DOI: 10.1002/anie.201300134

Organometallic Reactions

Migratory Insertion of Alkenes into Metal–Oxygen and Metal–Nitrogen Bonds

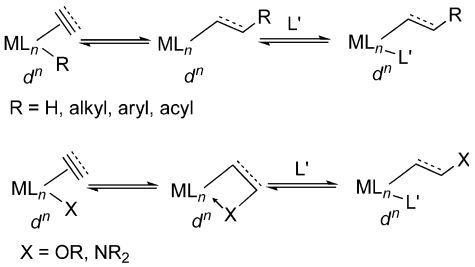
*Patrick S. Hanley and John F. Hartwig**

amination · organometallic reactions · palladium · insertion · reaction mechanisms

The insertion of an unsaturated ligand into a M–C or M–H bond proceeds through migratory insertion, a fundamental organometallic reaction. Recent literature documents evidence of the migratory insertion of alkenes into an M–O and M–N bonds for alkene alkoxylation and alkene amination reactions, respectively. Herein we provide an overview of the literature and a perspective on how these recent experiments relate to classic experiments on C–O and C–N bond formation with alkene complexes of the late transition metals.

Introduction

Migratory insertion is a fundamental organometallic reaction. It is a concerted reaction that combines an unsaturated ligand with an adjacent metal–ligand bond to form a product containing a new ligand with the unsaturated group formally inserted into the original covalent metal–ligand bond (Scheme 1). A variety of unsaturated ligands undergo migratory insertion, including carbon monoxide, carbon dioxide, alkenes, alkynes, ketones, aldehydes, and imines, and migratory insertion is a common step in numerous catalytic reactions, including hydroformylation,[1,2] hydrogenation,[3–5] polymerization,[6–9] hydroarylation,[10–14] difunctionalization of alkenes,[15–18] and the olefination of aryl halides (commonly termed the Mizoroki–Heck reaction).[19–22]



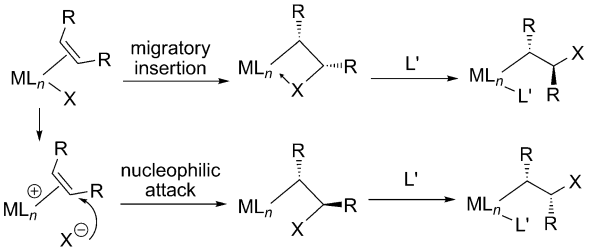
Scheme 1. Migratory insertion of an alkene or alkyne into M–R and M–X bonds.

In most cases, the unsaturated ligand inserts into a metal–carbon (M–C) or metal–hydrogen (M–H) bond. Related insertions of alkenes into metal–oxygen (M–O) and metal–nitrogen (M–N) bonds are much less common (Scheme 1). Over the past decade, however, several papers have described palladium-catalyzed alkene alkoxylation and alkene amination reactions for which stereochemical data implies that migratory insertion of an alkene occurs into an M–O or M–N bond. Moreover, the first isolated transition metal amido complexes that insert unactivated alkenes have been reported in the past few years. These recent publications on isolated amido complexes include information on the factors controlling the rate of insertion.

Although the first examples of insertion of an alkene into a metal–heteroatom bond were reported more than two decades ago, experiments on the insertions of alkenes into isolated metal amido complexes are rare. An open coordination site is necessary for alkene coordination prior to insertion, and many alkoxo and amido complexes form stable multinuclear structures if the metal center is coordinatively unsaturated. Thus, preparation of monomeric amido complexes containing an open coordination site to bind and subsequently insert alkenes is difficult, and the absence of such complexes has meant that the factors which control insertions of alkenes into metal–heteroatom bonds have been poorly understood.

Many alkene complexes have been prepared and react with nucleophiles by attack onto the coordinated alkene. As discussed below, the classic Wacker reaction has been proposed to occur by this elementary reaction, rather than migratory insertion. Although the product of migratory insertion and nucleophilic attack on a coordinated alkene

[*] Dr. P. S. Hanley, Prof. J. F. Hartwig
Department of Chemistry, University of Illinois Urbana-Champaign
Urbana, IL 61801 (USA)
Prof. J. F. Hartwig
University of California, Department of Chemistry
718 Latimer Hall, Berkeley, CA 94720 (USA)
E-mail: jhartwig@berkeley.edu



Scheme 2. Migratory insertion of an alkene into M–X bonds versus nucleophilic attack of X onto a coordinated alkene.

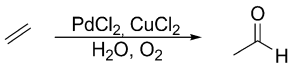
contain the same connectivity, the stereochemistry of the products of the two reactions is different. As shown in Scheme 2, the migratory insertion pathway leads to the opposite relative configurations of the α- and β-carbon atoms of the resulting alkyl complex. Ongoing work has sought to reveal what complexes and reaction conditions lead to insertion and what complexes and reaction conditions lead to nucleophilic attack on the coordinated alkene. Recent data that begins to address this issue are included in this Minireview.

To develop new, selective metal-catalyzed olefin alkoxylation and amination reactions, fundamental knowledge of the factors that control the rate and stereoselectivity of the insertion of alkenes into M–O and M–N bonds is needed. These factors are just beginning to be revealed. Thus, one aim of this Minireview is to provide a perspective on how these recent experiments relate to classic experiments on C–O and C–N bond formation with alkene complexes of the late transition metals, and to summarize the existing literature on chemistry involving migratory insertion of alkenes into the M–N and M–O bonds of isolated metal amido and metal alkoxo complexes, respectively. We will also describe mechanistic studies of catalytic amination and alkoxylation reactions, that offer insight into the migratory insertion step.

We have separated this review into two sections. The first section is divided into two subsections: 1) The description of catalytic reactions for which evidence of alkene insertion into an M–O bond has been gained, and 2) the description of stoichiometric reactions of alkoxo complexes with alkenes. The second section describes chemistry involving migratory insertions of alkenes into M–N bonds. Because more data have been published on alkene insertions into M–N bonds, the section on this topic is divided into three subsections: 1) The description of catalytic reactions involving insertions of alkenes into bonds between nitrogen and lanthanide, actinide, alkaline earth, and early transition metals, 2) the description of catalytic reactions involving the insertion of alkenes into late-transition-metal–nitrogen bonds, and 3) the description of reactions of discrete amido complexes with alkenes that likely occur by a migratory insertion of the alkene into the M–N bond.

Reactions Occurring by Migratory Insertion of Olefins into M–O Bonds

The oxidative functionalization of alkenes is the one of the most widely used processes catalyzed by soluble transition-metal complexes. The oxidation of ethylene in water with a palladium catalyst, commonly termed the Wacker process, is used to produce 2×10^6 tons of acetaldehyde annually



Scheme 3. The Wacker process.

(Scheme 3).[23] The metal-mediated formation of new C–O bonds by the addition of an oxygen nucleophile to an olefin was thought for many years to occur exclusively by nucleophilic attack of an oxygen nucleophile onto a metal-coordinated olefin. Well-characterized metal olefin complexes had been prepared, and alcohols were shown to add to the alkene of these complexes at the face opposite the metal center.[24–27] Thus, metal-catalyzed additions of oxygen nucleophiles to olefins were typically assumed to occur by *anti* addition. However, alkoxometal olefin complexes that react by migratory insertion have recently been identified. In this section, we describe catalytic reactions, including the Wacker process, for which mechanistic data implies that the C–O bond is formed by insertion of an alkene into an M–O bond. Stoichiometric reactions of alkoxo complexes with alkenes will be discussed in detail.

John Hartwig is the Henry Rapoport Professor at the University of California, Berkeley. His group seeks to discover new reactions catalyzed by transition-metal complexes and to reveal new reaction mechanisms. He recently authored the textbook "Organotransition Metal Chemistry: From Bonding to Catalysis". He is the 2006 recipient of the ACS Award in Organometallic Chemistry and the 2013 ACS H.C. Brown Award in Synthetic Methods. He was elected to the National Academy of Sciences in 2012.

Patrick Hanley received his B.S. from West Virginia University in 2008 under the direction of Prof. Jeffrey L. Petersen. He completed his Ph.D. in 2012 at the University of Illinois at Urbana-Champaign under the direction of Prof. John F. Hartwig, studying new carbon–nitrogen bond-forming reactions of palladium. Currently, he is a Senior Chemist at The Dow Chemical Company in Michigan.

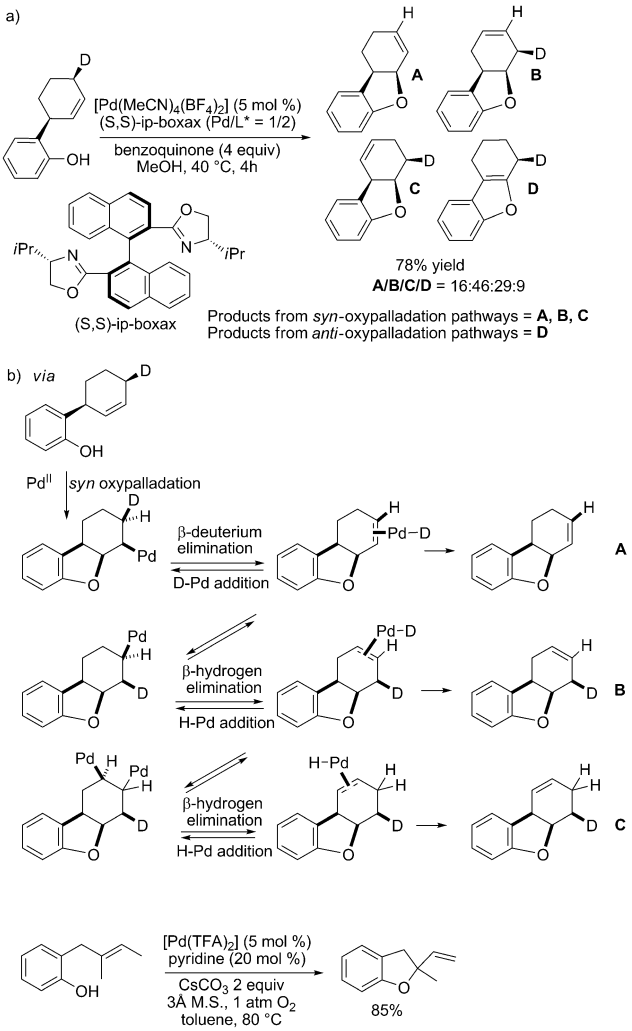
Catalytic Reactions Involving Alkene Insertion into M–O Bonds

