would be desirable to use allyl alcohol as the allylating agent. Several palladium systems have been reported to be able to use allyl alcohol as an allylating agent [7–11]. However, in the cases where phenols are used as the substrate, stoichiometric amounts of base are necessary to induce chemoselectivity towards O-allylation, inevitably resulting in inorganic waste [9]. In the absence of base, C-allylation occurs [10], a feature also observed with ruthenium-based systems [12]. We have developed a catalytic system based on ruthenium that catalyzes both O- and C-allylation of phenols; we have shown that the O-allylated products are reversibly formed, while C-allylated products are produced irreversibly [13]. For this ruthenium-based system a large variety of bidentate phosphine ligands has been used [13,14].

Apart from the observation that selectivity of the reaction is time-dependent, the role of the ligand appeared to be of great importance for the activity as well as the selectivity; it was shown that with only minor changes in the ligand-structure dramatic effects on both activity and selectivity were accomplished. Restricted coordination space at the ruthenium center favors the formation of the O-allylated product, which could be achieved using ligands that either have a large bite angle [13] and/or form kinetically stable chelates [14]. For palladium however, the use of Pd(OAc)₂ for the allylation of phenol-type substrates has only been reported with monodentate phosphine ligands [8–10].

In this paper a palladium system with a selection of bidentate phosphine ligands is reported (Fig. 1); the activity and selectivity for O-allylation as a function of the ligand is discussed.

2. Experimental

2.1. General

All reactions were performed under an argon atmosphere using standard Schlenk techniques. Solvents were dried and distilled using standard procedures and were stored under argon. The phosphine ligands with phenyl substituents (dppm, dppe, dppp, dppb and PPh₃) and triphenylphosphite were commercially available and used as received. Pd(OAc)₂ and Pd(dba)₂ were purchased from Strem Chemicals. The ligands dppdmp [15] and dppdep [16] were earlier described in literature. The ligands *o*-MeOdppp [17], *o*-MeOdppdmp [18], *p*-MeOdppp [19], *o*-Medppp [20] and trisani-sylphosphine [21] were a gift from Shell Global Solutions and used as received. Allyl-1,1-*d*₂ alcohol was synthesized as reported [22].

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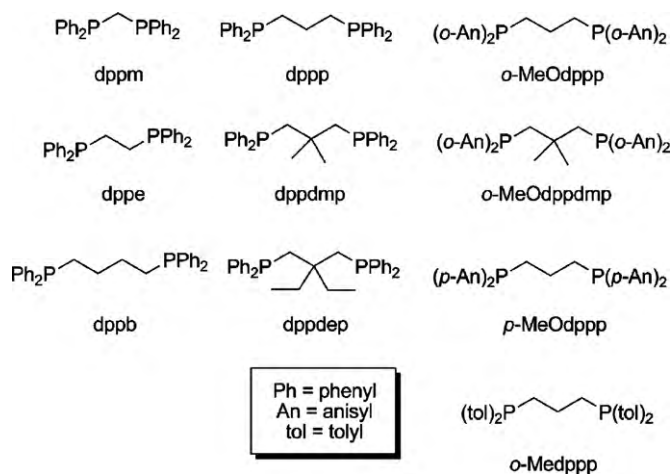


Fig. 1. Overview of the bidentate phosphine ligands employed in this study and their abbreviations.

^1H NMR spectra (300 MHz), ^{13}C NMR (75.5 MHz) and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra (121.4 MHz) were measured on a Bruker DPX-300 spectrometer. Chemical shifts are reported in ppm. The spectra were taken at room temperature. Mass spectrometry was performed on a Finnigan MAT 900 spectrometer equipped with an electrospray interface.

2.2. General procedure for catalytic reactions with $\text{Pd}(\text{OAc})_2$

5 mmol of 4-*tert*-butylphenol (or an aliphatic alcohol or an amine), 5 μmol of $\text{Pd}(\text{OAc})_2$ and 20 μmol of bidentate phosphine ligand (or 40 μmol of PPh_3) were charged into the reaction vessel which was then flushed with argon. Degassed and dried toluene or *n*-heptane (5 ml) was added and the mixture was stirred for 5 min. The allyl donor (10 mmol) was added and the reaction mixture was heated to 100 °C. Samples were taken at certain time intervals and were analyzed by gas chromatography.

