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# Procedures for and Possible Mechanisms of Pd-Catalyzed Allylations of Primary and Secondary Amines with Allylic Alcohols

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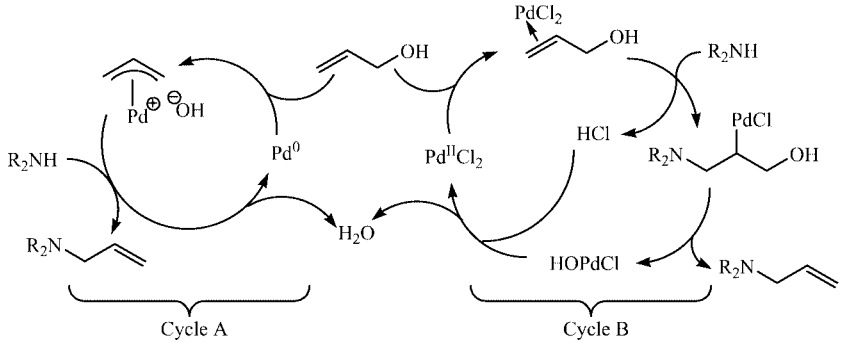
**Keywords:** Allylic alcohol / Allylic amine / Allylation / Palladium / Promoter / Reaction mechanisms

This review describes the different Pd-catalyzed methods that afford allylic amines from intermolecular reactions between allylic alcohols and amines and, with personal comments, the mechanisms that have been proposed. Allylic amines are an important class of compounds, while a wide structural variety of allylic alcohols are commercially available and are abundant in nature. The advantages of the use of allylic alcohols over that of their derivatives such as allylic esters or carbonates are the high atom efficiency and the formation only of water as the by-product.


## Introduction

We have recently covered the Pd-catalyzed reactions of alcohols in a series of reviews.[1–4] A small part of this topic concerned the formation of C–N bonds from reactions between primary and secondary amines and allylic alcohols.[2,5] Such reactions have been explained in terms of the addition of the amine to either $\eta^2$- or $\eta^3$-complexes, as illustrated in an oversimplified way in Scheme 1 (Cycles A and B). Cycle A relates to a Tsuji–Trost-type reaction, while aminopalladation of the double bond followed by β-OH elimination are the key steps in Cycle B. Cycle B involves only $Pd^{II}$ species and has only been ascribed to intramolecular *N*-alkylations catalyzed by palladium chloride.[2,8] Since $Pd^{II}$ salts have Lewis acid properties, it is rather surprising that intramolecular $S_N2'$ substitution of the allylic




Scheme 1. Pd-catalyzed reactions between allyl alcohol and amines via $\eta^2$- or $\eta^3$-complexes.

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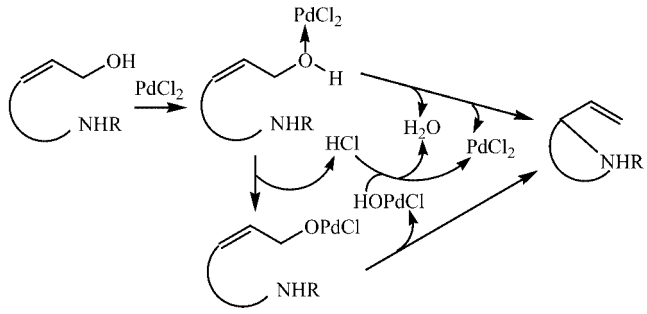
alcohol or of the corresponding allyoxypalladium complex (Scheme 2) has not really been considered. Indeed, such a substitution mediated by acetic acid has been reported.[9]




Scheme 2. Alternative mechanism for the $Pd^{II}$-catalyzed synthesis of azacycles.

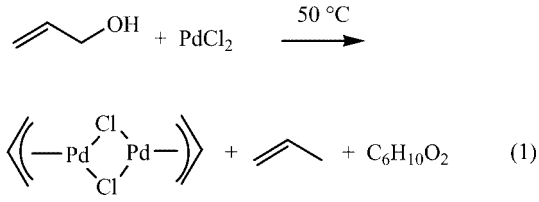
In the context of "Green Chemistry", the main interest of these reactions is their use of allylic alcohols rather than their derivatives, such as allylic esters or carbonates, the high atom efficiency, and the formation only of water as byproduct. Furthermore, allylamines are valuable synthetic intermediates[10] for the preparation of numerous compounds, such as amino acids,[11] piperidines,[12] and azacarbohydrates,[13] and also for reactions involving ring-closing alkene metathesis methodology.[14]

Since the acceptance of our reviews,[15] the synthesis of allylic amines from allylic alcohols via $\eta^3$-allylpalladium intermediates has been the subject of new reports and it seems of interest to highlight this topic in commenting on the reaction mechanisms. Indeed, Cycle A can be induced under various experimental conditions, also giving rise to the proposal of a variety of transient species.

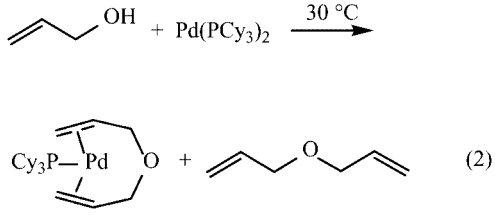
## Stoichiometric Formation of $\eta^3$-Allylpalladium Complexes from Allyl Alcohol

Before description of the catalytic reactions, an overview on the stoichiometric reactions between palladium and allyl alcohol (**1**), and the suggested corresponding reaction mechanisms is useful. Indeed, the results are highly dependent on the nature of the starting palladium species.

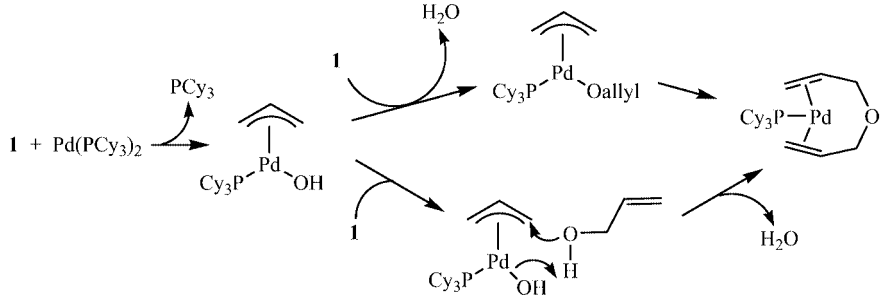
In 1959, Smidt and Hafner isolated $[(\eta^3\text{-allyl})PdCl]_2$,[16,17] propene, and a cyclic alcohol ($C_6H_{10}O_2$, undetermined structure) on treatment of **1** with $PdCl_2$ [Equation (1)]. It was proposed that the overall reaction was a disproportionation reaction with production of allyl anion resulting in the complex.[16]



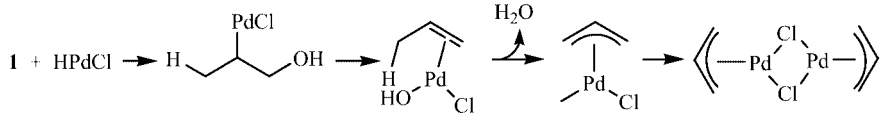

Using $Pd(PCy_3)_2$ as the palladium species, Yamamoto et al. obtained diallyl ether and its coordination product [Equation (2)].[18] According to the authors, the formation of Pd(diallyl ether)($PCy_3$) occurs through a $\eta^3$-allylpalladium complex (i.e., an oxidative addition of **1** to $Pd(PCy_3)_2$, and its reaction with **1** either at the Pd atom or at the $\eta^3$-allyl moiety as shown in Scheme 3).