The mechanism of the Wacker process has been disputed for the last four decades. Early kinetic data on the Wacker oxidation were consistent with a mechanism involving *syn* addition of a preformed palladium-hydroxo complex across ethylene.[28] However, experiments conducted by Akermark, Stille, Bäckvall, and co-workers demonstrated that palladium ligated with substituted or deuterium-labeled alkenes formed products by *anti* oxypalladation.[29–32] For example, the addition of CO to the combination of bis[(*cis*-$[D_2]$ethylene)$PdCl_2$] and H_2O in a buffered solution of $CuCl_2$ and NaOAc led to the formation of lactone products, and the configuration of the carbon atoms in the lactone indicated that an *anti* addition of the oxygen atom and palladium to the ethylene had occurred.[30] In fact, Bäckvall, Siegbahn, and co-workers stated that a hydroxymetal olefin complex is too unreactive to undergo *cis* migration of an OH ligand to a bound alkene.[33]

Henry and co-workers correctly noted that these experiments were conducted under reaction conditions distinct from those of the catalytic Wacker reaction. The Wacker process is typically conducted with low chloride concentrations. Henry and co-workers examined the hydroxylation of allylic alcohols and demonstrated that the stereochemical outcome of the oxypalladation step is different at high and low concentrations of chloride ion. At high chloride ion concentration, products from *anti* oxypalladation were observed, but at low chloride ion concentration the stereochemical configuration of the observed products indicated that *syn* oxypalladation, presumably by migratory insertion of an alkene into a metal–alkoxo bond, occurred.[34–39] Because two sets of products with different relative configurations were observed, the hydroxylation of allylic alcohols must occur by two different mechanisms. Despite these results, the mechanism of the Wacker process was described in leading textbooks as occurring by the attack of a free water molecule on a palladium-bound ethylene.[40]

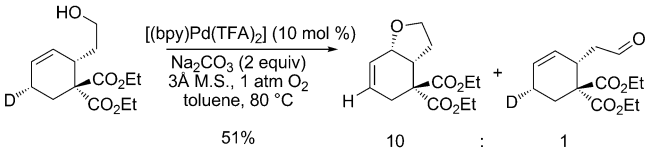
These studies of Henry were conducted on allylic alcohols to determine whether the addition occurred by a *syn* or *anti* oxypalladation process. Allylic alcohols might provide results that are biased toward one mechanism or another because they contain two binding sites and might isomerize under the reaction conditions. Thus, other researchers more recently have studied the stereochemistry of different Wacker reactions.

Hayashi et al. assessed the stereochemistry of the oxypalladation step in the oxidative cyclization of an *o*-allylphenol.[41] Stereospecifically deuterated, racemic 6-(2-hydroxyphenyl)-3-deuteriocyclohexenes underwent cyclization in the presence of $[Pd(MeCN)_4(BF_4)_2]$ as a precatalyst and (*S*,*S*)-2,2′-bis-(4-isopropyloxazolyl)-1,1′binaphthyl as a ligand with 4 equivalents of benzoquinone in MeOH at 40 °C (Scheme 4). In the absence of added LiCl, a series of cyclized products were obtained and formed by *syn* oxypalladation by migratory insertion, followed by a series of β-hydrogen elimination and insertion steps to generate the different product isomers. In the presence of added LiCl, different products formed. Under these reaction conditions, the major cyclized product resulted from *anti* addition of the palladium and oxygen across the internal alkene.



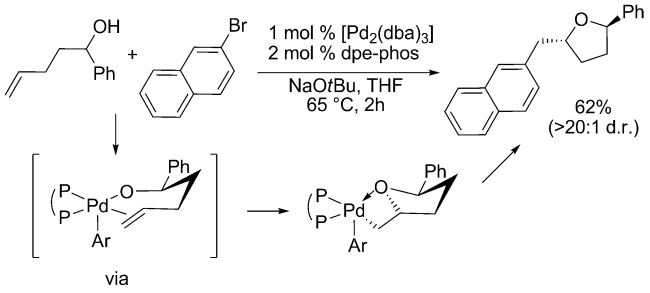
Scheme 4. a) Oxidative cyclization of 6-(2-hydroxy-phenyl)-3-deuteriocyclohexene. b) Mechanism for formation of products **A**–**C** after *syn* oxypalladation. M.S. = molecular sieves, TFA = trifluoroacetate.

Stereochemical evidence for a *syn* oxypalladation step also has been gained by Stoltz et al. for similar palladium-catalyzed cyclizations of phenols and primary alcohols.[42] Treatment of a deuterium-labeled unsaturated alcohol with 10 mol% [(bpy)Pd(TFA)] (bpy = 2,2′-bipyridine), 2 equivalents of Na_2CO_3, 1 atm of O_2, and 500 mg mol^{-1} of 3Å molecular sieves in toluene at 80 °C for 3 hours generated cyclized products in 51% overall yield (Scheme 5). Like the products of Hayashi's experiment, the products from Stoltz's experiment are best rationalized as forming by a *syn* oxypalladation (migratory insertion of the alkene into the Pd–O bond). However, the stereochemistry of the oxypalladation process, in this case, indicated that the reactions with or without added chloride anion both occurred by a *syn*-oxypalladation pathway. In addition, reactions conducted with nonchelating ligands based on pyridine occurred by a *syn*-oxypalladation pathway.



Scheme 5. Oxidative cyclization of *o*-allylphenol.

Wolfe and co-workers published a series of reports of alkoxyarylations of alkenes. The stereochemistry of the products from the palladium-catalyzed reaction of aryl bromides with γ-hydroxy alkenes indicated that these reactions also occur by a *syn* addition of the palladium and the oxygen atom across the alkene (Scheme 6).[43–45] These

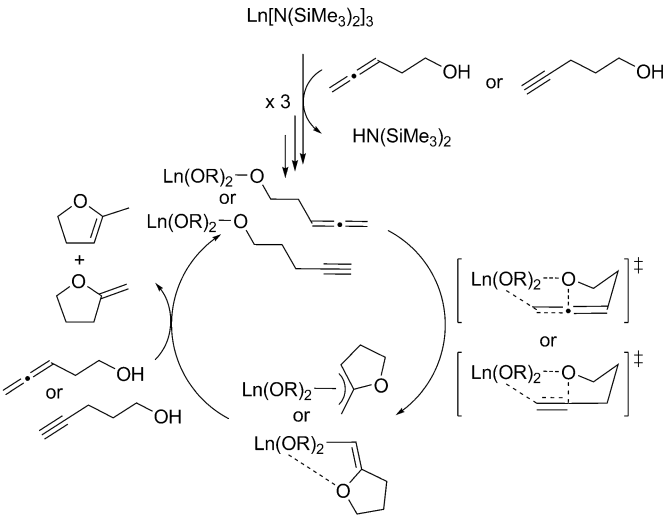


Scheme 6. Palladium-catalyzed reaction of aryl bromides with γ-hydroxy alkenes. dba = dibenzylideneacetone, dpe-phos = bis[2-(diphenylphosphino)phenyl]ether.

reactions are highly regio- and stereoselective, thus forming the *trans*-2,5-disubstituted furan products. The selectivity of these products is inconsistent with a mechanism involving *trans* hydroxypalladation of the alkene. The *anti*-hydroxypalladation pathway would generate *syn*-1′,2-disubstituted products, which are not observed. The proposed mechanism for these reactions begins with oxidative addition of the aryl bromide to a Pd^0 species ligated by a bis(phosphine) and subsequent transmetalation to generate a [Pd(Ar)(OR)] intermediate. This intermediate undergoes selective migratory insertion of the pendant alkene into the Pd–O bond over the PdAr bond, and the resulting alkylpalladium aryl complex undergoes C–C bond-forming reductive elimination to generate the tetrahydrofuran product.

Catalytic olefin alkoxylation reactions proposed to proceed by a migratory insertion pathway are not limited to palladium-catalyzed reactions. Marks and co-workers has reported the lanthanide-catalyzed hydroalkoxylation of alkynyl and allenyl alcohols.[46,47] The active lanthanide catalyst is formed by rapid protonolysis of the amide ligand of the $[Ln\{N(TMS)_2\}_3]$ precatalyst to generate a lanthanide alkoxo species, which undergoes turnover-limiting migratory insertion of the tethered alkyne into the Ln–O bond. The resulting vinyl ether is protonolyzed to release the cyclized product and regenerate the active catalyst.

These reactions are first order in catalyst and zero order in alkynyl or allenyl alcohol. These kinetic data are consistent



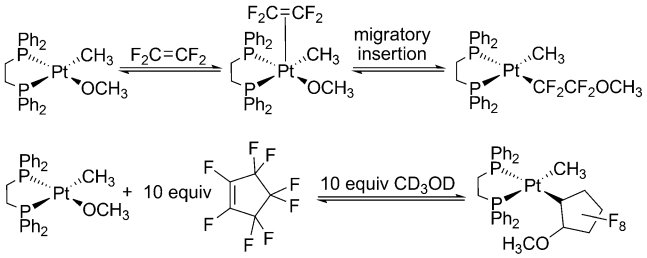
Scheme 7. Proposed reaction mechanism of lanthanide-catalyzed alkyne hydroalkoxylation.

with the proposed mechanism in Scheme 7. Although lanthanide-catalyzed cyclizations of alkenyl alcohols have been reported, these reactions do not proceed through a pathway involving migratory insertion of the alkene into an Ln–O bond.[48] The thermodynamics of the insertion of an alkyne and a terminal alkene into Ln–O bonds have been examined by calorimetry and these data predict that the insertion of an alkyne is exothermic ($\Delta H = -13$ kcal mol^{-1}), but the insertion of a terminal alkene is significantly endothermic ($\Delta H = +22$ kcal mol^{-1}).[49]

Reactions of Metal Alkoxo Complexes with Alkenes for which Direct Evidence has been Gained for Migratory Insertion into an M–O Bond

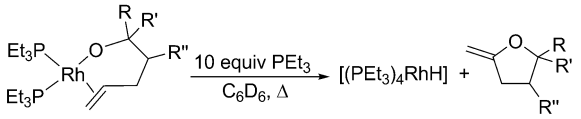
Although analysis of catalytic olefin alkoxylation systems provided stereochemical and kinetic evidence for a *syn*-oxypalladation step by migratory insertion of an alkene ligand into a M–O bond, the metal alkoxo complexes that were predicted to insert olefins have not been isolated and fully characterized. Until recently, only a single example of an alkoxide complex that reacts with an olefin was reported. Bryndza reported the reaction of $[(dppe)Pt(CH_3)(OCH_3)]$ [dppe = 1,2-bis(diphenylphosphanyl)ethane] with the highly activated alkene, tetrafluoroethylene (TFE), in $[D_8]$THF (THF = tetrahydrofuran) at 25 °C to generate $[(dppe)Pt(CH_3)(CF_2CF_2OCH_3)]$ in almost quantitative yield.[50] The reaction is first order in platinum methoxide and tetrafluoroethylene. At −80 °C, the chemical shift of the tetrafluoroethylene resonance in the ^{19}F NMR spectrum was found to vary linearly with the quantity of added TFE, thus indicating that tetrafluoroethylene interacts with the platinum methoxide complex. Tetrafluoroethylene was proposed to bind to the platinum methoxide to form a five-coordinate olefin complex. Upon warming to 25 °C, the observed alkene complex formed a product from insertion of the alkene ligand into the Pt–O bond to form an alkylplatinum complex.