The spectroscopic data of the compounds **3–6** [13], allyl 1-octyl ether, allyl cyclohexyl ether [23], *N*-allylaniline, *N,N*-diallylaniline, *N*-allyloctan-1-amine and *N,N*-diallyloctan-1-amine [24] corresponded with the data reported in literature. Spectroscopic data for allyl-1,1- d_2 4-*tert*-butylphenyl ether and allyl-3,3- d_2 4-*tert*-butylphenyl ether (13 + 14); mixture of products: ^1H NMR (CDCl_3): δ 7.28 (d, 4H, $J=9$ Hz, ArH), 6.85 (d, 4H, $J=9$ Hz, ArH), 6.05–6.02 (m, 2H, H-allyl), 5.39 (dd, 1H, $J=2$ and 17 Hz, H-allyl), 5.27 (dd, 1H, 2 and 9 Hz, H-allyl), 4.51 (d, 1H, $J=6$ Hz, OCH_2), 1.28 (s, 9H, tBu). ^{13}C NMR

(CDCl_3): δ 133.5 (=CH), 129.2 (ArH), 117.6 (=CH₂), 114.2 (ArH), 68.8 (OCH_2), 31.5 (tBu). MS (ESI) $m/z=193.37$ [$\text{M}+\text{H}$]⁺

2.3. General procedure for catalytic reactions with $\text{Pd}(\text{dba})_2$

5 mmol of 4-*tert*-butylphenol, 5 μmol of $\text{Pd}(\text{dba})_2$ and 20 μmol of bidentate phosphine ligand (or 40 μmol of monodentate ligand) were charged into the reaction vessel which was then flushed with argon. Degassed and dried toluene (5 ml) was added and the mixture was stirred for 5 min. Allyl alcohol (10 mmol) was added and the reaction mixture was heated to 100 °C. Samples were taken at certain time intervals and analyzed by gas chromatography.

2.4. Procedure for mercury test

The general procedure for catalytic reactions with $\text{Pd}(\text{OAc})_2$ was followed with the difference that after 1 h reaction time, 100 mg (0.5 mmol) of mercury was added. The reaction mixture was stirred vigorously and the reaction was continued at a temperature of 100 °C. Stirring was temporarily halted while taking samples to prevent sampling of mercury droplets.

3. Results and discussion

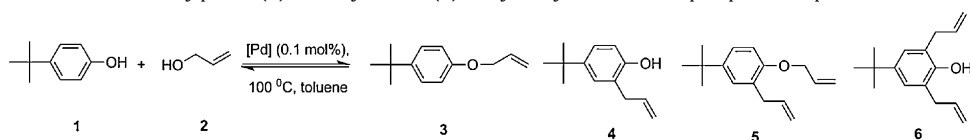
3.1. Catalysis with $\text{Pd}(\text{OAc})_2$ as catalyst precursor

The palladium precatalysts were formed *in situ* by addition of a bidentate phosphine ligand to $\text{Pd}(\text{OAc})_2$. This results in the initial formation of the species $[\text{Pd}(\text{II})(\text{OAc})_2(\text{PP})]$, but it has been reported that these complexes can be reduced in the presence of an excess of phosphine ligand to form Pd(0) complexes, acetic anhydride and phosphine oxide [25,26]. This process is slower for bidentate ligands than for monodentate ligands and does not occur without an excess of phosphine ligand. Immediate stabilization of the formed Pd(0) species with ligand or substrate, or subsequent uptake into the catalytic cycle is highly beneficial for the reduction reaction to occur [26]. Surprisingly it was found that the reduction of palladium(II) requires the presence of phosphine ligands, despite the presence of a large excess of allyl alcohol, usually also considered as a reducing agent.

A palladium over diphosphine ligand ratio of 1/4 was found to give optimal activity for the allylation reaction shown in Table 1. The use of $\text{Pd}(\text{OAc})_2$ to bidentate phosphine ratios of 1/2 or 1/1 results in a lower stability of the catalyst; the conversions are significantly lower and precipitation of metallic palladium (plating) is

Table 1

Reaction of 4-*tert*-butylphenol (**1**) with allyl alcohol (**2**) catalyzed by different Pd–diphosphine complexes.^a



| Entry | Pd(OAc) ₂ + PP PP = | Conversion of 1 (%) | | | Selectivity (%) | | | | | | |
|-------|-----------------------------------|----------------------------|-----|-----|-----------------|-----|------------|-----|----------|------------|-----|
| | | 1 h | 3 h | 6 h | 3 | | 4–6 | | 3 | 4–6 | |
| | | | | | 1 h | 3 h | 3 h | 6 h | | 3 h | 6 h |
| 1 | dppm | 2 | 6 | 13 | 100 | 0 | 100 | 0 | 100 | 0 | |
| 2 | dppe | 0 | 0 | 2 | – | – | – | – | 100 | 0 | |
| 3 | dppp | 15 | 20 | 26 | 100 | 0 | 100 | 0 | 100 | 0 | |
| 4 | dppb | 21 | 35 | 53 | 100 | 0 | 87 | 13 | 72 | 28 | |
| 5 | 2 PPh ₃ | 28 | 44 | 56 | 65 | 35 | 29 | 71 | 16 | 84 | |

^a Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/ $\text{Pd}(\text{OAc})_2$ /PP = 1000/2000/1/4, toluene, 100 °C.