The cationic complex [PdCl][OTf], formed in situ from $PdCl_2(MeCN)_2$ and AgOTf, afforded $[(\eta^3\text{-allyl})PdCl]_2$ and [5-(allyloxy)-4-methyltetrahydrofuran-2-yl]methanol [Equation (3)].[19] According to Hosokawa et al., the ($\eta^3$-allyl)palladium complex is obtained by addition of HPdCl to the double bond, β-OH elimination, and abstraction of an allylic hydrogen by the OH ligand (Scheme 4). The formation of HPdCl species is not due to a β-H elimination from an

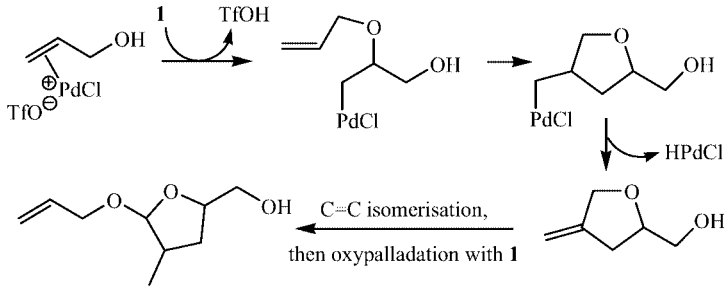



Scheme 3. Postulated reaction mechanisms for the formation of Pd(diallyl ether)($PCy_3$).



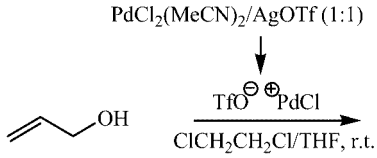

Scheme 4. Hydropalladation of allyl alcohol to afford $[(\eta^3\text{-allyl})PdCl]_2$.

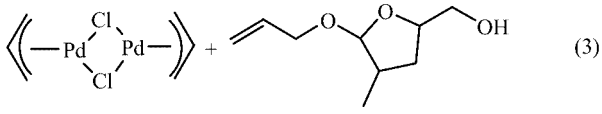
  




Scheme 5. Formation of HPdCl species from allyl alcohol and [PdCl][OTf].

(allyoxy)PdCl intermediate, because no or only a trace of aldehyde was detected.[20] They would arise from the pathways leading to the tetrahydrofuran derivative (Scheme 5).

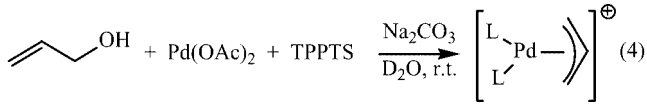



(3)

Ozawa et al. synthesized a cationic ($\eta^3$-allyl)palladium complex from **1** and a hydridopalladium complex obtained in situ by treatment of (DPCB)PdMe(OTf) with $HSiMe_2Ph$ in aqueous dichloromethane (DPCB = 1,2-diphenyl-3,4-bis-[(2,4,6-tris(*tert*-butylphenyl)phosphanylidene]cyclobutene; Scheme 6).[21,22] According to the authors, the allylpalladium complex is obtained through coordination of **1** to the $Pd^{II}$ complex (DPCB)PdH(OTf) rather than to the $Pd^0$ complex (DPCB)Pd. This was followed by proton transfer from the palladium to the hydroxy group, finally producing the cationic allylpalladium complex and water (Scheme 7).

Recently, Oshima et al. reported that treatment of allyl alcohol with $Pd(OAc)_2$/TPPTS in basic $D_2O$ provided a cationic($\eta^3$-allyl)palladium complex [Equation (4)].[23] Theoretical calculations have revealed the importance of hydration of the hydroxy group for the generation of the complex.

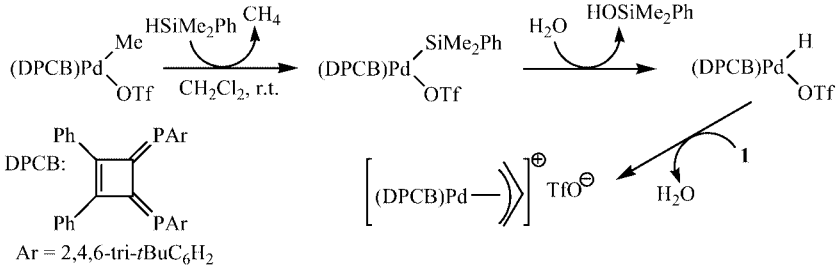



(4)

## $Pd^0$-Catalyzed Allylations in the Absence of Activator

This section is devoted to allylic aminations mediated only by $Pd^0$ species. In many cases the starting Pd species are neutral $Pd^{II}$ compounds, the corresponding active $Pd^0$ species being obtained in situ and stabilized by phosphanes.[24]

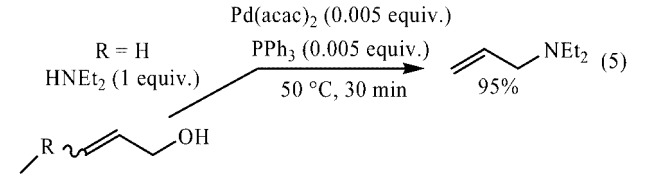
In 1970, Atkins et al. disclosed the formation of C–N bonds in the reactions between diethylamine and allyl alcohol or but-2-ene-1,4-diol in the presence of $Pd(acac)_2$/$PPh_3$ as the catalytic system and in the absence of solvent [Equations (5) and (6)].[25] However, the teams of Bäckvall[26] and Mortreux[27] were unable to reproduce the allylation of diethylamine under such conditions [Equation (7)]. Furthermore, Bergbreiter et al. obtained only a 5% yield for the allylation of piperidine with allyl alcohol in the presence of a heterogeneous polystyrene-bound palladium catalyst at 100 °C under neat conditions.[28]

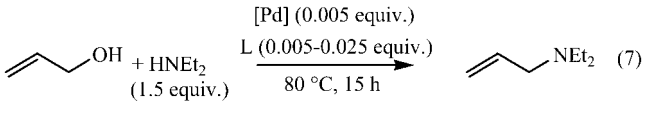



Scheme 6. Ozawa's synthesis of a cationic ($\eta^3$-allyl)palladium complex.


Scheme 7. Proposed mechanism for the formation of Ozawa's complex.

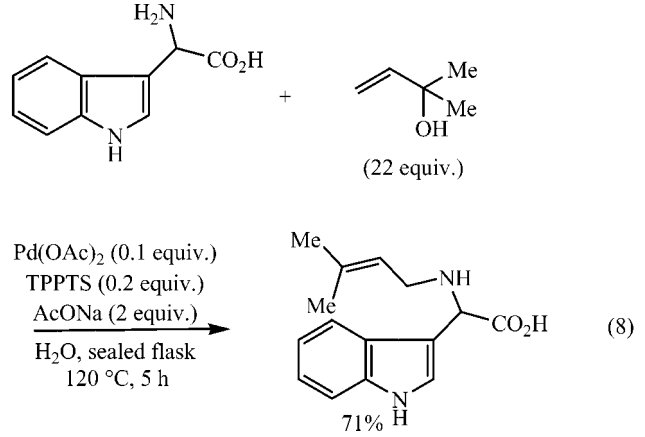
  



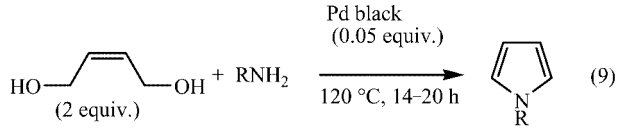




Pd(acac)$_2$, PPh$_3$ (0.005 equiv.), neat: 5%
Pd(OAc)$_2$, PPh$_3$ (0.025 equiv.), MeCN: 8%
Pd(OAc)$_2$, dppb (0.015 equiv.), PhMe: 46%