In addition, a labeling experiment showed that the dppp-ligated platinum complex reacts to form a new alkyl complex in the presence of 10 equivalents of CD_3OD and perfluorocyclopentene with less than 8% incorporation of the OCD_3 group (Scheme 8). This result indicates that the methoxide ligand does not dissociate from the platinum complex and subsequently attack a coordinated olefin by an *anti*-oxyplatination pathway.



Scheme 8. Reactions of platinum methoxide complexes with perfluorinated alkenes.

More recently, the first well-characterized alkoxo complexes that undergo migratory insertion of unactivated olefins were reported.[51] A series of triethylphosphine-ligated rhodium alkoxide complexes, formed by the reaction of the rhodium(I) silylamido complex $[(PEt_3)_2RhN(SiMe_3)_2]$ with α, ω-enols at room temperature or below, led to $HN(SiMe_3)_2$ and the alkoxorhodium olefin complex in Scheme 9. A crystal

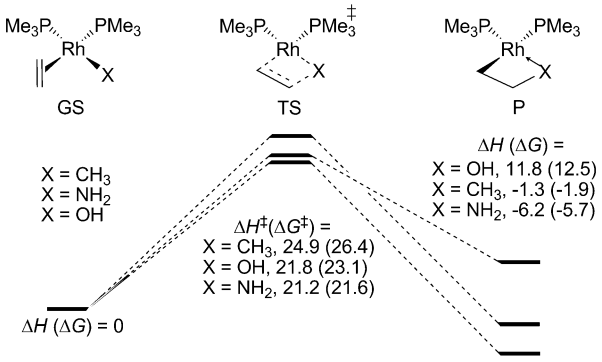


Scheme 9. Reactions of alkoxorhodium alkene complexes.

structure of the olefin complex of a more stable analogue, which does not undergo insertion, was obtained. This complex adopts a square-planar geometry, and the alkene moiety of the homoallylic alkoxide ligand is bound perpendicular to square plane. Upon warming to 25 °C in the presence of added PEt_3, a series of alkoxo-olefin complexes formed functionalized tetrahydrofurans and $[(PEt_3)_4RhH]$ in good yields by sequential migratory insertion of the alkene into the Rh–O bond and β-hydrogen elimination (Scheme 9).

The mechanism of the oxypalladation step was assessed by a series of kinetic and stereochemical experiments. The rate of the reaction was first order in rhodium and zero order in PEt_3. In addition, the reaction was slightly faster in less-polar solvents than in more-polar solvents. This solvent effect is inconsistent with a mechanism involving formation of an ionic intermediate by dissociation of the alkoxide and subsequent nucleophilic attack of the alkoxide on a rhodium-coordinated olefin. Finally, the reaction of an alkoxo olefin complex containing a deuterium-labeled, dimethyl-substituted alkenyl alcohol generated a single isomer of the *trans*-deuterio tetrahydrofuran. The isomer formed is consistent with cyclization by a migratory insertion pathway. Thus, this study provided the first evidence for reaction of an alkene with a directly observed metal alkoxo complex to form a new C–O bond by migratory insertion of the alkene into a M–O bond. More important, the modest activation barrier for insertion into a Rh–O bond implies that many catalytic olefin oxidation reactions believed to occur by nucleophilic attack of an alkoxide onto a metal-coordinated olefin might occur, instead, by migratory insertion of a an alkene into a metal–alkoxide bond.

A series of computational studies on the relative rates for migratory insertion of alkenes into square-planar methyl, amido, and hydroxo complexes of rhodium have also been published.[52] The calculated free-energy barriers for migratory insertion of the alkene into the M–X bond of the rhodium complexes $[(PMe_3)_2Rh(\eta^2\text{-}CH_2{=}CH_2)(X)]$ (X = CH_3, NH_2, OH) follow the trend Rh–NH_2 < Rh–OH ≪ Rh–CH_3 (Scheme 10). This trend was attributed to the



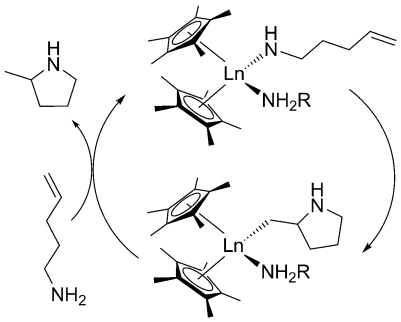
Scheme 10. Optimized ground-state and transition-state energies for ethylene insertion into rhodium–alkyl, rhodium–amido, and rhodium–hydroxy bonds.

presence of an M–X dative bond in the transition state and immediate insertion product. The M–N or M–O bond of an X-type ligand in the starting complex becomes an M–N or M–O bond of an L-type ligand during the insertion step. Because the M–X (X = NH_2, OH) bond is transformed into a different type of bond during this process, rather than cleaved, the barrier to migratory insertion is lower when X = NH_2 and OH than when X = CH_3. When X = CH_3, the M–X bond is broken in the product, and the M–X bond order in the transition state is lower.

Reactions Involving Migratory Insertion of Olefins into M–N Bonds

Catalytic reactions that proceed by migratory insertion of an alkene into an M–N bond are much more common than those that proceed by migratory insertions into M–O bonds. Moreover, a series of palladium amido complexes have been isolated and insert olefins with moderate activation barriers. In addition, thermochemical analysis of the bond enthalpies of bis(pentamethylcyclopentadienyl) samarium complexes

shows that insertions into a samarium amide should be considerably less endothermic than insertions into samarium alkoxides,[49] and multiple reports describe lanthanide- and actinide-catalyzed hydroamination reactions, which are proposed to occur by migratory insertion of an alkene into the M–N bond. In addition, several published reports hypothesize that Group IV transition-metal-catalyzed hydroaminations can proceed by a migratory insertion pathway, although the mechanism of the insertion step is still being debated. This section describes examples of catalytic reactions for which experimental evidence has been gained in support of migratory insertion as a step of the catalytic cycle. In addition, we describe in detail the reactions of well-characterized metal amido complexes with alkenes.



Scheme 11. Proposed reaction mechanism of lanthanide-catalyzed hydroamination.

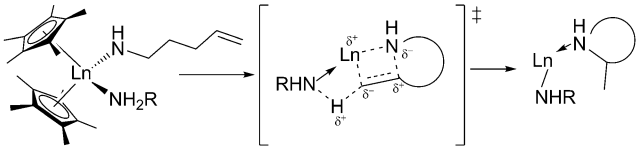
Catalytic Reactions Involving Insertions into the Metal–Nitrogen Bonds of Lanthanide, Actinide, Alkaline-Earth, and Early Transition Metal Complexes

The mechanism of lanthanide-catalyzed hydroamination is typically believed to occur by migratory insertion of an alkene into a Ln–N bond.[53–57] However, closer evaluation of the kinetic data obtained from many of these systems suggests that a reevaluation of some of the steps of the reaction mechanism is appropriate. A large kinetic isotope effect (KIE) is observed for reactions of N-deuterated aminoalkenes in many cases, and these data are inconsistent with a simple migratory insertion reaction being the turnover-limiting step. Assistance by a coordinated amine was proposed initially to account for the kinetic isotope effect. Recent results from Sadow and others[53] show that hydroaminations by alkaline-earth- and early-transition-metal systems also occur with a large kinetic isotope effect. Sadow proposed that these systems react through a six-membered transition state, not through a simple migratory-insertion pathway.

In this section, we present examples of lanthanide- and actinide-catalyzed hydroamination reactions. Although these reactions were proposed to occur by migratory insertion of an alkene into a M–N bond, it is possible that these systems react through the same six-membered transition state proposed for reaction of the alkaline-earth- and early-transition-metal systems. We will summarize the mechanistic data collected for each system in light of the recent proposals.

A seminal report on hydroamination by Marks and co-workers described intramolecular reactions of aminoalkenes catalyzed by a series of bis(pentamethylcyclopentadienyl) lanthanide complexes, including those of lanthanum, neodymium, samarium, yttrium, and lutetium.[53] Reactions with catalysts containing the larger lanthanides occurred faster than those with catalysts containing the smaller lanthanides. These hydroaminations were found to be first order in catalyst and zero order in aminoalkene. This result is consistent with rapid proton transfer to generate a lanthanide amide, followed by turnover-limiting migratory insertion of the pendant alkene into the Ln–N bond (Scheme 11).

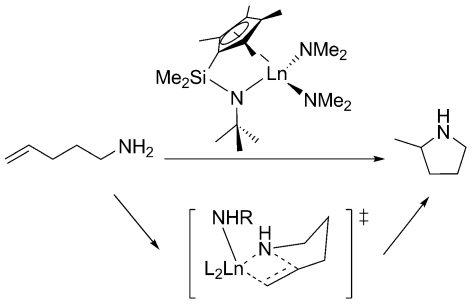
Amido complexes lacking a pendant alkene were prepared by the reaction of $[Cp^*_2LaCH(TMS)_2]$ ($Cp^* =$ pentamethylcyclopentadienyl, TMS = trimethylsilyl) and HNR_2. ^{1}H NMR spectroscopy and X-ray crystallography confirmed the presence of an additional coordinated amine. Eyring analysis of the rate of cyclization of 1-aminopent-4-ene catalyzed by $[Cp^*_2LaCH(TMS)_2]$ over a 25–60 °C temperature range revealed an activation barrier for migratory insertion of $\Delta H^{\neq} = (12.7 \pm 1.4)$ kcal mol^{-1} and $\Delta S^{\neq} = (-27.0 \pm 4.6)$ cal mol^{-1}. These values are consistent with a highly ordered transition state. Reactions conducted with N-deuterium-labeled aminoalkenes revealed a primary KIE of 2.7–5.2. If migratory insertion by a concerted pathway involving a four-membered transition state were turnover limiting, a primary KIE would not be observed. Therefore, the authors propose that a proton on the coordinated amine ligand stabilizes the transition state for migratory insertion by protonating the forming Ln–C bond as the alkene inserts into the Ln–N bond (Scheme 12).



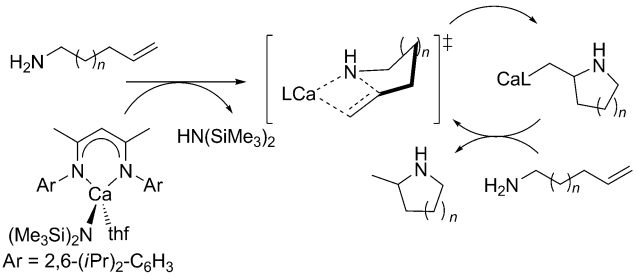
Scheme 12. Proposed proton-assisted mechanism of alkene insertion into an Ln–N bond.