Table 2
Reaction of 4-*tert*-butylphenol (**1**) with allyl alcohol (**2**) catalyzed by different Pd–diphosphine complexes starting from Pd(OAc)₂.^a

| Entry | Pd(OAc) ₂ + PP PP = | Solvent | Conversion of 1 (%) | | | Selectivity (%) ^b | | | |
|----------------|-----------------------------------|-------------------|----------------------------|-----|------|------------------------------|------|------------|------------|
| | | | | | | 3 | | 4-6 | |
| | | | 1 h | 6 h | 22 h | 6 h | 22 h | 3 | 4-6 |
| 1 | dppp | Toluene | 15 | 26 | 38 | 100 | 0 | 94 | 6 |
| 2 | dppdmp | Toluene | 16 | 41 | 58 | 99 | 1 | 95 | 5 |
| 3 | dppdep | Toluene | 14 | 38 | 50 | 99 | 1 | 99 | 1 |
| 4 ^c | dppdmp | Toluene | 0 | 0 | 0 | – | – | – | – |
| 5 | dppdmp | <i>n</i> -Heptane | 11 | 31 | 54 | 100 | 0 | 99 | 1 |
| 6 | dppdep | <i>n</i> -Heptane | 9 | 23 | 56 | 99 | 1 | 97 | 3 |
| 7 ^d | dppdep | <i>n</i> -Heptane | 4 | 43 | 80 | 99 | 1 | 85 | 15 |

^a Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/Pd(OAc)₂/PP = 1000/2000/1/4, toluene, 100 °C.

^b For all entries the selectivity after 1 h 100% for **3**.

^c *p*-Toluenesulfonic acid was added (10 eq. on Pd).

^d Diallyl ether was used as the allyl donor (ratio 4-*tert*-butylphenol/diallyl ether = 1/1).

more pronounced. The results of the use of different phosphine ligands with Pd(OAc)₂ in the catalytic allylation of 4-*tert*-butylphenol (**1**) are summarized in Table 1.

The addition of dppm as a bidentate phosphine ligand to Pd(OAc)₂ (entry 1) results in the formation of a selective catalyst for O-allylation of phenol with allyl alcohol, but, the conversion of **1** is relatively low. The solution turned intensely red, indicating the formation of Pd(I) dimers [27,28]. When dppe is used as the ligand (entry 2), the resulting catalytic activity is very low. Formation of [Pd(dppe)(OAc)₂] is slow, due to the relatively high stability of a [Pd(dppe)₂](OAc)₂ intermediate [29]. This phenomenon clearly slows down the formation of the active catalyst. However, when [Pd(dppe)(OAc)₂] is synthesized *ex situ* and used as a catalyst in the presence of three equivalents of dppe (as the fourth equivalent is already present in the complex) to obtain a similar catalytic system as the *in situ* formed catalytic system, activity for allylation remains very low.

Indeed, when the bridge length of the bidentate ligand is increased to a C₃-fragment in dppp (entry 3) the conversion increases, with maintenance of the very high selectivity. Only O-allylation is observed, making this the first Pd-based catalyst that is selective for O-allylation without the need for any stoichiometric additives.

When using the C₄-bridged ligand dppb (entry 4), the conversion of **1** is even higher, but the selectivity for O-allylation is decreased. Finally, the catalyst with the monodentate ligand triphenylphosphine (entry 5) has a low selectivity for the desired O-allyl ether; after 6 h mainly C-allylated products are obtained, in agreement with earlier studies with similar substrates [10].

A dramatic effect on both activity and selectivity is thus observed by simply changing the bridge length of the bidentate ligand. A drying agent is not required and high catalytic activity is observed even with a low catalyst concentration of 0.1 mol% of Pd on **1**. However, the stability of these palladium catalysts is different from the Ru-complexes previously reported by us [13,14]. For the ruthenium-based catalysts high turnover numbers could be achieved when using high substrate over catalyst ratios. For the Pd-based catalysts described here increasing the substrate over catalyst ratio does not lead to significantly higher turnover numbers and a maximum TON of ~800 is reached. During all reactions some plating of palladium metal was visible, which most likely is the major deactivation pathway of the catalyst.