On modifying Atkins' conditions (i.e., using a different catalytic system and a solvent), Mortreux et al. obtained no more than a 46% yield in the allylation of diethylamine [Equation (7)].[27] Nevertheless, the allylation of diethylamine occurs effectively in the presence either of Pd(OAc)$_2$/diphosphane (dppe or dppb) in propylene glycol[29,30] or of Pd(OAc)$_2$/TPPTS in aqueous pentane at 110 °C.[34] The Pd(OAc)$_2$/TPPTS-catalyzed allylation can even occur in only water as the solvent, as reported for the reactions between tryptophan [Equation (8)][35] or 4-bromotryptophan[35,36] and dimethylallyl alcohol.[37]



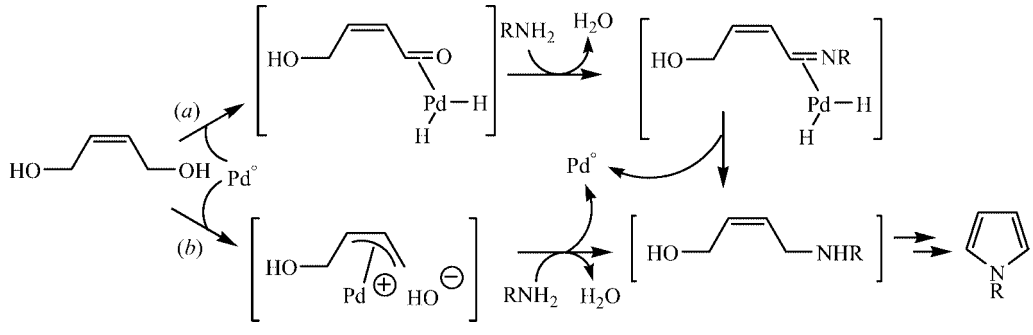

In 1974, Murahashi et al. reported the synthesis of *N*-substituted pyrroles from (*Z*)-but-2-ene-1,4-diol and primary amines in the presence of palladium black as the catalyst at 120 °C in the absence of solvent [Equation (9)].[39] The authors proposed the formation of 4-(alkylamino)but-2-en-1-ols as intermediates, the first step of the cascade reaction being the dehydrogenation of one hydroxy group (Scheme 8, path *a*). Instead of this proposal, we suggest the nucleophilic addition of the amine to a cationic $\eta^3$-allylpalladium complex (Scheme 8, path *b*) as another possibility for the formation of this intermediate.




R = $(CH_2)_2OH$ (87%), $cC_6H_{11}$(89%), $nC_6H_{13}$ (93%), Ph (46%)

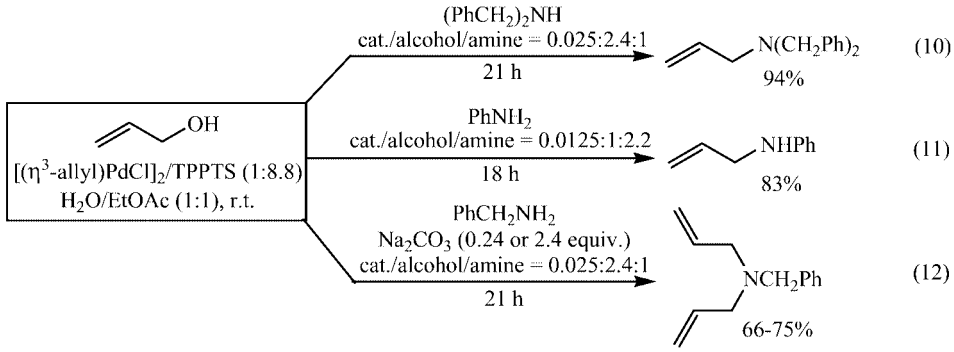
Whereas Pd(PPh$_3$)$_4$[40–42] and the Pd(OAc)$_2$/PPh$_3$[43] or [($\eta^3$-allyl)PdCl]$_2$/PPh$_3$[44] combination are not efficient, either at room temperature in THF[40,42,44] or $CH_2Cl_2$[41] or at reflux in PhH,[43] [($\eta^3$-allyl)PdCl]$_2$/TPPTS can be highly effective, in an aqueous medium, for room temperature C–N bond formation.[23] Under these mild conditions, the reaction is limited to hydrophilic allylic alcohols [Equations (10)–(14)], no reaction being observed with hydrophobic substrates such as cinnamyl alcohol. The requirement for substrates with hydrophilic properties allowed the selective monoamination of (*Z*)-but-2-ene-1,4-diol and 2-(hydroxymethyl)prop-2-en-1-ol with dibenzylamine [Equation (14)], the substitution of one hydroxy group producing a hydrophobic compound.

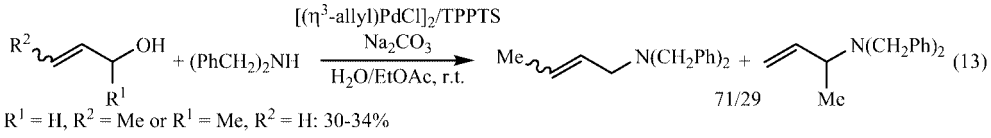
The formation of the same mixture both from but-2-en-1-ol and from but-1-en-3-ol [Equation (13)] indicated the presence of a common $\eta^3$-allyl intermediate. Although usually carried out in the presence of $Na_2CO_3$ [Equations (12)–(14)], the process also takes place under neutral conditions [Equations (10) and (11)], thus excluding the formation of transient allyl hydrogenocarbonate from **1** and $CO_2$ liberated from $Na_2CO_3$. The involvement of allyl acetate through transesterification with EtOAc was excluded from the successful reaction, in $H_2O/Et_2O$, between allyl alcohol and a C-nucleophile. From these observations, Oshima et al. suggested that water activates the substrate through hydration of the hydroxy group and stabilizes the hydroxide ion, resulting in the formation of the cationic $\eta^3$-allylpalla-

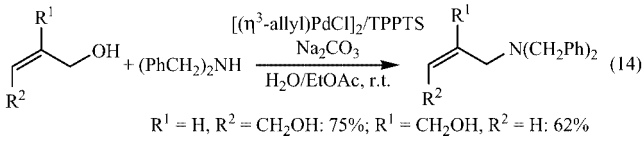


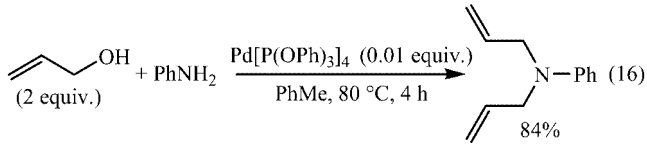

Scheme 8. Two possible pathways for the formation of *N*-substituted pyrroles from (*Z*)-but-2-ene-1,4-diol and primary amines.



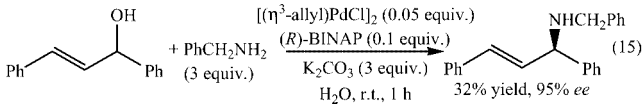




dium complex (Scheme 9). Such a proposal was consolidated by theoretical calculations.[23]

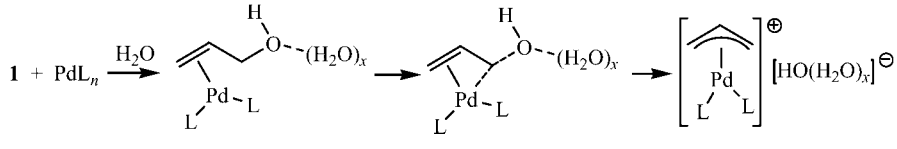
In fact, amination in water can been carried out without a water-soluble phosphane, as reported by Sinou's group, who studied the enantioselective amination of 1,3-diphenylprop-2-en-1-ol under such conditions. A high enantiomeric excess but only a moderate chemical yield were obtained with (*R*)-BINAP as the ligand [Equation (15)].[45]




The effective diallylation of aniline in the presence of small amounts of $Pd[P(OPh)_3]_4$ at 80 °C in toluene [Equation (16)] was mentioned briefly by Ikariya et al.[46]