Fragalá, Marks, and co-workers have also studied the mechanism of these hydroamination reactions by computational methods. They calculated the enthalpic and free-energy activation barriers for intramolecular hydroamination of aminoalkenes. The computed barriers indicate that the migratory insertion step is turnover limiting.[58] The activation parameters computed for the cyclization of 1-aminopent-4-ene were $\Delta H^{\neq} = 11.3$ kcal mol^{-1}, $\Delta G^{\neq} = 12.5$ kcal mol^{-1}, and $\Delta S^{\neq} = -14.6$ cal mol^{-1}. Because the catalytic hydroamination requires temperatures higher than room temperature, either the free energy is calculated incorrectly, or migratory insertion is not the turnover-limiting step. In addition, the computed transition state for the migratory insertion step did not include the proposed proton assistance from a coordinated amine ligand to account for the primary isotope effect.

Marks and co-workers also investigated hydroaminations catalyzed by actinide complexes ligated by constrained-geometry ligands (Scheme 13). The activity of these organo-



Scheme 13. Actinide-catalyzed hydroamination of aminoalkenes.



Scheme 14. Proposed mechanism of calcium-catalyzed hydroamination of aminoalkenes.

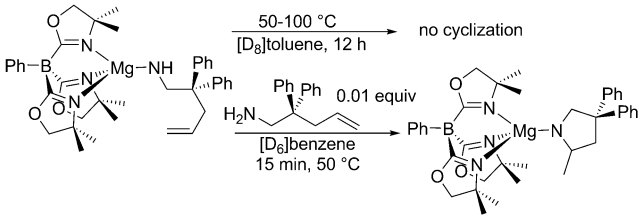
actinide catalysts is similar to that of the most active lanthanide catalysts and exceeds that of most Group IV transition-metal systems. The scope of these systems includes aminoalkenes, aminoalkynes, aminoallenes, and aminodienes. The catalytic reaction was proposed to occur by migratory insertion of a pendant alkene into an An–N bond.[59,60]

A series of Group IV complexes that catalyze the cyclization/hydroamination of secondary amines also has been reported recently. Typically, hydroaminations catalyzed by early-transition-metal complexes occur by [2+2] cycloadditions of an alkene across a metal–imido bond.[61,62] However, hydroamination by this mechanism can only lead to the addition of primary amines to alkenes; a metal imido complex cannot form from a secondary amine.

Yet, Gribkov and Hultzsch reported the intramolecular hydroamination of secondary aminoalkenes catalyzed by $[Cp_2ZrMe]^+[MeB(C_6F_5)_3]^-$,[63] and Stubbert and Marks reported intramolecular hydroaminations of secondary aminoalkenes and aminoalkynes catalyzed by zirconium complexes ligated by the same constrained-geometry ligand shown in Scheme 13.[64] Both authors proposed that the new C–N bond forms by migratory insertion. In addition, Majumder and Odom reported the intramolecular hydroamination of primary aminoalkenes catalyzed by titanium and zirconium dipyrrolylmethane complexes.[65] Based on the competitive formation of products from hydroamination and oxidative amination, these reactions likely occur by insertion of an alkene into an M–N bond.

Hill and co-workers reported the first hydroamination of aminoalkenes catalyzed by alkaline-earth-metal complexes, and these reactions also are proposed to proceed by migratory insertion of the alkene into the M–N bond. Hill and co-workers examined the intramolecular hydroamination of aminoalkenes catalyzed by calcium amido and magnesium amido complexes ligated by β diketiminates (Scheme 14).[66,67] Kinetic analysis of the reaction catalyzed by the magnesium system revealed a first-order dependence on catalyst concentration and an inverse first-order dependence on the concentration of aminoalkene. Although preliminary, these data are consistent with a mechanism involving turnover-limiting insertion of alkene into the M–N bond, which occurs after dissociation of one substrate from the metal center.

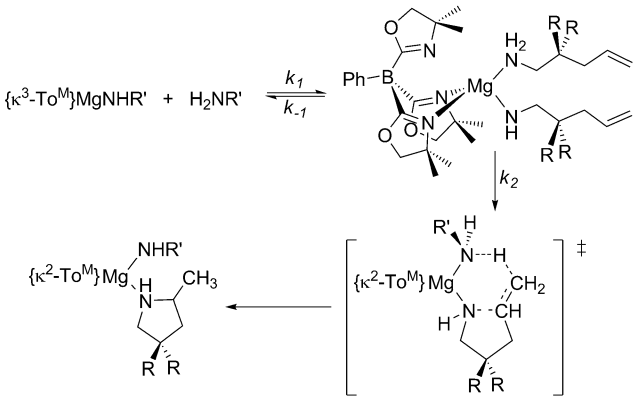
More recently, Sadow and co-workers gained evidence for an alternative pathway for C–N bond formation in hydroaminations catalyzed by d^0 systems. They reported the hydroamination of aminoalkenes catalyzed by a magnesium(II) amido complex ligated by tris(4,4-dimethyl-2-oxazolinyl)phenylborate ([To^M]).[68] The reaction of [To^M]MgMe and aminoalkenes occurs with a large primary KIE, like the KIE Marks and co-workers[53] obtained for the hydroamination catalyzed by lanthanide metallocene complexes. However, the rates of these hydroaminations are first order in Mg and first order in aminoalkene, thus suggesting that binding of the substrate occurs reversibly prior to cyclization. However, the isolated [To^M]Mg primary amido complex containing a tethered alkene did not undergo cyclization in the absence of added amine. The complex underwent cyclization in the presence of a catalytic amount of primary amine to form an amido complex containing the cyclized product bound through the secondary amine function (Scheme 15). Thus, an additional amine ligand is necessary to promote cyclization.



Scheme 15. Reactions of [To^M]Mg amido complexes in the presence and absences of added amine.

On the basis of these data, Sadow and co-workers[68] proposed that cyclization of the [To^M]Mg amido complex occurs by substitution of one arm of the [To^M] ligand for an amine, followed by concerted rate-limiting C–N and C–H bond formation through a six-centered transition state (Scheme 16). By this proposed mechanism, hydroaminations would not proceed through the typical pathway involving migratory insertion of the alkene into a M–N bond.

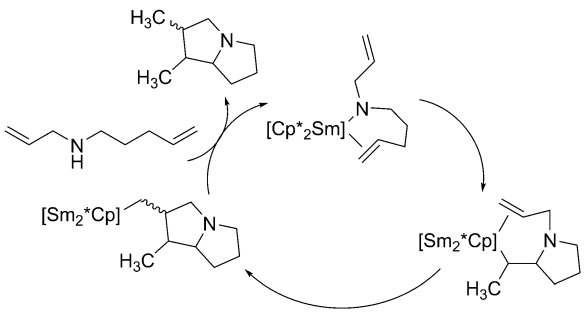
In addition, Sadow and co-workers reported that zirconium[69] and yttrium[70] complexes coordinated by similar ligand frameworks catalyze hydroamination, and the mechanistic data in this study imply that these reactions occur through the same six-membered transition state as that proposed for reactions of the alkaline earth systems. Sub-



Scheme 16. Proposed reaction mechanism of [To^M]Mg-catalyzed hydroamination of aminoalkenes.

sequently, Schafer and co-workers proposed a similar transition state for the hydroamination of primary and secondary aminoalkenes catalyzed by zirconium complexes ligated by a tethered bis(ureate).[71]

The proposed six-membered transition state accounts for the kinetic data obtained on the systems described by the groups of Sadow and Schafer and is a possible transition state for C–N bond formation by the Ln and An systems described by the group of Marks.[53,58–60] The orders in substrate, when combined with information on the resting state, and the KIE values suggest parallels between these systems. The large KIEs observed for many of the reactions suggest that cleavage of the N–H bond occurs in the turnover-limiting step. Although the computed barriers for alkene insertion are moderate, they do not account for cleavage of an N–H bond during the transition state. Thus, it seems possible that the mechanism of lanthanide-catalyzed hydroamination occurs through a related six-membered transition state. At the same time, the lanthanide systems described by Marks and co-workers.[72] have been shown to catalyze tandem C–N and C–C bond-forming additions to alkenes. As shown in Scheme 17, these data imply that the reactions, at least those of the secondary N-allylamines, form an intermediate containing a M–C bond. An alternate explanation for the primary kinetic isotope effect and zero-order dependence on substrate concentration is reaction by a mechanism involving turnover-limiting formation of a metal imido intermediate.[73,74]



Scheme 17. Bicyclization of an aminodiene, thus suggesting the presence of a M–C bond and a migratory insertion step.

Additional studies are clearly needed to delineate the relationships between the experimental data and mechanisms of hydroamination catalyzed by alkaline earth, group IV, and lanthanide complexes.

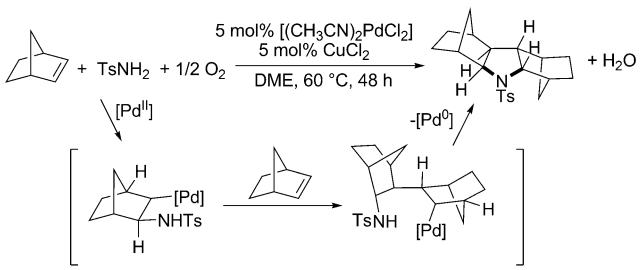
Catalytic Reactions Involving Insertions into Pd–N Bonds

Most published literature on palladium-catalyzed oxidative amination reactions of alkenes with amides, commonly termed the aza-Wacker reaction, state that the mechanism involves nucleophilic attack of a nitrogen nucleophile onto a metal-coordinated olefin. A number of early, elegant studies demonstrated that the addition of nitrogen nucleophiles to a palladium-coordinated alkene formed new C–N bonds by *anti* aminopalladation.[75–77] Hegedus and co-workers reported the first catalytic oxidative amination of alkenes with benzoquinone as an oxidant to regenerate the palladium(II), and proposed that these reactions occurred by *anti* addition of the palladium and the nucleophile across the alkene.[78] Over the next two decades, several studies described palladium-catalyzed amination reactions, but none contained evidence for a *syn* aminopalladation by migratory insertion of the alkene into a Pd–N bond.[79–82] Thus, migratory insertion was not thought to be part of the mechanism of palladium-catalyzed aminations of alkenes.

During the past ten years, however, this view of the mechanism has changed. Palladium-catalyzed amination reactions now thought to occur by a migratory insertion step include carboaminations,[83–86] oxidative aminations,[87–89] chloroaminations,[90] aminoacetoxylations,[91] diaminations,[92] and hetero-Heck-type transformations.[93] In some cases, stereochemical evidence for *syn* aminopalladation by migratory insertion has been gained. Because reviews detailing known examples of palladium-catalyzed reactions involving an aminopalladation step are available,[94,95] this review focuses on the migratory insertion step.