It has been found previously that the use of kinetically stable chelating bidentate phosphine ligands in cationic ruthenium complexes results in very selective O-allylation of phenols with allyl alcohol [14]. Although the selectivity of the palladium system is already high when dppp is used as the ligand, the use of kinetically more stable chelating ligands might aid in further stabilization of the intermediate zerovalent palladium complexes

and in preventing the formation of palladium black. The results of the catalytic reactions using the *gem*-dialkyl ligands are shown in Table 2.

The conversion of **1** by the catalytic system with dppp increases when longer reaction times (22 h) are used (entry 1). For the catalyst with dppdmp (entry 2) as the bidentate phosphine ligand, initial conversion after 1 h is very similar to that of the reaction with dppp as the ligand. This indicates a similar rate constant and thus a comparable activity of these catalysts. Higher conversions after 6 and 22 h are observed for the catalyst with dppdmp, indicating the formation of a more stable catalyst compared to Pd(OAc)₂ with dppp. The use of the *gem*-diethyl substituted phosphine ligand dppdep (entry 3), also leads to higher conversion of **1**. When a yield of about 50% of **3** is obtained, equilibrium is reached and further conversion of **1** into **3** is halted. In contrast to the cationic ruthenium-based system, the addition of a strong acid to the reaction mixture does not increase the rate of the reaction, but actually inhibits the catalyst for allylation (entry 4). When the acid is added after 1 h reaction time, the reactivity of the catalyst is completely halted from that moment on, including conversion of O-allylated products into the thermodynamically favored C-allylated products.

The equilibrium reaction of O-allylation is governed by the amount of water that is soluble in the reaction mixture. The use of the apolar solvent toluene limits the solubility of this water in the reaction mixture and the water forms a separate phase. The more apolar solvent *n*-heptane can also be used as a solvent (entries 5–6); this results in a lower conversion after 1 and 6 h, but after 22 h conversions are very similar to those obtained for the reactions in toluene. Apparently, activation of the catalyst proceeds less efficient in *n*-heptane than in toluene. The use of dppdmp or dppdep in this reaction medium results very similar selectivities for O-allylation after 22 h. Unlike most of the reported studies, which need to remove water from the reaction mixture, a water scavenger is not necessary as in this apolar system the water forms a separate phase. However, complete water removal from the system would probably be beneficial to obtain higher yields of **3** in a batch process and higher conversion per pass in a continuous process. When diallyl ether is used as the allylating agent (entry 7), the conversion of **1** and the yield of **3** after 22 h is indeed increased significantly in agreement with the lower quantity of water produced relative to that using allyl alcohol as allylation agent. However, at high phenol conversion and very long reaction time, C-allylated product **4** is also formed.

3.2. Catalysis with Pd(*dba*)₂ as catalyst precursor

The use of phosphine ligands that are not oxidized easily, such as *o*-anisylphosphines previously used for Pd-catalyzed olefin–carbon monoxide copolymerization [30], or the use of triphenylphos-

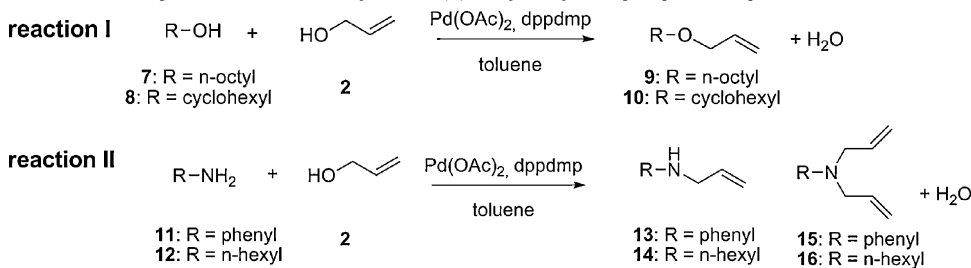
Table 3Reaction of 4-*tert*-butylphenol (**1**) with allyl alcohol (**2**) catalyzed by different Pd–diphosphine complexes starting from Pd(dba)₂.^a

| Entry | Pd(dba) ₂ + PP | Conversion of 1 after 22 h (%) | Selectivity after 22 h (%) | |
|-------|---------------------------------|--|-------------------------------|------------|
| | | | 3 | 4–6 |
| 1 | dppdmp | 49 | 96 | 4 |
| 2 | <i>o</i> -MeOdppp | 10 | 100 | 0 |
| 3 | <i>o</i> -MeOdppdmp | 12 | 100 | 0 |
| 4 | 2 P(<i>o</i> -An) ₃ | 17 | 100 | 0 |
| 5 | <i>p</i> -MeOdppp | 38 | 100 | 0 |
| 6 | <i>o</i> -Medppp | 72 | 71 | 29 |
| 7 | 2 P(OPh) ₃ | 11 | 100 | 0 |