## $Pd^0$-Catalyzed Allylations in the Presence of Promoters

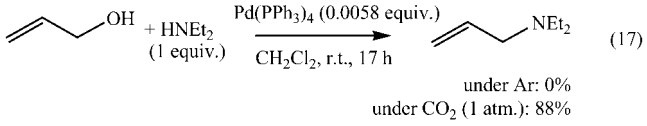
The low lability of the hydroxy group has resulted in testing of various additives to promote the Pd-catalyzed allylation of amines by allylic alcohols. As mentioned in the previous section, even water can have a significant influence on the efficiency of the process (Scheme 9). To the best of our knowledge, the first use of a promoter, namely carbon dioxide, for Pd-catalyzed allylation of amines by allylic alcohols was disclosed in 1992 by Tokito in a Japanese patent.[47] Subsequently, Yamamoto et al. tested various $Pd^0$/phosphane and $Pd^{II}$/phosphane combinations, at room temperature under 1 atm of $CO_2$, in the reaction between **1** and diethylamine in $CH_2Cl_2$. Under these conditions, the best catalyst was $Pd(PPh_3)_4$ and no allylation took place in the absence of $CO_2$ [Equation (17)].[41] The reaction was also efficient in acetone (96% yield) and even in the absence of solvent (70–80% yield). According to the authors, the




Scheme 9. Allyl-OH bond cleavage assisted by hydration.

promotion effect of $CO_2$ is due to the formation of the reactive allyl hydrogen carbonate (i.e., to the conversion of the OH moiety into a more labile leaving group; Scheme 10). Verification of the presence of this adduct was unsuccessful, but the authors showed that the cationic complex $[(\eta^3\text{-}(2\text{-methylallyl})Pd(PMe_3)_2][OCO_2H]$ reacts with diethylamine at room temperature to afford *N*,*N*-diethyl-2-methylprop-2-enylamine.

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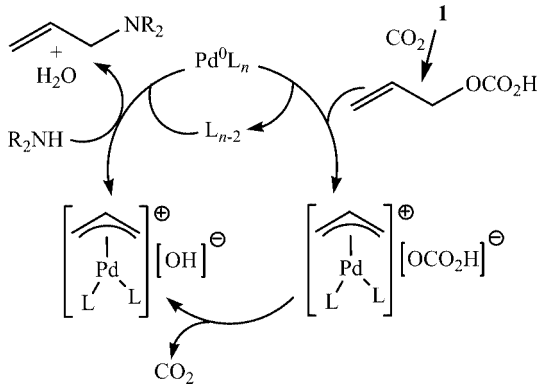
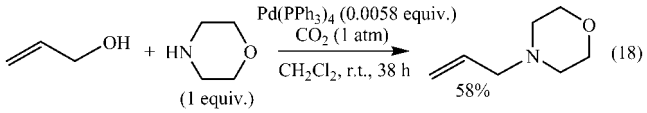


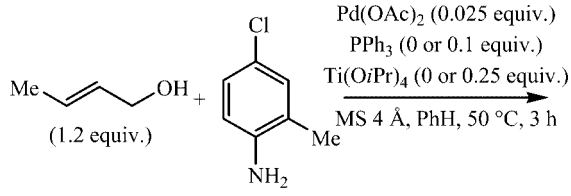

Scheme 10. Proposed role of $CO_2$ as promoter.

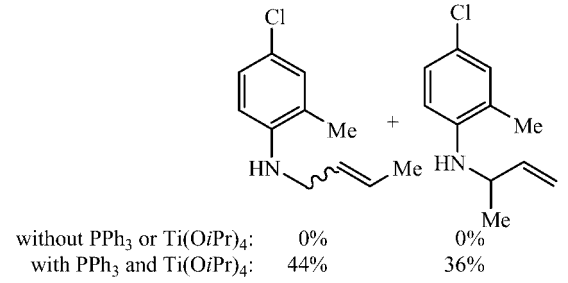
Yamamoto's process is compatible with the use of morpholine [Equation (18)] and other alcohols (2-methylprop-2-en-1-ol, but-2-en-1-ol), but steric hindrance of the reagents resulted in a decrease in the yields.[41]




(18)

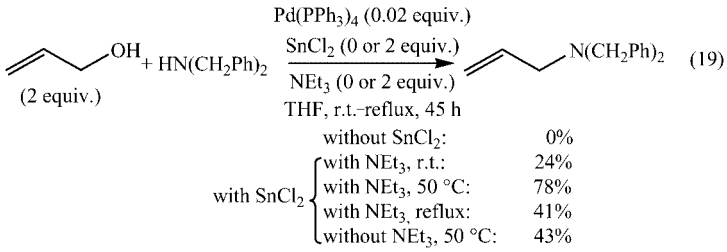
Masuyama et al. used overstoichiometric amounts of tin(II) chloride as the promoter; $SnBr_2$ was less effective while no reaction occurred with $SnF_2$ and $Sn(OAc)_2$. As above, the best catalyst was $Pd(PPh_3)_4$, but the reaction required heating to 50 °C in THF or DMF and the presence of triethylamine to be efficient [Equation (19)].[42] These experimental conditions are compatible with the use of various allylic alcohols [Equation (20)] and secondary and primary amines [Equation (21)], but the reactivities of aromatic amines are lower than those of aliphatic amines, no allylation being observed with an amine possessing weak nucleophilic properties such as diphenylamine. The formation only of *N*,*N*-dibenzylbut-2-en-1-ylamine (55–64% yields) from the reaction of dibenzylamine with but-2-en-1-ol and but-1-en-3-ol indicated a $\eta^3$-allylpalladium intermediate. The authors suggest, without further comment, that $SnCl_2$ promotes the formation of such a complex. As a slight amount of water inhibited the reaction,[42] we suspect the coordination of the hydroxy group of the substrate to the Lewis acid, namely $SnCl_2$; this would result in a decrease of the allyl–O bond energy that facilitates the formation of the $\eta^3$-allylpalladium complex. We propose that water causes hydration or destruction of $SnCl_2$.




(21)

Yang et al. have intensively developed the use of titanium(IV) isopropoxide and molecular sieves as additives for the allylation of primary and secondary arylamines with

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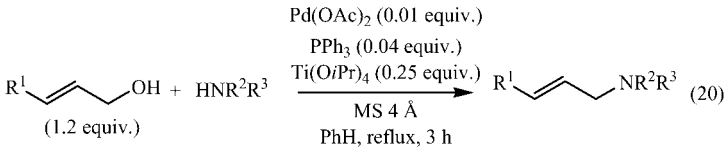
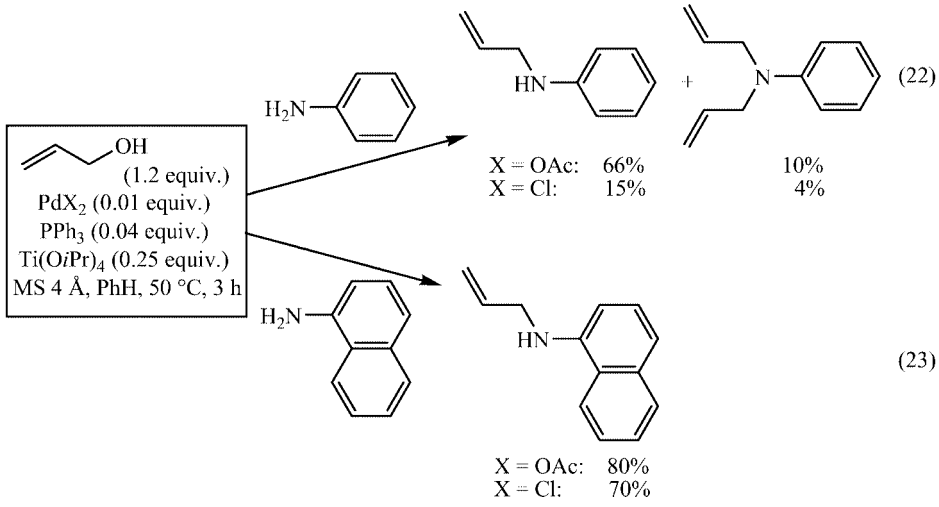