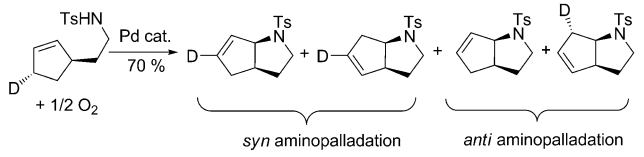
Stahl and co-workers reported the first palladium-catalyzed intermolecular oxidative amination of unactivated alkenes with amides.[91] The stereochemistry of the product that arose from the oxidative amination of norbornene was consistent with a mechanism involving *syn* aminopalladation. The oxidative coupling of two norbornenes and *p*-toluenesulfonamide in the presence of 5 mol% [$(CH_3CN)_2PdCl_2$] in DME under 1 atm of O_2 and 5 mol% $CuCl_2$ at 60 °C formed a cyclic product with relative configurations in the product that are consistent with norbornene insertion into the Pd–N bond (Scheme 18).[96]

Stahl and co-workers subsequently investigated the mechanism of palladium-catalyzed oxidative amination reactions with several palladium catalysts under varied reaction conditions.[88] In most cases, the relative configuration of the products from the oxidative cyclization of a deuterium-labeled, sulfonamide-substituted aminoalkene are consistent with a mechanism involving *syn* aminopalladation (migratory insertion; Table 1). Amination of substrates containing a nosyl group instead of a tosyl group formed products exclusively derived from *syn* aminopalladation. Because the NH proton of the nosyl group is more acidic than the NH proton of the



Scheme 18. Proposed reaction mechanism of the palladium-catalyzed oxidative amination of norbornene. DME = dimethoxyethane, Ts = 4-toluenesulfonyl.

Table 1: Oxidative amination of a sulfonamide-substituted aminoalkene.



Entry	Pd catalyst[a]	*t* [h]	Yield [%]	Product ratio *syn* amino-palladation	Product ratio *anti* amino-palladation
1	$Pd(OAc)_2$/DMSO	15	70	100:0	–
2	$Pd(OAc)_2$/py	15	84	98:2	–
3	$Pd(O_2CCF_3)_2$/py	15	85	88:12	–
4	$Pd(IMes)(O_2CCF_3)_2$/BzOH	72	60	43:8	37:12
5	$Pd(O_2CCF_3)_2$/sp	72	72	59:41	–

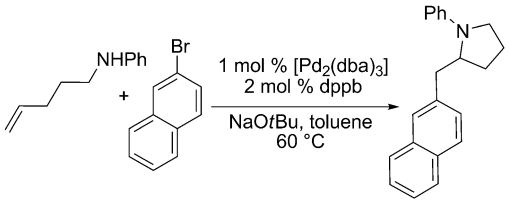
[a] IMes = 1,3-di(2,4,6-trimethylphenyl)imidazolin-2-ylidene, py = pyridine, sp = sparteine.

tosyl group, the palladium amido species is formed more readily with a nosylamide than with a tosylamide. Lower stereoselectivity from the oxidative cyclization of tosyl-substituted carboxamide substrates was observed with most catalyst combinations, although the origin of the selectivity is not well understood.

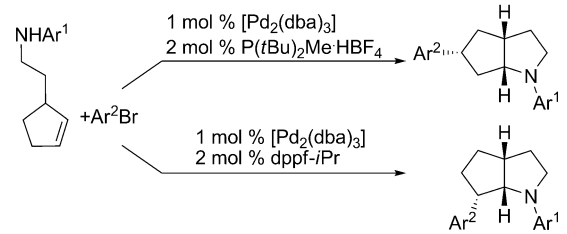
Further mechanistic investigation on the intramolecular amidation of alkenes catalyzed by $[(IMes)Pd(O_2CCF_3)_2H_2O]$, which forms products from both *syn*- and *anti*-amidopalladation pathways (Table 1; entry 4), revealed that reactions conducted in the presence of Na_2CO_3 exclusively formed products from a *syn*-amidopalladation pathway.[97] In the absence of base, reaction by both *syn* amidopalladation by formation of a palladium sulfonamidate complex and subsequent migratory insertion and an *anti* amidopalladation by a nucleophilic attack on a coordinated alkene occur. In the presence of Na_2CO_3, a threefold rate enhancement was observed. In the presence of base, the product from the *syn*-amidopalladation pathway presumably forms exclusively because the base promotes formation of a palladium sulfonamidate complex.

Recently, Weinstein and Stahl investigated the enantioselectivity of both the *syn* and *anti*-amidopalladation pathways catalyzed by a palladium complex ligated by chiral, nonracemic pyridine oxazoline ligands.[98] In these examples, reactions that occurred by migratory insertion of an alkene into a Pd–N bond formed the product with low enantioselectivity. However, amidocyclization reactions that occured primarily by *trans* amidopalladation formed products with excellent enantioselectivity (96%).

Ney and Wolfe investigated the stereochemistry of palladium-catalyzed carboamination of N-arylaminoalkenes with aryl bromides. The reaction of N-arylaminoalkenes with aryl bromides in the presence of 1 mol% $[Pd_2(dba)_3]$, 2 mol% dppb ligand, and 1.2 equivalents NaO*t*Bu, in toluene at 60 °C generated carboaminated products (see Scheme 19 for a representative example).[99] By conducting the reaction with a substrate containing a cyclic alkene, they gained strong evidence that the C–N bond-forming step of these multicomponent reactions occurs by migratory insertion of the alkene into a Pd–N bond. Careful selection of the phosphine ligand resulted in selective synthesis of either the 5-aryl or 6-aryl carboaminated products (Scheme 20).[84] Reactions catalyzed by the combination of $[Pd_2(dba)_3]$ and the chelating phosphine dppf-*i*Pr provided primarily the 6-aryl octahydrocyclopenta[β]-pyrrole product. However, analogous reactions conducted with the combination of $[Pd_2(dba)_3]$ and $P(tBu)_2Me{\cdot}HBF_4$ generated the 5-aryl isomer with high diastereoselectivity.



Scheme 19. Palladium-catalyzed carboamination of N-arylaminoalkenes with aryl bromides.



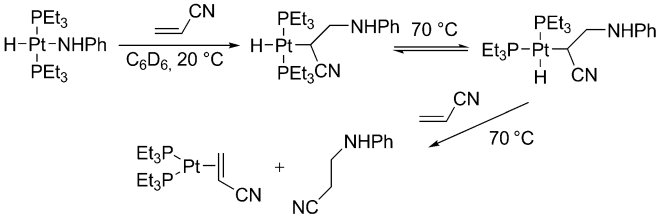
Scheme 20. Palladium-catalyzed carboamination of N-arylaminoalkenes to form either 5-aryl or 6-aryl products. dppf = 1,1′-bis(diphenylphosphino)ferrocene.

In addition, the group of Wolfe reported examples of asymmetric palladium-catalyzed carboamination reactions to form enantiomerically enriched 2-(arylmethyl)- and 2-(alkenylmethyl)pyrrolidines, which likely occur by migratory insertion into a Pd–N bond.[85] In contrast to the amidocyclization reactions, reported by Stahl and co-workers,[98] which form the product with low enantioselectivity when they occur by migratory insertion, the cyclizations reported by Mai and Wolfe, which occur by migratory insertion, form the products with up to 94% *ee*.

Reactions of Metal Amido Complexes with Alkenes for which Direct Evidence has been Gained on Migratory Insertion into an M–N Bond

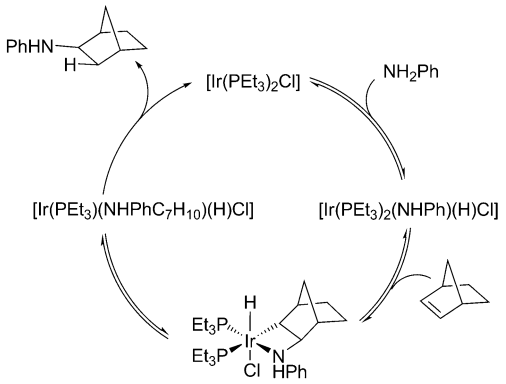
Although stereochemical and kinetic analysis of many of the catalytic reactions described in this review provide convincing evidence that alkene insertion into an M–N bond occurs as part of the mechanism, direct evidence of insertion has not been gained for any of these systems. In none of these cases was a metal amido complex isolated and shown to react with an alkene to transfer an amido group to the olefin. However, a few examples of metal amido complexes that react with alkenes to generate metal alkyl complexes or that react with alkenes to form organic products that have relative configurations consistent with a *syn* amidometallation, have recently been reported, and these examples are included as part of the next section.

Cowan and Trogler reported the first example of an isolated metal amido complex that reacts with an alkene to generate products resulting from the "formal" insertion of an unsaturated C=C double bond into an M–N bond.[100] The PEt_3-ligated platinum complex $[(PEt_3)_2Pt(H)(NHPh)]$ was shown to react with acrylonitrile at 20 °C in C_6D_6 to generate an alkyl complex by 2,1-insertion of the acrylonitrile (Scheme 21). Upon warming to 70 °C, this complex underwent C–H bond-forming reductive elimination to generate the product from one cycle of hydroamination. Although this reaction is reported to occur by a migratory insertion mechanism, no evidence was presented that would rule out direct attack of the amido complex onto the activated acrylonitrile. Reactions with less activated olefins did not occur.



Scheme 21. Proposed reaction mechanism of platinum amides with acrylonitrile.

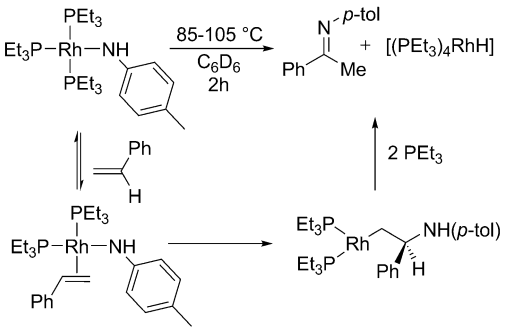
In 1988, Milstein and co-workers reported strong evidence for migratory insertion of an alkene into a M–N bond as part of studies on an iridium-catalyzed addition of aniline to norbornene (Scheme 22).[101] Addition of aniline to a slurry of norbornene and $[Ir(PEt_3)_2(C_2H_4)_2Cl]$ in refluxing Et_2O resulted in the formation of a well-characterized azametallacyclic iridium complex. This intermediate was proposed to form by oxidative addition of the N–H bond in aniline to $[Ir(PEt_3)_2(C_2H_4)_2Cl]$, with subsequent migratory insertion of the norbornene into the Ir–N bond. The precursor to the insertion step was not observed, but the addition of excess PEt_3 to the azametallacycle, or the reaction of $[Ir(PEt_3)_3Cl]$, aniline, and norbornene, formed the related, coordinatively saturated complex $[Ir(PEt_3)_3(NHPh)(H)Cl]$. Warming of the



Scheme 22. Proposed reaction mechanism of iridium-catalyzed addition of aniline to norbornene.

azametallacyclic iridium complex to 45 °C resulted in C–H bond-forming reductive elimination to release *exo*-2-(phenylamino)norbornane. Catalytic addition of aniline to norbornene was also observed, with 10 mol% $[Ir(PEt_3)_2(C_2H_4)_2Cl]$ and 0.2 mol% $ZnCl_2$, to form *exo*-2-(phenylamino)norbornane with an average of six turnovers. Recently, several examples of enantioselective, iridium-catalyzed hydroamination reactions of strained bicyclic alkenes were reported, along with evidence that the reactions occur by migratory insertion of the alkene into an Ir–N bond.[102–105]

More recently, Hartwig and co-workers reported the transfer of an amido group to alkenes and vinylarenes from an isolated rhodium amido complex.[106] A series of triethylphosphine-ligated rhodium amido complexes react with vinylarenes at 60 °C to from the corresponding N-aryl imine and a dimeric hydridorhodium amide complex (Scheme 23).