^a Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/Pd(dba)₂/PP = 1000/2000/1/4, toluene, 100 °C.

phite in combination with Pd(OAc)₂ does not yield active catalysts for allylation. In combination with the Pd(0) precursor Pd(dba)₂, (dba = dibenzylideneacetone) however, the use of these ligands does result in an active catalytic system and the results are shown in Table 3.

When dppdmp is added to Pd(dba)₂ (entry 1), a similar conversion with high selectivity is reached compared to the reactions in which Pd(OAc)₂ is used as precursor, indicating that *in situ* the same catalyst is obtained. For *o*-MeOdppp (entry 2) and *o*-MeOdppdmp (entry 3), the anisyl analogues of dppp and dppdmp, only a very low conversion is observed, albeit with high selectivity for **3**. The addition of monodentate tris(*o*-anisyl)phosphine as the ligand (entry 4) results in a slightly higher conversion of **1**, but when compared to its unsubstituted analogue triphenylphosphine in combination with Pd(II) (Table 1; entry 5), the resulting catalyst reaches considerably lower conversion. In order to investigate steric vs. electronic effects of the different ligands on the catalytic results, *p*-MeOdppp was used as ligand (entry 5). In this case the conversion of **1** is considerably higher than for *o*-MeOdppp and comparable to that observed for the combination of Pd(OAc)₂ with dppp as the ligand (Table 1; entry 3); therefore an electronic effect can be excluded. The addition of *o*-Medppp (entry 6) results in a considerably higher conversion than when *o*-MeOdppp is used. The increase of steric bulk around the palladium centre therefore seems not to be the sole reason for the low activity of the catalyst with *o*-anisyl ligands, since an *o*-tolyl group is considered to cause similar steric hindrance around the metal centre compared to an *o*-anisyl group.

Table 4Reaction of nucleophilic substrates with allyl alcohol (**2**) catalyzed by Pd–diphosphine complexes.^a

| Entry | Reaction | Nucleophilic substrate | Reaction time | Conversion of 7–8 or 11–12 (%) | Selectivity in reaction II (%) | |
|----------------|----------|------------------------|---------------|--|--------------------------------|--------------|
| | | | | | 13–14 | 15–16 |
| 1 | I | 1-Octanol | 20 | 94 | – | – |
| 2 | I | Cyclohexanol | 20 | 11 | – | – |
| 3 | II | Aniline | 20 | 100 | 25 | 75 |
| 4 | II | Aniline | 3 | 85 | 77 | 23 |
| 5 ^b | II | Aniline | 3 | 16 | 100 | 0 |
| 6 | II | <i>n</i> -Octylamine | 20 | 81 | 75 | 25 |

^a Reaction conditions: ratio substrate/allyl alcohol/Pd(OAc)₂/dppdmp = 1000/2000/1/4, toluene, 100 °C.^b Ratio substrate/allyl alcohol/Pd(OAc)₂/dppdmp = 1000/500/1/4.

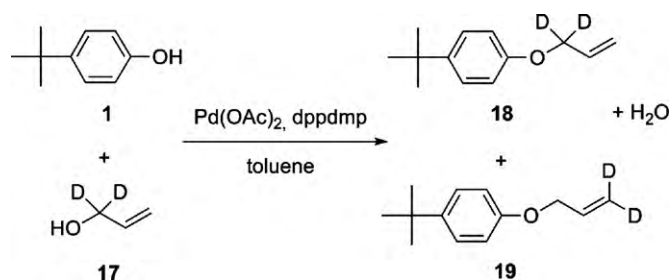
If such steric hindrance would pose a limiting factor on activation, the catalyst with *o*-Medppp would be less active compared to the catalyst with dppp, which is not the case. Most likely coordination of the methoxy group, as already reported for similar complexes [31], hampers activation of allyl alcohol at the palladium centre and thus results in lower catalytic activity. The use of electron-withdrawing triphenylphosphite as the ligand (entry 7) for catalytic allylation also results in very low conversion of **1**. From these results it is clear that addition of unsubstituted phenylphosphine ligands, in particular the bidentate ligands dppp, dppdmp and dppdep, to either a source of Pd(II) or Pd(0) yields the most active and selective catalysts for the allylation of phenols.