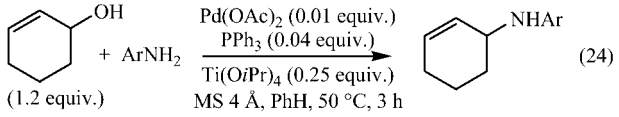

(20)

$R^1$ = H, $R^2$ = $R^3$ = Ph: 68%; $R^1$ = $R^2$ = H, $R^3$ = *o*-$O_2NC_6H_4$: 84%;
$R^1$ = $R^2$ = $R^3$ = Ph: 83%; $R^1$ = Ph, $R^2$ = H, $R^3$ = *o*-$O_2NC_6H_4$: 78%



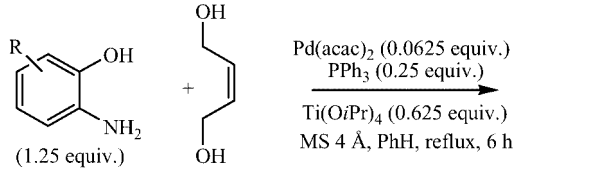

various allylic alcohols[43,48–55] [Equation (20)].[55] No reaction was observed without the titanium alkoxide [Equation (21)],[43] and the yields decreased greatly in the absence of the molecular sieves.[48,51] The best catalytic system would be highly dependent on the structure of the amine; for an example, the reaction between **1** and aniline in benzene gave much better results with $Pd(OAc)_2/PPh_3$ than with $PdCl_2/PPh_3$ [Equation (22)],[48] while the yields were similar with 1-aminonaphthalene [Equation (23)].[53] Good yields were obtained from primary and secondary linear allylic alcohols, while the efficiency with cyclohex-2-enol strongly depended on the structure of the amine [Equation (24)].[51,53,55]

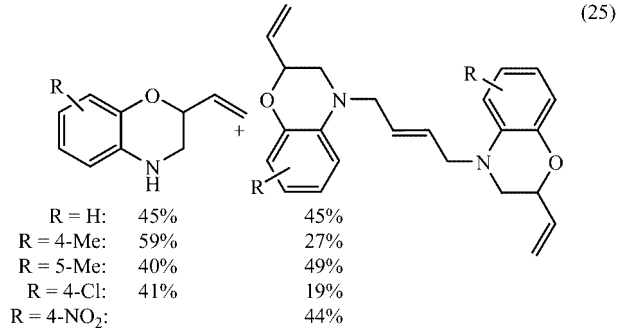


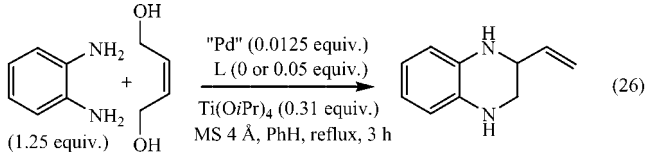

Ar = 1-$O_2NC_6H_4$ (5%), 2-$O_2NC_6H_4$ (34%), 3-$O_2NC_6H_4$ (34%), 3-$CNC_6H_4$ (27%), 4-Cl-2-$MeC_6H_3$ (98%), 1-naphthyl (18%)

The $PdL_n/Ti(OR)_4$/MS procedure has been applied to the synthesis of heterocycles from (*Z*)-but-2-ene-1,4-diol and 2-aminophenols [Equation (25)],[50,54] *o*-phenylenediamines [Equation (26)],[52] or 2,3-diaminonaphthalene.[53,56]

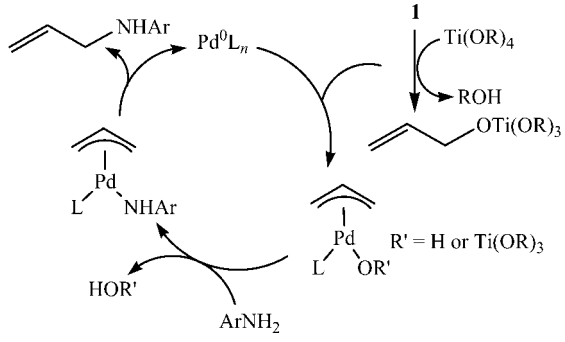
Other $Ti(OR)_4$ variants can be used,[52–54] while use of $TiCl_4$ resulted either in no reaction[52] or in low yields.[53,54] This is consistent with Yang's proposal of the formation of an allylic titanate through an exchange reaction between the allylic alcohol and $Ti(OR)_4$, the allylic titanate giving rise to the $\eta^3$-allylpalladium intermediate.[43,51,54] According to the authors, the allylic amine would be produced through coordination of the amine to palladium, followed by reductive elimination (Scheme 11).[43,51,58] The possible formation of the Pd–N bond by ligand exchange between ($\eta^3$-allyl)PdLOR′ and $Ti(HNAr)_n(OR)_{4-n}$ generated in situ has been envisaged.[43] Yang and Chung suggest that the role of the molecular sieves would be to prevent catalyst deactivation by water formed during the reaction.[48,51] We suspect



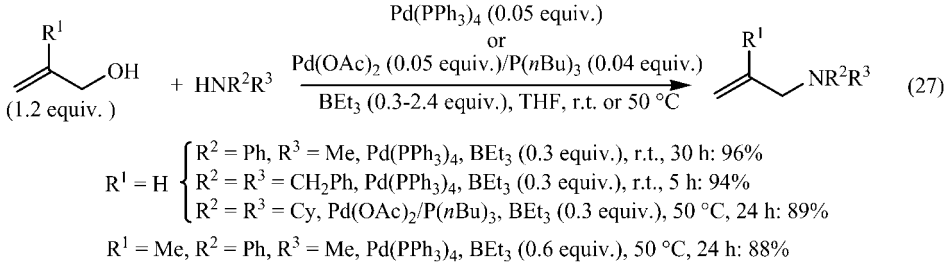



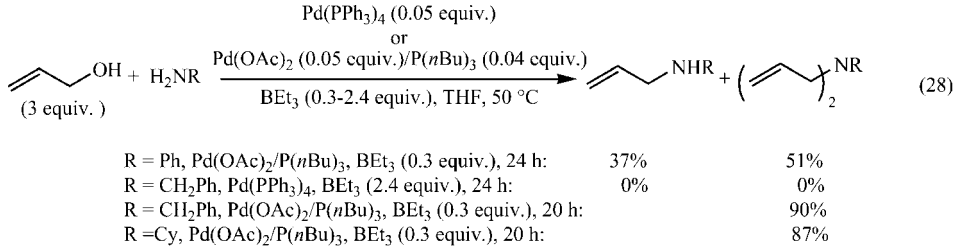

$Pd(acac)_2$: 0%, $Pd(acac)_2/PPh_3$: 95%, $PdCl_2(MeCN)_2/PPh_3$: 92%, $Pd(OAc)_2$/(*R*)-BINAP: 58%, 19% *ee* (*S*)

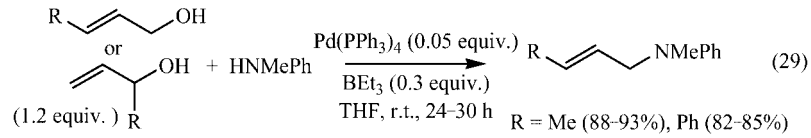



Scheme 11. Proposed role of $Ti(OR)_4$ as promoter.