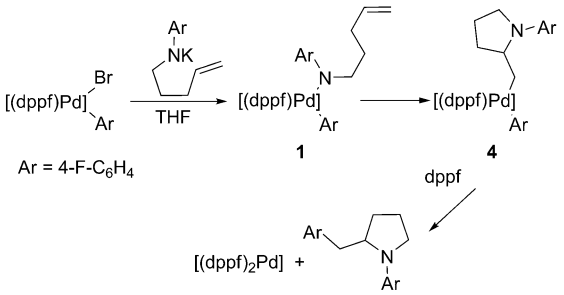
Scheme 23. Reactions of rhodium amides with vinylarenes.

These complexes also react with propylene to form N-arylimine products at 95 °C. The rate of the reaction of $[(PEt_3)_3RhNHAr]$ with styrene was determined to be first order in the concentration of the rhodium amido complex and styrene, and inverse first order in the concentration of PEt_3. These data are consistent with the mechanism shown in Scheme 23, involving reversible exchange of styrene for PEt_3 in the starting complex and subsequent irreversible migratory insertion of the vinylarene into the Rh–N bond.

Although the stoichiometric reactions of alkenes with iridium amido, platinum amido, and rhodium amido com-

plexes demonstrated that alkene insertion into a late-transition-metal–nitrogen bond is feasible, only recently have palladium amido complexes been reported to react with an olefin to generate a new C–N bond. In 2010, reports from Wolfe and co-workers[107] and Hartwig and co-workers[108] described two different phosphine-ligated palladium amido complexes proposed to react with unactivated alkenes by a migratory insertion pathway. These reports, along with subsequent studies[109,110] on the effect of the ancillary and amido ligands on the rate of the insertion step, provide detailed information on the factors controlling the rates of migratory insertion of an alkene into a metal–heteroatom bond.

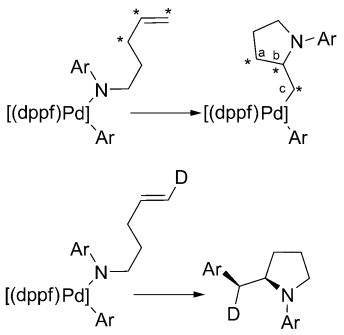
Wolfe and co-workers reported studies on the potential amido intermediate in palladium-catalyzed carboamination reactions. To examine the mechanism of these reactions, they prepared a palladium amido complex and studied the migratory insertion of a tethered alkene into the Pd–N bond in situ.[107] Upon mixing [(dppf)Pd(4-F-C_6H_4)Br] and KN(4-F-C_6H_4)(CH_2)$_3$CH=CH_2 in THF at room temperature, the [(dppf)Pd(4-F-C_6H_4)][N(4-F-C_6H_4)(CH_2)$_3$CH=CH_2] complex (**1**) was formed (Scheme 24; see Scheme 26 for compounds **2**



Scheme 24. Proposed reaction mechanism of arylpalladium halide complexes with KN(Ar)(CH_2)$_3$CH=CH_2.

and **3**). They characterized this complex by the presence of a pair of doublet resonances at $\delta = 24.9$ ppm ($J = 38.1$ Hz) and $\delta = 9.0$ ppm ($J = 35.5$ Hz) in the ^{31}P NMR spectrum and two new resonances at $\delta = -123.7$ and $\delta = -137.3$ ppm in the ^{19}F NMR spectrum. This complex underwent migratory insertion of the pendant alkene into the Pd–N bond to generate a new intermediate proposed to be an alkylpalladium aryl complex. This complex decomposed by C–C bond-forming reductive elimination to form the pyrrolidine product and [(dppf)$_2$Pd] at a rate comparable to that by which it formed.

The structure of the alkylpalladium aryl intermediate was cleverly elucidated by preparation of a complex containing an amido ligand bearing a pendant, ^{13}C-labeled alkene (Scheme 25). The chemical shifts of the labeled carbon atoms in the proposed alkylpalladium amido intermediate were inconsistent with those of a coordinated alkene. The chemical shift of C_β ($\delta = 61.9$ ppm) indicated that it is adjacent to a heteroatom. This connectivity is inconsistent with a six-membered palladacycle that would result from alkene insertion into the palladium–aryl bond. Instead, this con-



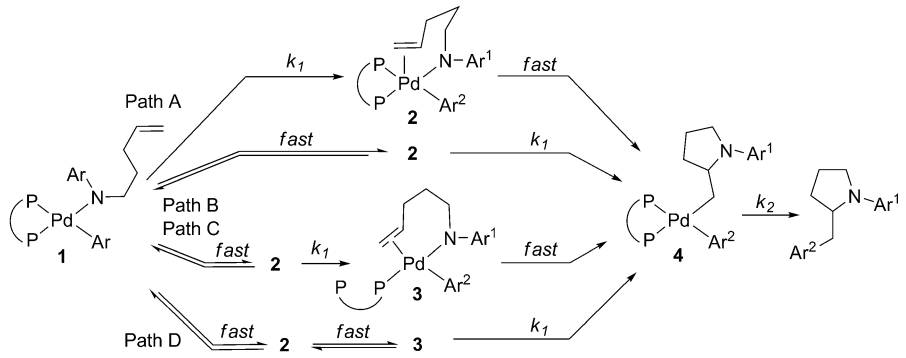
Scheme 25. Reactions of [(dppf)Pd] amide complexes containing isotopically labeled alkenes.

nectivity is consistent with the product of alkene insertion into a Pd–N bond (**4** of Scheme 24). Therefore, the authors concluded that this reaction occurs by a pathway involving aminopalladation of the alkene. The stereochemical configuration of the pyrrolidine products formed from the reaction of a palladium amido complex containing a *trans*, deuterium-labeled alkene indicated that net *syn* addition of the aryl group and the nitrogen atom occurred across the alkene.

The concentration of the amido complex, alkylpalladium aryl intermediate, and pyrrolidine were monitored over the course of the reaction. Because the rates of each step are within an order of magnitude of each other, the rate constant for each step was determined by fitting the rate equations for consecutive first-order reactions. Eying plot analysis indicated that the enthalpic barrier for alkene insertion into the Pd–N bond was 24.8 kcal mol^{-1}.

In a subsequent article, Wolfe and co-workers[110] reported the electronic and steric effects of the ancillary, amido, and aryl ligands on the rate constants, k_1 and k_2, for formation and consumption, respectively, of the aminoalkyl intermediate (Scheme 26). Complexes containing electron-donating substituents on the N-aryl group converted from **1** into **4** by migratory insertion and formed the carboaminations product by reductive elimination from **4** more rapidly than complexes containing electron-withdrawing substituents on the N-aryl group. A Hammett analysis using the σ_p parameters generated linear plots of $\log(k_R/k_H)$ with good fits from which $\rho = (-2.5 \pm 0.2)$ and $\rho = (-9.2 \pm 0.06)$ were obtained for k_1 and k_2, respectively. A clear correlation was not observed between complexes containing varying substituents on the aryl ligand. The effect of the electronic properties of the ancillary ligand on the conversion of **1** into **4** was also investigated. The complex ligated by the least electron donating of the dppf derivatives (the ligand containing *p*-CF_3 substituents, dppf-*p*-CF_3) underwent conversion from **1** into **4** about 1.5 times faster than the complex ligated by the unsubstituted dppf.

The effect of bite angle on the reactivity of arylpalladium amido complexes was examined, but quantitative rate data were not obtained. Qualitative studies showed that amido complexes ligated with bis(phosphine)s containing large bite angles (*N*-methyl-nixanthphos and xantphos) formed pyrrolidine products rapidly at room temperature. In contrast, amido complexes ligated with bis(phosphine)s containing small bite angles (dppe, dpp-benzene, dppp, binap) failed to



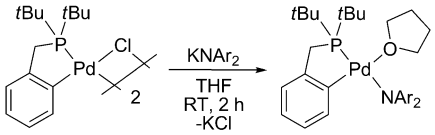
Scheme 26. Possible pathways of aminopalladation in dppf-ligated arylpalladium amido complexes.

react at elevated temperatures (60 °C) or decomposed. In addition, the authors demonstrated that a complex containing an amido ligand tethered to a 1,1-disubstituted alkene reacts to generate the corresponding pyrrolidine product, although this reaction occurred more slowly than that of the analogous complex containing a monosubstituted alkene. Complexes containing *cis*- or *trans*-1,2-disubstituted alkenes did not react.

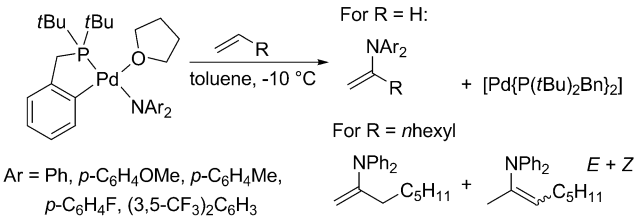
Several mechanisms were considered for the conversion of the amido complex **1** into the aminoalkyl complex **4**. Four pathways are outlined in Scheme 26, two of which involve a five-coordinate intermediate and two of which involve dissociation of half of the chelating phosphine. Several pieces of data suggest that the insertion occurs by path C. A positive entropy of activation was measured for the conversion of **1** into **4**. One would expect a negative entropy of activation for reaction by path A because the overall order of the system is greater in the transition state from **1** to **4**, whereas one would expect a positive $\Delta S^{\ddagger}$ for Path C involving rate-limiting dissociation of phosphine. Moreover, the conversion of **1** into **4** was faster for complexes containing less-donating bis(phosphine) ligands than more-donating bis(phosphine) ligands, and dissociation of one arm of a less-donating phosphine ligand should be faster than dissociation of one arm of a more-donating phosphine. If Wolfe's conclusion is valid, then the kinetic data reveal the electronic effects on the dissociation of the phosphine, rather than the migratory insertion step.