3.3. Allylation of other nucleophiles

Apart from 4-*tert*-butylphenol, other nucleophiles have been explored for their reactivity in the presence of the Pd(OAc)₂ with dppdmp and the results are summarized in Table 4. The aliphatic alcohol 1-octanol is efficiently allylated (Table 4; entry 1), while the secondary alcohol cyclohexanol is much less reactive (entry 2); only low conversion towards the allyl ether is observed. Not only alcohols are readily allylated, but also nitrogen-containing substrates such as aniline can be efficiently allylated with allyl alcohol. After 20 h, conversion is complete when an excess of allyl alcohol is used and mainly the *N,N*-bisallylated product is obtained (entry 3). After 3 h the conversion already is quite high, and mostly monoallylated aniline is present (entry 4). The high conversion after only 3 h is illustrative for the much higher reactivity of aniline compared to hydroxyl-containing substrates, which need considerably longer reaction times to achieve similar conversions. By reducing the amount of allyl alcohol, *N*-monoallylated aniline is formed selectively, although the conversion is considerably lower (entry 5). Finally, apart from aromatic amines, also alkylamines can be allylated, as shown for *n*-octylamine, which is less reactive than aniline (entry 6).

3.4. Homogeneous complexes vs. heterogeneous nanoparticles

When using zerovalent transition metal complexes as catalysts, the question arises whether the active catalyst is truly a homogeneous metal complex or whether catalytic activity is caused by the formation of heterogeneous nanoparticles or clusters. Especially in the case of Pd(0) catalysts this should be investigated, since numer-



Scheme 1. Reaction of **1** with deuterated allyl alcohol **12** in the presence of a Pd(PP) catalyst.

ous reactions have been reported to be catalyzed by heterogeneous nanoparticles, such as hydrogenation [32], Heck-reactions [33,34] as well as allylic alkylations [33,34].

The strong effect of the ligand on the activity and selectivity of the palladium catalysts as described above indicates that a homogeneous complex is responsible for catalytic activity, although ligand-dependent nanoparticle formation cannot be excluded. The use of heterogeneous Pd(0) on carbon as the catalyst does not result in conversion of allyl alcohol, giving another indication that a homogeneous complex is the active catalyst. Finally, when mercury is added to the reaction mixture after 1 h, the catalytic system remains active, indicating that truly a homogeneous catalyst is responsible for the observed catalytic activity. The addition of mercury is often used to indicate the presence of active heterogeneous Pd(0) particles, as it leads to the formation of an amalgam with the surface of a heterogeneous catalyst, thereby blocking any catalytic activity [35].

3.5. Mechanistic considerations

The excess of bidentate phosphine ligand (4 equivalents on Pd; 8 equivalents of P on Pd) added to the reaction mixture is necessary to prevent plating of metallic palladium, which leads to loss and therefore deactivation of the catalyst. One equivalent of bidentate phosphine ligand is consumed in the reduction of Pd(II)(OAc)₂ to the active Pd(0) species and one bidentate ligand is present on the Pd centre throughout the catalytic cycle. This means that the remaining two equivalents of bidentate ligand will assist in keeping the Pd(0) species in the homogeneous phase when allyl alcohol, diallyl ether or allyl phenyl ether is not coordinated, forming most likely a tetrakisphosphine palladium(0) compound. Allylation of the phosphine groups can occur, but it has been reported to be a reversible process in the presence of Pd(0) catalysts [36,37]. For the reactions with Pd(dba)₂ as catalyst precursor, a Pd(0) species is already present and consumption of a phosphine ligand for activation does not take place. The phosphine ligands replace the dba ligands, and one phosphine ligand then needs to be replaced by allyl alcohol to form the active Pd(0) catalyst.