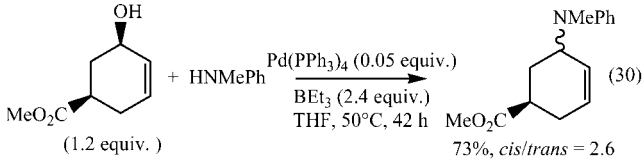


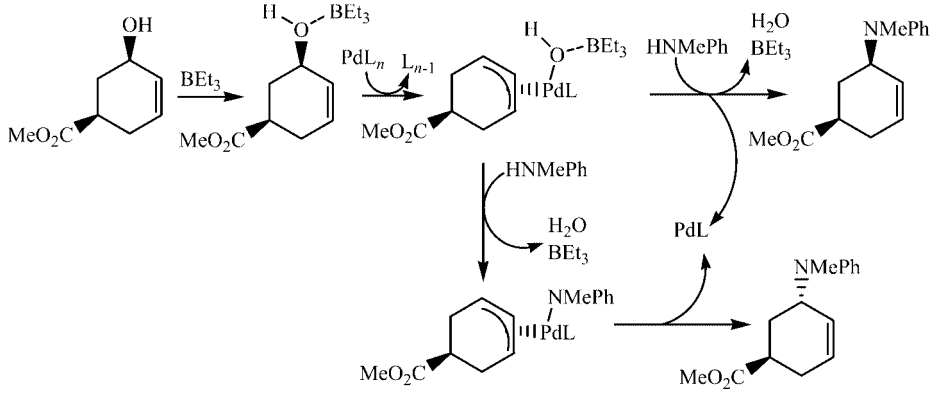




rather that the molecular sieves prevent the hydrolysis of $Ti(OR)_4$.

Kimura, Tamaru, et al. have used triethylborane (0.3 to 2.4 equiv.) as an additive with either $Pd(PPh_3)_4$ or $Pd(OAc)_2/P(n\text{-}Bu)_3$ as the catalyst.[59] The optimum catalyst, amount of $BEt_3$, reaction temperature, and reaction time depend on the natures of both alcohol and amine [Equations (27) and (28)].[60] The results obtained from isomeric allylic alcohols depicted in Equation (29) indicated $\eta^3$-allylpalladium intermediates, while a mixture of *cis* and *trans* adducts was obtained from methyl *cis*-5-hydroxycyclohex-3-ene-1-carboxylate and *N*-methylaniline [Equation (30)]. The authors interpreted their results as outlined in Scheme 12. Coordination of $BEt_3$ to the hydroxy group of the substrate would help the oxidative addition, resulting in the $\eta^3$-allylpalladium. This intermediate would react through *trans* attack of the amine or, as in Scheme 11, through coordination of the amine to palladium. Pd-catalyzed *trans* to *cis* isomerization of the $\eta^3$-allylpalladium intermediate is also a possibility.[61]

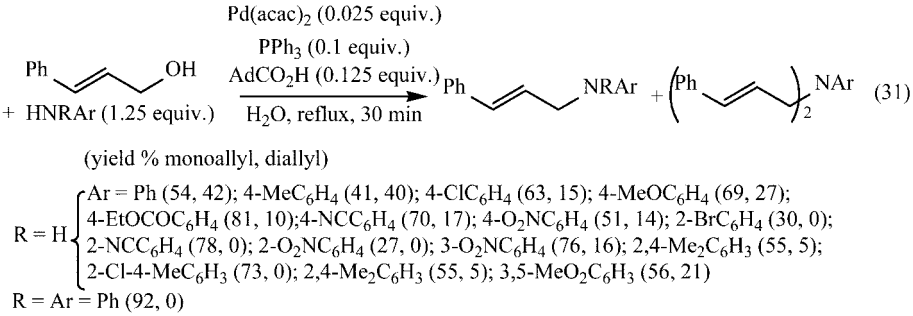


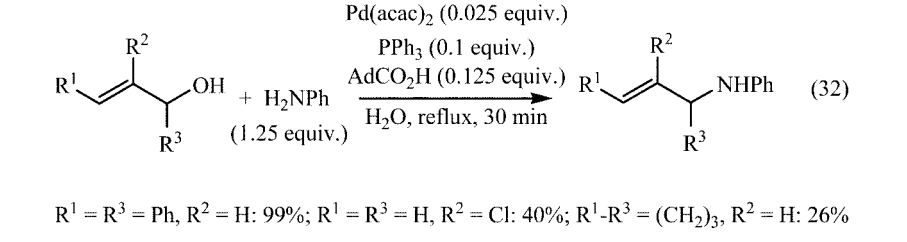

Yang's team, who had previously used the $PdL_n/Ti(OR)_4$/MS procedure in benzene for allylation of anilines,[40,48–51,55] has recently reported the use of a carboxylic



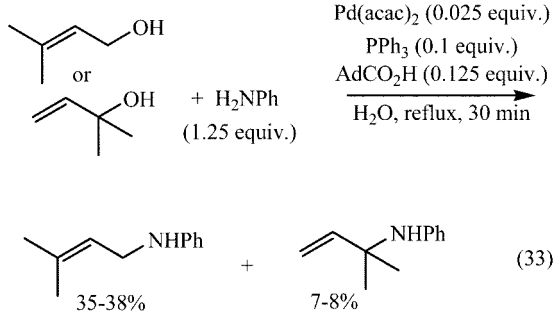

Scheme 12. Proposed role of $BEt_3$ and reaction pathways for the addition of *N*-methylaniline.



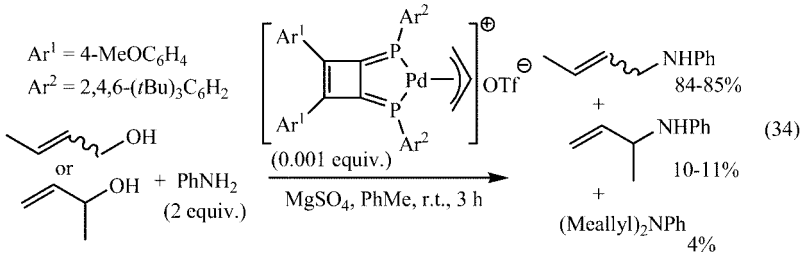

acid as the additive at reflux in water [Equations (31)–(33)].[62] A screening of carboxylic acids and palladium/ligand combinations resulted in the retention of adamantane-1-carboxylic acid ($AdCO_2H$) and $Pd(acac)_2/PPh_3$ for the performance of various allylic aminations. No more than a 10% yield of allylation product was obtained from aniline and cinnamyl alcohol in the absence of the carboxylic acid. In keeping with the proposal of Oshima et al.,[23] the authors envisaged the activation of the allylic alcohol by water, but they also suspected protonation of the alcohol by the acid. The mechanism finally proposed, which involves a $\eta^3$-allylpalladium intermediate as suggested by the results shown in Equation (33), was similar to the one depicted in Scheme 11 but with R′ = H or COAd.



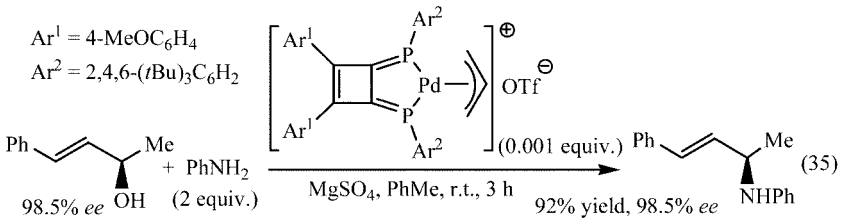

## Use of Cationic $Pd^{II}$ Catalysts

In 2002, Ozawa's and Yoshifuji's teams reported the efficient use of a cationic $\eta^3$-allylpalladium complex bearing a diphosphanylidenecyclobutene ligand, namely [(DPCB-OMe)($\eta^3$-allyl)Pd][OTf], for the allylation, at room temperature, of aniline with allylic alcohols [Equations (34) and (35)].[21] Interestingly, allylation with an enantiomerically enriched chiral alcohol occurred with retention of the configuration of the chiral center, and without loss of optical purity [Equation (35)].