Concurrent with the work from Wolfe, Hartwig and co-workers described a series of palladium diarylamido complexes which react with unactivated alkenes to form enamine products.[108] These reactions were shown to occur by intermolecular migratory alkene insertion into the Pd–N bond. To promote the formation of monomeric amido complexes and discourage C–N bond-forming reductive elimination, complexes containing a cyclometallated, monoanionic benzylphosphine were studied. Stable thf-ligated amido complexes were prepared from the reaction of $[\{(P\text{-}C)PdCl\}_2]$ with $KNAr_2$ in THF at room temperature (Scheme 27). A series of complexes were synthesized containing different diarylamido ligands, and these complexes were isolated and fully characterized by X-ray crystallography.

The thf-ligated amido complexes reacted with ethylene at −10 °C and with 1-octene at 80 °C to form enamine products in good yields (Scheme 28). Complexes containing more-electron-donating amido groups reacted faster than those



Scheme 27. Synthesis of thf-ligated palladium diarylamido complexes.

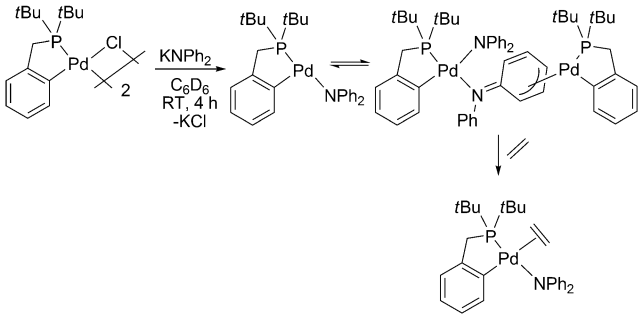


Scheme 28. Reactions of thf-ligated palladium amides with ethylene and octene.

containing less-electron-donating amido groups. For example, the complex containing a di-*p*-ansiylamide reacted 10 times faster than the complex containing a less electron-donating diphenyl or di-*p*-fluorophenylamide.

The mechanism of the reaction of ethylene with the palladium amides was examined by kinetic experiments and an assessment of the stereochemical outcome of the insertion step. The reaction was found to be first order in palladium amide and ethylene, and inverse first order in thf. These data are consistent with ligand substitution of ethylene for thf and subsequent migratory insertion of the alkene into the Pd–N bond of a four-coordinate ethylene amido intermediate. Reaction of the palladium amide with *cis*-$[D_2]$ethylene generated enamine products with an alkene geometry expected to result from a concerted migratory insertion into the Pd–N bond and subsequent β-hydrogen elimination, C–H bond-forming reductive elimination, and binding of the added phosphine to form the observed Pd^0 product.

An analogous diarylamido complex lacking a thf ligand was prepared from the reaction of $[\{(P\text{-}C)PdCl\}_2]$ with $KNAr_2$ in benzene. In solution at room temperature, this complex is a three-coordinate monomer. In solution at low temperature and in the solid state, the complex is an unsymmetrical dinuclear species (Scheme 29). Addition of ethylene to the

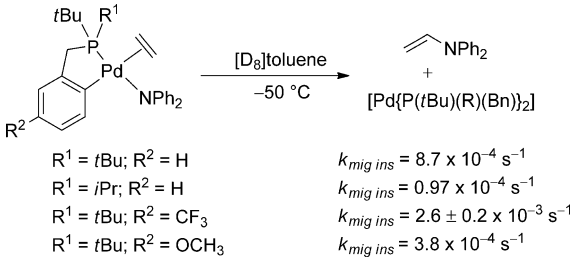


Scheme 29. Preparation of thf-free and ethylene-bound palladium amides.

thf-free, three-coordinate palladium amide at −65 °C generated a four-coordinate ethylene amido intermediate, which undergoes migratory insertion at −40 °C. The ethylene amido intermediate was characterized by NMR spectroscopy at low temperature, including the observation of a new, broad resonance at $\delta = 106.5$ ppm in the ^{13}C NMR spectrum at −65 °C when the thf-free, palladium amido complex was treated with $^{13}CH_2{=}^{13}CH_2$.

A full account of the mechanism by which these complexes react with ethylene was recently reported, and the steric and electronic effects imparted by the ancillary ligand on the rate of migratory insertion were described.[109] Addition of varying excess amounts of ethylene to the three-coordinate amido complex revealed that binding of ethylene to form an olefin adduct is rapid and reversible. To allow the rate of migratory insertion to be measured directly, reaction conditions were established under which the alkene amido complex was the major complex in solution. With an excess of ethylene (150 equiv) at −50 °C, the alkene amido complex comprised over 85 % of the complexes in solution, and the rate of migratory insertion could be measured directly. The proposed reaction mechanism of these palladium amides with ethylene is illustrated in Scheme 30. The rate constant for the migratory insertion step was found to have a $\Delta G^{\ddagger}$ of 16.0 kcal mol^{-1}.

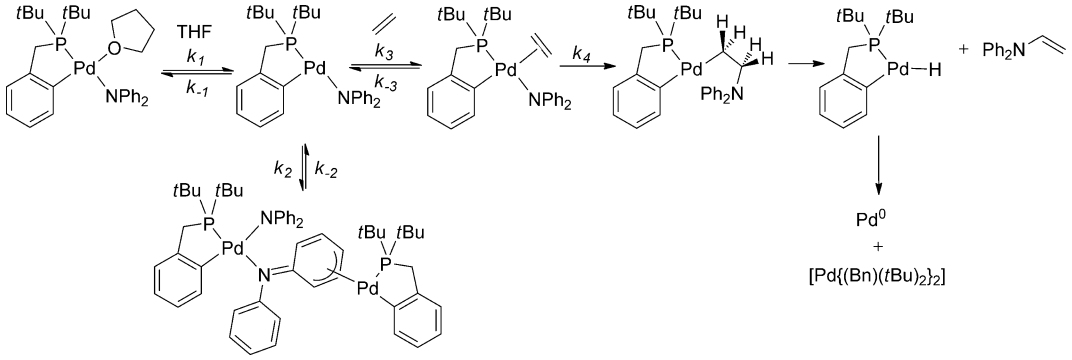
To examine the steric effects of the ancillary ligand on the rate of migratory insertion, an amido complex ligated by a cyclometallated benzyl(isopropyl)(*tert*-butyl)phosphine ligand was prepared, and the reactivity of this complex was compared to that of the 2-$(t\text{Bu})_2\text{PCH}_2\text{C}_6\text{H}_4$-ligated complex by both experimental and computational methods. The rate constant for migratory insertion of the less sterically encumbered 2-$(t\text{Bu})(i\text{Pr})\text{PCH}_2\text{C}_6\text{H}_4$-ligated complex was almost an order of magnitude smaller than the rate constant for migratory insertion of the 2-$(t\text{Bu})_2\text{PCH}_2\text{C}_6\text{H}_4$-ligated complex (Scheme 31).



Scheme 31. Rate constants for migratory insertion reactions of amido-palladium ethylene complexes. DMSO = dimethylsulfoxide.

Computational studies helped reveal the effect of the steric properties of the ligand on the individual steps of the migratory insertion pathway. The computed free-energy barriers for the reaction of these complexes and for the reaction of an analogous complex ligated by a truncated 2-$(CH_3)_2\text{PCH}_2\text{C}_6\text{H}_4$ were computed with DFT methods. The calculated barriers were consistent with those measured experimentally. The bulky substituents on the phosphine create stronger steric interactions in the ground state than in the transition state for migratory insertion. Thus, the reactions of complexes ligated by more bulky ancillary ligands undergo migratory insertion with a lower barrier than those of complexes ligated by less bulky ancillary ligands.

Because the reactions of the two thf-ligated analogues of these complexes occur with similar rate constants at −10 °C, this steric effect imparted by the ancillary ligand on the migratory insertion step must be counterbalanced by the steric effect on the binding of the alkene to the three-coordinate complex. The K_{eq} for binding of thf to the complex of the less sterically demanding ligand 2-$(t\text{Bu})(i\text{Pr})\text{PCH}_2\text{C}_6\text{H}_4$ was found to be two times greater than the K_{eq} for binding of thf to the more sterically demanding ligand 2-



Scheme 30. Proposed reaction mechanism of benzylphosphine-ligated palladium amides with ethylene.

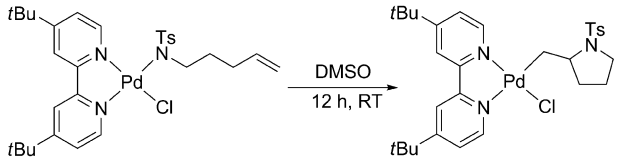
$(t\text{Bu})_2\text{PCH}_2\text{C}_6\text{H}_4$. Similarly, K_{eq} for binding of ethylene to the less sterically congested complex was 13 times greater than the K_{eq} for binding of thf to the more sterically congested complex. Thus, the equilibrium constants measured for each complex counterbalance the relative rate constants for migratory insertion, and the overall rate constants for the reaction of ethylene with the two thf-ligated amides are similar to each other.

To evaluate the electronic effect of the ancillary ligands on the rate constant for migratory insertion, amido complexes ligated by cyclometalated di-*tert*-butylbenzylphosphine ligands containing *meta*-trifluoromethyl and *meta*-methoxy substituents on the aryl ring were studied. The effect of the electronic parameters of the alkene on the rate of insertion was examined by reacting the thf-ligated palladium amide with a series of vinylarenes containing different substituents on the aryl ring. Complexes ligated by more weakly donating ancillary ligands underwent migratory insertion faster than those containing more electron-donating phosphines (Scheme 31).

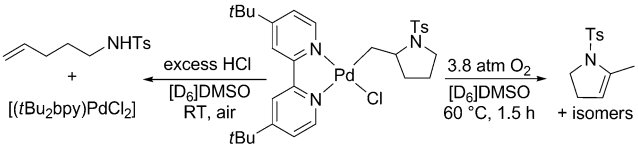
Finally, to evaluate the electronic effect of the alkene on the rate constant for migratory insertion, palladium amides were allowed to react with a series of vinylarenes containing electron-donating and electron-withdrawing substituents. The reactions of more-electron-poor vinylarenes occurred faster than those of more-electron-rich vinylarenes. A Hammett analysis revealed a ρ value of 1.04. Thus, an accumulation of negative charge or a decrease in the partial positive charge on the olefin occurs during the migratory insertion process. Thus, this study on the insertion of alkenes into this palladium amido complex provides an unusually detailed view into the effect of the steric and electronic properties of the alkene, reactive ligand, and ancillary ligands on the rate of the reaction.