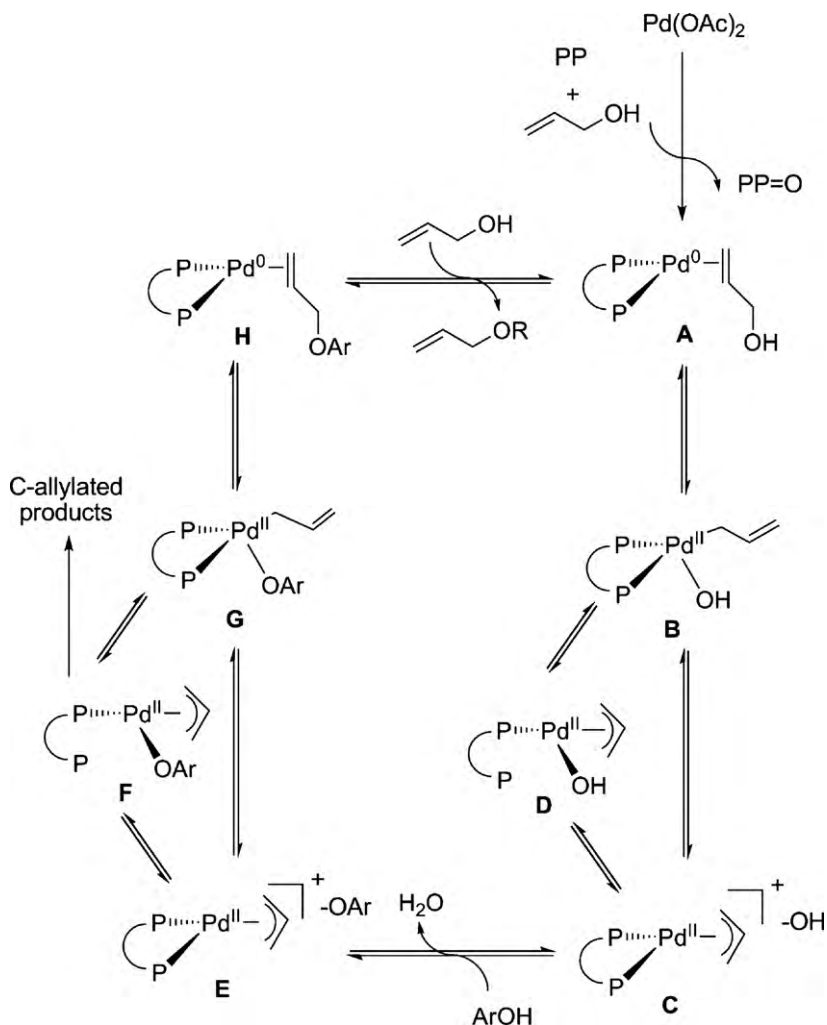
Several mechanisms have been proposed for allylation reactions with allyl alcohol as the allylating agent [7–9]. We propose the formation of an initial Pd(II)(σ-allyl) species immediately after oxidative addition of allyl alcohol, which rapidly isomerises to a π-allyl species with either phosphine or anion dissociation to maintain a stable 16 e Pd(II) species, depending on the chelate stability of the bidentate phosphine ligand. It has been reported that σ-allyl species are indeed formed in the presence of phosphines and coordinating anions [37]. In order to investigate if a π-allyl species is present at some point in the catalytic cycle, the reaction of **1** was performed with allyl-1,1-d₂ alcohol **17** (Scheme 1). This resulted in an approximate 1/1 mixture of allyl-1,1-d₂ 4-*tert*-butylphenyl ether and allyl-3,3-d₂ 4-*tert*-butylphenyl ether (Scheme 1; products **18** and **19**). The observation of scrambling

in formation of the deuterated allyl products indicates that a metal π-allyl species must be present somewhere in the catalytic cycle. The dissociation of a phosphine moiety is also believed to play a key role in the mechanism: a strong ligand-structure effect is observed and especially the use of phosphine ligands that do not form kinetically stable chelates on Pd(II), in this case dppb and monodentate triphenylphosphine, results in lower selectivity for O-allylation. In analogy with the Ru-based catalytic system previously reported [13,14], it is proposed that (at least partial) dissociation of one phosphine moiety of the diphosphine is needed to accommodate the transition state for intramolecular attack of O–CH moiety of the phenolate by the allyl fragment, and thus for C-allylation to occur. The proposed catalytic cycle is shown in Scheme 2.

After formation of the Pd(0) species by means of phosphine oxidation, allyl alcohol coordinates to form species **A**. It is thought that despite the use of excess of (di-)phosphine over Pd, the active organo-Pd species will contain one chelating di-phosphine ligand. Although bis-(bidentate phosphine) Pd(0) complexes will certainly exist as resting states, the pseudo zero-order kinetics in ligand concentration suggests that in the applied ligand to Pd ratio of 1–4 and large excess of the allylic substrate, one diphosphine is easily displaced by the allylic substrate, thus reflecting the relatively high “back donation” binding energy of olefin (relative to that of a phosphine moiety) to Pd(0) species. Dissociation of the first diphosphine ligand is expected to be much less energy demanding than dissociation of the single remaining diphosphine ligand at Pd.