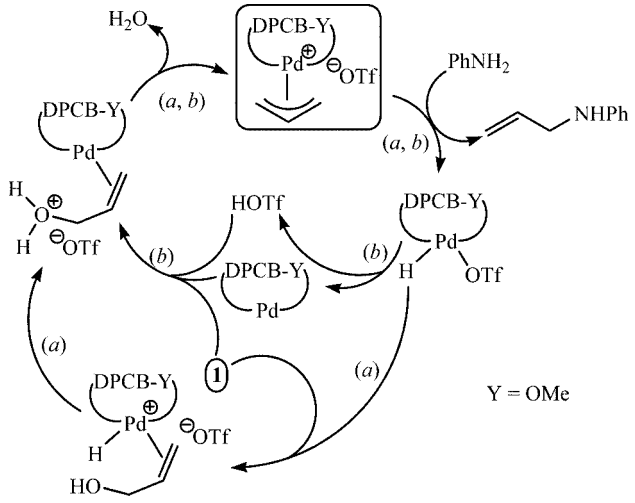
By comparison with the reactivity of a platinum analogue, Ozawa and Yoshifuji proposed the mechanism depicted in Scheme 13, path *a*.[21,22,63] The addition of aniline to the catalyst would afford a hydridopalladium intermediate, and after coordination of allyl alcohol to this intermediate, the transfer of proton to the hydroxy group would be facilitated by the strong π-accepting ability of the DPCB-OMe ligand.[64] This would be followed by the regeneration of the starting catalyst with elimination of water. The retention of configuration observed with a chiral alcohol as the substrate [Equation (35)] demonstrates the *anti* nucleophilic attack by the amine on the $\eta^3$-allylpalladium intermediate.[65] Kinetic examinations resulted in the observation of significant increases in the rate constant with increasing amounts of water.[21] According to the authors, the exact



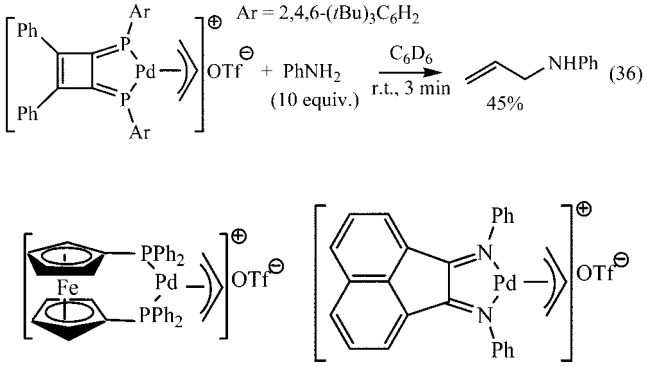



reason for this unexpected effect of water is unclear but is in agreement with a catalysis involving ionic intermediates. From Oshima's report[23] we suspect some stabilization of intermediates by coordination of water as shown in Scheme 9. The reductive elimination of TfOH from (DPCB-Y)HPdOTf to afford a $Pd^0$ complex that would evolve to [($\eta^3$-allyl)Pd(DPCB-Y)][OTf] through reaction with allyl alcohol (Scheme 13, path *b*) has been discounted.[21]



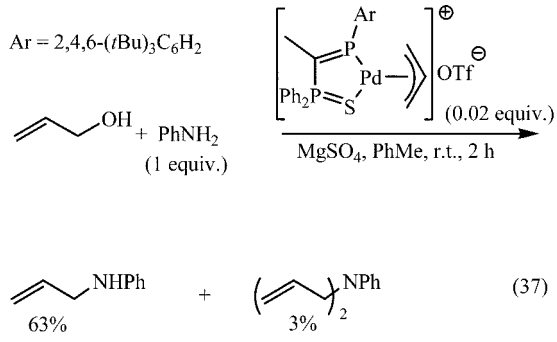

Scheme 13. Possible mechanisms for the allylation of aniline via a hydridopalladium(II) intermediate.

The particular effect of the DPCB-OMe ligand has been demonstrated in a stoichiometric reaction with a similar cationic $\eta^3$-allylpalladium complex [Equation (36)]. The allylation occurred in 3 min at room temperature, while no reaction was observed over 24 h with the two complexes shown in Scheme 14 under similar conditions.[63]

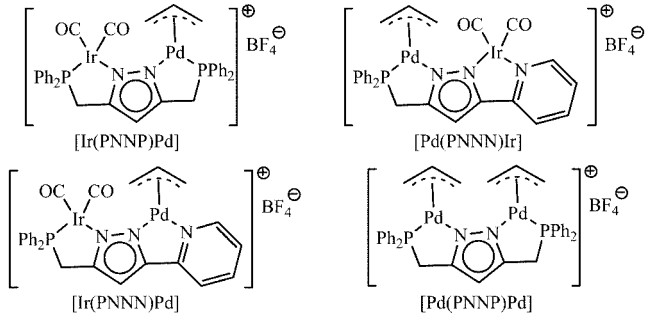



Scheme 14. Two inefficient cationic complexes.

Another complex with a *P,S*-chelating ligand that would also have π-back-bonding properties, again for the allylation of aniline but with an increased catalyst loading, was subsequently reported by Yoshifuji et al. [Equation (37)].[66]



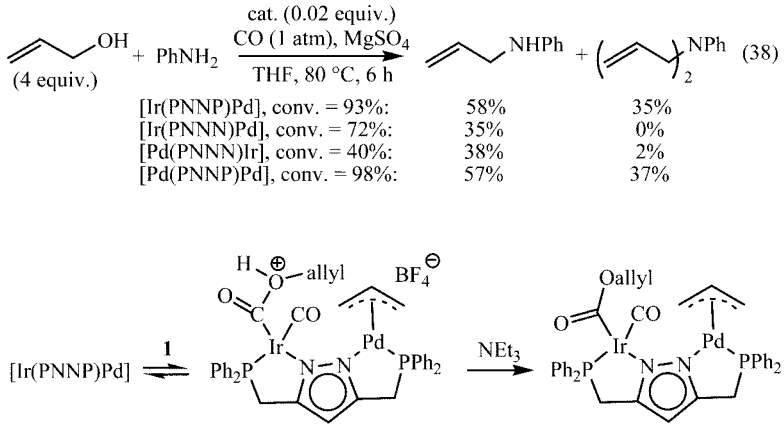

Akita et al. used a series of cationic dinuclear complexes with bridging *P,N,N,N* and *P,N,N,P* ligands (Scheme 15) to catalyze the same reaction [Equation (38)], albeit carried out under CO to suppress decomposition of the catalytic species and with an excess of the alcohol.[67] Study of the reaction mechanism remains under way, but the stoichiometric reaction between **1** and [Ir(PNNP)Pd], followed by treatment with $NEt_3$, nevertheless afforded a complex with an (allyloxy)carbonyl-Ir moiety (Scheme 16).



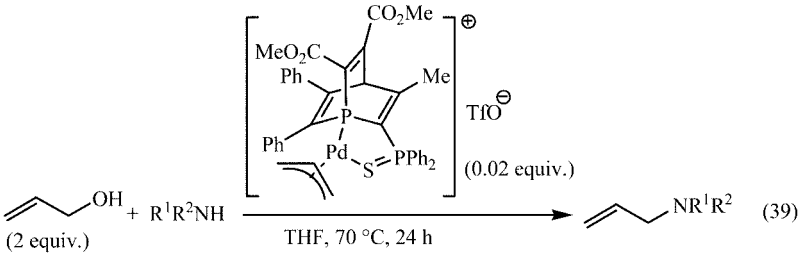

Scheme 15. Four efficient cationic dinuclear complexes.

A cationic palladium complex with a phosphabarrelene-phosphanylsulfide ligand, that should also have a significant π-acceptor capacity, has been synthesized and used for the allylation of secondary amines by Le Floch et al. [Equation (39)].[68] The crucial role of this particular ligand was exemplified by the absence of any reaction when the cationic complex [($\eta^3$-allyl)Pd(S = $PPh_2CH_2PPh_2$)][OTf], bearing a different *P,S* bidentate ligand, was used as the catalyst under the same experimental conditions.



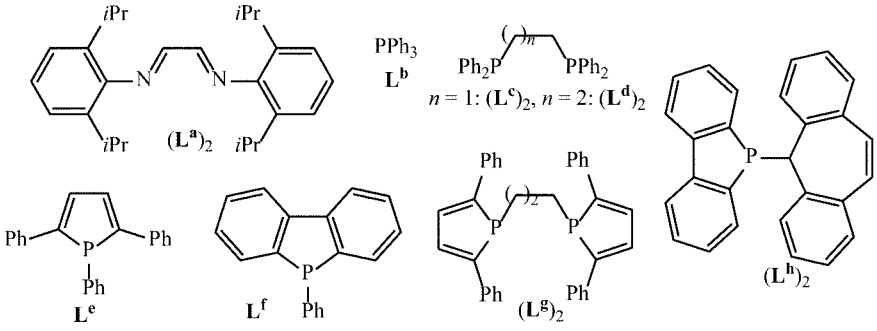

Scheme 16. Stoichiometric reaction between [Ir(PNNP)Pd] and allyl alcohol.




$R^1$ = Ph, $R^2$ = Me: 85%, $R^1$ = $R^2$ = $CH_2Ph$: 57%, $R^1$-$R^2$ = $(CH_2)_2O(CH_2)_2$: 86%

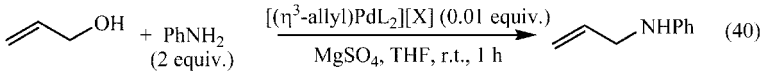
These observations prompted Le Floch's team to investigate the performance of a range of cationic palladium complexes – $[(\eta^3\text{-allyl})PdL_2][X]$ (X = OTf or $NTf_2$) – possessing mono- or bidentate ligands featuring phosphanes and phospholes (Scheme 17) in the reaction between aniline and allyl alcohol.[69] The increase in catalytic activity with the π-acceptor properties of the ligand was supported by DFT calculations and demonstrated by experiment [Equation (40)]. The best catalyst, $[(\eta^3\text{-allyl})Pd(\mathbf{L^e})_2][NTf_2]$, was used for the bis-allylation of aniline (up to 100% yield) and for reactions with other allylic alcohols and amines [Equations (41) and (42)]. The reactions were usually carried out in the presence of $MgSO_4$, although the absence of this water scavenger resulted only in a small depletion in the conversion. A significant decrease in the catalytic activity was observed with disubstituted amines such as morpholine and dibenzylamine [Equation (42)] and with α-substitution in the alcohol, as in the case of 2-methylprop-2-en-1-ol.

Very recently, Le Floch et al. returned to the mechanism depicted in Scheme 13, path *a*, originally proposed by Ozawa and Yoshifuji. DFT and CDA calculations led them to retain a different catalytic cycle (Scheme 18), closer to that currently accepted for nucleophilic allylic substitutions.[70,71] The addition of the amine to the starting catalyst would afford the corresponding allylammonium salt and a transient dicoordinated $Pd^0$ complex that, with allyl alcohol, would produce $(allylOH)PdL_2$. A key step of Le Floch's mechanism is the intermolecular protonation of the alcohol functionality of this complex by the ammonium to deliver the allylamine, water, and the allyl complex precursor. Calculations also indicated that the process should be sensitive to the nature of the ligand and the basicity of the amine.

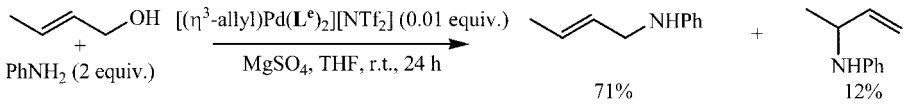


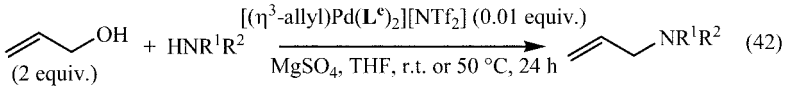

Scheme 17. Mono- and bidentate ligands used by Le Floch's team.



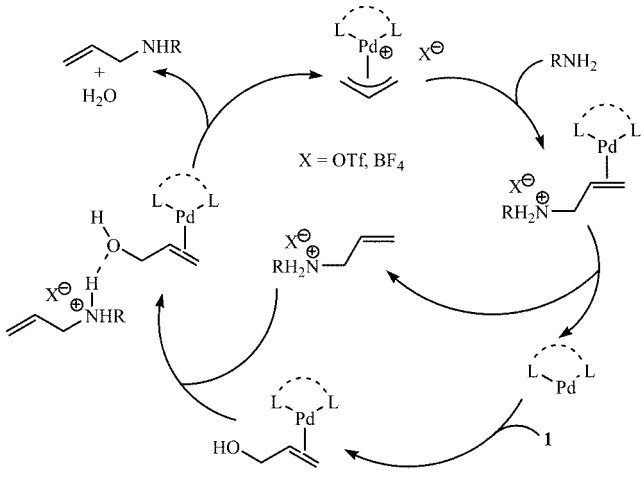

with X = OTf, $(\mathbf{L^a})_2$: 0%, $(\mathbf{L^b})_2$: 47%, $(\mathbf{L^e})_2$: 72%, $(\mathbf{L^f})_2$: 52%, $(\mathbf{L^g})_2$: 18%
with X = $NTf_2$, $(\mathbf{L^a})_2$: 0%, $(\mathbf{L^b})_2$: 27%, $(\mathbf{L^e})_2$: 100%, $(\mathbf{L^f})_2$: 34%, $(\mathbf{L^g})_2$: 13%, $(\mathbf{L^h})_2$: 30%




$R^1$ = Ph, $R^2$ = Me, r.t.: 100%; $R^1 = R^2 = CH_2Ph$, r.t.: 11%; $R^1 = R^2 = CH_2Ph$, 50 °C: 44%
$R^1$-$R^2$ = $(CH_2)_2O(CH_2)_2$, r.t.: 28%; $R^1$-$R^2$ = $(CH_2)_2O(CH_2)_2$, 50 °C: 100%

On the basis of these computational studies, new cationic palladium complexes were synthesized and tested; one of them – namely $[(\eta^3\text{-allyl})Pd(P(OPh)_3)_2][OTf]$ – was particularly effective for the allylation of aniline at room temperature while, consistently with the theoretical studies, no conversion was observed with *n*-butylamine even after 24 h at 50 °C.[70]




Scheme 18. Le Floch's proposal for the promotion of allyl-OH bond cleavage.

## Conclusions

Various Pd-catalyzed procedures for the allylation of amines by allylic alcohols have been reported, but their efficiencies are often dependent on the nature of the amine, while their mechanisms and the need for promoters are highly dependent on the catalyst. Nevertheless, allylic alcohols are viable alternatives to allylic esters and carbonates for such reactions. According to the literature, the reaction between the amine and the allyl fragment occurs at the $\eta^3$-allylpalladium intermediate stage but can involve two reaction paths: either direct addition on the allyl or coordination to the Pd atom followed by reductive elimination. Moreover, the mechanism of the formation of the $\eta^3$-allylpalladium intermediate can often be much more complicated than usually accepted.

**Note Added in Proof** (May 9, 2007): Štěpnička et al. have reported the synthesis of *N*-(2-hydroxyethyl)pyrrole from (*Z*)-2-butene-1,4-diol and 2-aminoethanol using various supported Pd catalysts, at 100–140 °C, in the absence of solvent.[72] Leaching of metal from the support has been observed. Such a cyclization has previously been disclosed by Murahashi et al. [Equation (9)].[39]

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