Oxidative addition takes place to initially form the σ-allyl Pd(II) species **B**, which is in equilibrium with the isomeric π-allyl intermediates **C** and **D**. Due to exchange of the anion via an acid–base reaction, the phenolate Pd(II) species **E**, **F** and **G** are formed. The reductive elimination towards O-allylated products is believed to take place from intermediate **G**, in agreement with the Tsuji–Trost mechanism, in which it is proposed that hard nucleophiles, such as phenolate, coordinate to the metal centre prior to reductive elimination [6]. After this step, an intermediate in which the allyl phenyl ether product is bound to Pd(0), (**H**) is formed. As indicated, C-allylated products are most likely formed via a (mono)phosphine dissociation step (**F**). Finally, the product is replaced with a molecule of allyl alcohol to complete the catalytic cycle.

The catalysts with the highest selectivity have ligands with C₃-based bridging groups, being dppp, dppdmp and dppdep, for which stable chelation is expected in the Pd(II) intermediates **E** and **G**. This is most likely caused by the fact that the natural bite angle of these ligands is close to 90°, which is also the optimal angle required for cis-coordination in a square-planar Pd(II) complex, making the chelate ring free of strain and relatively stable under the reaction conditions. The introduction of alkyl substituents at C₂ of the C₃-bridging group of the ligand is less important for selectivity, as the unsubstituted dppp ligand already gives highly selective O-allylation. Note, however that bulkier di-Et C₂-backbone substituents yield a small but measurably higher selectivity for O-allylation. However, more distinctly, the stability of the complex improves by the use of *gem*-dialkyl substituted ligands. Deactivation via plating to Pd-black will be related to phosphine dissociation of the ligand and thus due to a more stable chelation, catalyst deactivation is prevented. The ligands which create a large P–Pd–P angle (>90°), such as dppb or two monodentate PPh₃ ligands, result in a catalyst with a relatively low selectivity. Since the P–Pd–P angle deviates from the preferred 90°, chelation of this type of ligands is weaker than that of ligands with C₃-based bridging groups. Intermediate **F** most likely is lower in energy and will be more abundant. C-allylation requires sufficient coordination space on the Pd(II)(allyl) intermediate in order to activate the *ortho*-position of the phenolate-anion and in species **F** this space is provided.



Scheme 2. Proposed mechanism for Pd-catalyzed allylation of phenols.

Addition of acid at any time during the reaction immediately inhibits the allylation reaction. It has been reported that Pd(II)-hydride species are formed from a Pd(0) species and *p*-toluenesulfonic acid [38]; this would prevent the catalyst to return to the Pd(0) state, which is the active species.

The nucleophilicity of the alcoholate/phenolate formed plays an important role in the reactivity of substrates with hydroxyl groups. This is illustrated by the large increase in conversion observed when *4-tert*-butylphenol is replaced with 1-octanol. When instead of *4-tert*-butylphenol, a more acidic phenol is used, such as *p*-nitrophenol or pentafluorophenol, conversion is not observed due to the low nucleophilicity of the formed phenolate. A unique feature of the Pd catalysts – distinguishing them from the ruthenium catalysts that we investigated before – is the benefit that stronger nucleophiles, such as primary and secondary amines, can also be efficiently allylated. This again can be seen as a consequence of the strong (back donating) binding energy of the olefinic moiety of allyl alcohol to Pd(0), relative to that of the N-coordination of amines. This allows an easy approach of allyl alcohol to the Pd(0) centre without much competition by the nitrogen compound. In fact, strong nitrogen coordination is thought to be the reason why strongly Lewis acidic cationic Ru catalysts [13,14], are unsuitable for allylation of amines: strong coordination compounds between Ru and the basic amine exist.

4. Conclusions

Pd-phosphine complexes show good catalytic activity in allylation reactions with allyl alcohol as the allylating agent in the absence of additives. Complexes with a chelating phosphine ligand and with C₃-based bridging groups show high selectivity towards O-allylation of phenols. Introduction of *gem*-dialkyl substituents on C2 of the ligand backbone results in an increase of the conversion of the reaction, most likely due to an enhanced stability of the Pd(0) species. The use of diallyl ether as allylating agent results in an increase in the conversion while maintaining the high selectivity for O-allylation. Both Pd(II)(OAc)₂ as well as Pd(0)(dba)₂ can be used as catalyst precursor in combination with phosphine ligands. Catalysts having phosphine ligands with non-substituted phenyl rings show higher activity compared to catalysts with phosphine ligands with *ortho*-methoxy substituted phenyl rings, possibly due to coordination of the methoxy groups. Apart from *4-tert*-butylphenol, also aliphatic alcohols are efficiently allylated, as well as aromatic or aliphatic amines.

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