Most recently, White and Stahl reported the intramolecular migratory insertion of an unactivated olefin into the Pd–N bond of a well-defined palladium sulfonamidate complex.[111] The air-stable palladium amidate complex was prepared from the reaction of $[(t\text{Bu}_2\text{bpy})\text{PdCl}_2]$ and a single equivalent of $\text{NaN(Ts)}[(\text{CH}_2)_3\text{CH=CH}_2]$ in CH_2Cl_2 at room temperature, and was fully characterized by NMR spectroscopy and X-ray crystallography. The reaction of the sulfonamidate complex in DMSO over 12 hours formed an alkylpalladium chloride complex. This complex was proposed to form by dissociation of the chloride ligand and subsequent migratory insertion of the pendant alkene into a Pd–N bond through a four-coordinate intermediate (Scheme 32). Under aerobic conditions at 60 °C, the alkyl complex underwent β-hydrogen elimination to yield a mixture of N-tosylpyrrole and N-tosylpyrrolidine products (Scheme 33). Reaction of a palladium sulfonamidate complex containing a stereochemically defined, deuterium-labeled amido ligand formed products resulting from *syn* aminopalladation.

Addition of excess HCl to the aminoalkylpalladium chloride complex resulted in the rapid formation of 4-pentenyl tosylamide and $[(t\text{Bu}_2\text{bpy})\text{PdCl}_2]$ (Scheme 33). Thus, the alkyl complex undergoes de-insertion of the sulfonamide (β-amidate elimination) faster than β-hydrogen elimination, and the resulting palladium amidate complex is protonated by

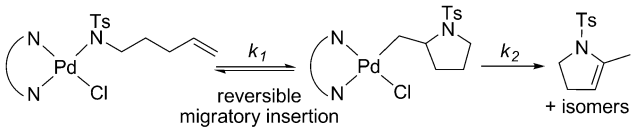


Scheme 32. Reaction of palladium sulfonamidate complex.



Scheme 33. Reactions of di-*tert*-butylpyridine-ligated palladium alkyl complex.

HCl. This result implies that alkene insertion into the palladium–amidate bond is reversible. Indeed, the reactions of a series of palladium sulfonamidate complexes containing different *para*-substituted benzenesulfonamidate groups were monitored by ^{1}H NMR spectroscopy. These sulfonamide complexes underwent migratory insertion to form an equilibrium mixture of aminoalkyl palladium and sulfonamidate palladium complexes. These complexes decayed in concert with the formation of heterocylic products (Scheme 34). The



Scheme 34. Proposed reaction mechanism of palladium sulfonamidate complexes.

rate constant for the migratory insertion step was measured for each complex, and the complexes containing more electron-donating groups on the amidate ligand reacted more rapidly than those containing less electron-donating groups. This trend parallels that observed for the insertion of ethylene into palladium diarylamido bonds.

Conclusions

Recently, a series of catalytic aminations and alkoxylations of alkenes have been reported and appear to occur by migratory insertion of an alkene into either an M–N or M–O bond as one step of the proposed catalytic cycle. In addition, examples of isolated amido and alkoxo complexes that react with alkenes were reported. The propensity of amido and alkoxo complexes to form stable N- or O-bridged dimeric or oligomeric species makes the formation of amido and alkoxo complexes possessing a binding site for the alkene challenging.

During the last few years, however, several papers have described a series of palladium amido complexes that undergo migratory insertion reactions with unactivated olefins. The

experiments in these studies provide direct evidence that migratory insertion of an alkene into a late-metal–nitrogen bond occurs with moderate activation barriers. The systems studied by the groups of Stahl, Wolfe, and Hartwig undergo migratory insertion at or below room temperature, and these moderate activation barriers are similar to those obtained for insertions into M–C bonds.

Although most authors have proposed that metal-catalyzed olefin amination and alkoxylation reactions occur by attack of the heteroatom nucleophile onto a metal-coordinated olefin, many of these reactions likely occur by migratory insertion of the alkene into an M–O or M–N bond. The low barriers now measured directly for the migratory insertions explain why catalytic reactions, which would be expected to occur by external attack of a nucleophile based on earlier mechanistic studies, actually occur by migratory insertion of an alkene into the M–O or M–N bond. In fact, migratory insertions of alkenes into M–O and M–N bonds occur with barriers similar to those for insertions into M–C bonds.

Likewise, a reevaluation of the mechanism of lanthanide-catalyzed hydroamination seems warranted based on recent evidence for a six-membered transition state involving the simultaneous participation of an amide and amine ligand. However, if the reactions of lanthanides with alkenes occur by this six-membered transition state, then the insertions of alkenes into metal–amide bonds of lanthanide complexes would not be as facile as initially thought. Clearly much information remains to be gained before these reactions are understood as well as the migratory insertion of alkenes into M–C bonds.

Acknowledgement

We thank the Department of Energy (DE-FG02-96ER14678) for support of our fundamental studies on migratory insertion into palladium–nitrogen bonds. Our work at Berkeley was supported by the Director, Office of Science, of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231.

Received: January 8, 2013
Published online: July 5, 2013

[1] B. C. a. W. A. Herrmann, *Applied Homogeneous Catalysis with Organometallic Compounds, Vol. 1*, Wiley-VCH, Weinheim, **2002**.
[2] R. V. Chaudhari, *Top. Catal.* **2012**, *55*, 439.
[3] D. Evans, J. A. Osborn, F. H. Jardine, G. Wilkinson, *Nature* **1965**, *208*, 1203.
[4] F. H. Jardine, J. A. Osborn, G. Wilkinso, J. F. Young, *Chem. Ind.* **1965**, 560.
[5] R. H. Morris, *Handbook of Homogeneous Hydroamination, Vol. 1*, Wiley-VCH, Weinheim, **2007**.
[6] R. H. Grubbs, G. W. Coates, *Acc. Chem. Res.* **1996**, *29*, 85.
[7] S. D. Ittel, L. K. Johnson, M. Brookhart, *Chem. Rev.* **2000**, *100*, 1169.
[8] V. C. Gibson, S. K. Spitzmesser, *Chem. Rev.* **2003**, *103*, 283.
[9] S. Mecking, *Angew. Chem.* **2001**, *113*, 550; *Angew. Chem. Int. Ed.* **2001**, *40*, 534.
[10] R. K. Thalji, K. A. Ahrendt, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2001**, *123*, 9692.
[11] K. L. Tan, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2002**, *124*, 13964.
[12] R. A. Periana, X. Y. Liu, G. Bhalla, *Chem. Commun.* **2002**, 3000.
[13] J. Oxgaard, R. A. Periana, W. A. Goddard, *J. Am. Chem. Soc.* **2004**, *126*, 11658.
[14] M. Lail, C. M. Bell, D. Conner, T. R. Cundari, T. B. Gunnoe, J. L. Petersen, *Organometallics* **2004**, *23*, 5007.
[15] Y. Nakao, Y. Hirata, T. Hiyama, *J. Am. Chem. Soc.* **2006**, *128*, 7420.
[16] Y. Nakao, S. Ebata, A. Yada, T. Hiyama, M. Ikawa, S. Ogoshi, *J. Am. Chem. Soc.* **2008**, *130*, 12874.
[17] Y. Nakao, H. Idei, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2009**, *131*, 5070.
[18] M. P. Watson, E. N. Jacobsen, *J. Am. Chem. Soc.* **2008**, *130*, 12594.
[19] I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009.
[20] C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314.
[21] R. F. Heck, *Acc. Chem. Res.* **1969**, *2*, 10.
[22] R. F. Heck, *Acc. Chem. Res.* **1979**, *12*, 146.
[23] G. M. F. Eckert, R. Jira, H. M. Bolt, K. Golka, *Ullmann's Encyclopedia of Industrial Chemistry, Vol. 1*, Wiley-VCH, Weinheim, **2012**, p. 191.
[24] M. Green, J. K. K. Sarhan, I. M. Alnajjar, *J. Chem. Soc. Dalton.* **1981**, 1565.
[25] B. L. Shaw, *Chem. Commun.* **1968**, 464.
[26] M. Green, R. I. Hancock, *J. Chem. Soc. A* **1967**, 2054.
[27] J. K. Stille, R. A. Morgan, *J. Am. Chem. Soc.* **1966**, *88*, 5135.
[28] P. M. Henry, *J. Am. Chem. Soc.* **1964**, *86*, 3246.
[29] B. Akermark, B. C. Soderberg, S. S. Hall, *Organometallics* **1987**, *6*, 2608.
[30] J. K. Stille, R. Divakaruni, *J. Am. Chem. Soc.* **1978**, *100*, 1303.
[31] J. E. Bäckvall, B. Akermark, S. O. Ljunggren, *J. Chem. Soc. Chem. Commun.* **1977**, 264.
[32] J. E. Bäckvall, B. Akermark, S. O. Ljunggren, *J. Am. Chem. Soc.* **1979**, *101*, 2411.
[33] J. E. Bäckvall, E. E. Bjorkman, L. Pettersson, P. Siegbahn, *J. Am. Chem. Soc.* **1984**, *106*, 4369.
[34] O. Hamed, P. M. Henry, C. Thompson, *J. Org. Chem.* **1999**, *64*, 7745.
[35] O. Hamed, C. Thompson, P. M. Henry, *J. Org. Chem.* **1997**, *62*, 7082.
[36] O. Hamed, P. M. Henry, *Organometallics* **1997**, *16*, 4903.
[37] K. Zaw, P. M. Henry, *Organometallics* **1992**, *11*, 2008.
[38] J. W. Francis, P. M. Henry, *Organometallics* **1992**, *11*, 2832.
[39] J. W. Francis, P. M. Henry, *Organometallics* **1991**, *10*, 3498.
[40] R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals, 5th ed.*, Wiley, Hoboken, **2009**.
[41] T. Hayashi, K. Yamasaki, M. Mimura, Y. Uozumi, *J. Am. Chem. Soc.* **2004**, *126*, 3036.
[42] B. M. Stoltz, R. M. Trend, Y. K. Ramtohul, *J. Am. Chem. Soc.* **2005**, *127*, 17778.
[43] M. B. Hay, J. P. Wolfe, *J. Am. Chem. Soc.* **2005**, *127*, 16468.
[44] M. B. Hay, A. R. Hardin, J. P. Wolfe, *J. Org. Chem.* **2005**, *70*, 3099.
[45] J. P. Wolfe, M. A. Rossi, *J. Am. Chem. Soc.* **2004**, *126*, 1620.
[46] S. Y. Seo, X. H. Yu, T. J. Marks, *J. Am. Chem. Soc.* **2009**, *131*, 263.
[47] X. H. Yu, S. Seo, T. J. Marks, *J. Am. Chem. Soc.* **2007**, *129*, 7244.
[48] A. Dzudza, T. J. Marks, *Chem. Eur. J.* **2010**, *16*, 3403.
[49] S. P. Nolan, D. Stern, T. J. Marks, *J. Am. Chem. Soc.* **1989**, *111*, 7844.
[50] H. E. Bryndza, *Organometallics* **1985**, *4*, 406.

[51] P. J. Zhao, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 9642.
[52] J. W. Tye, J. F. Hartwig, *J. Am. Chem. Soc.* **2009**, *131*, 14703.
[53] M. R. Gagne, C. L. Stern, T. J. Marks, *J. Am. Chem. Soc.* **1992**, *114*, 275.
[54] Y. W. Li, T. J. Marks, *J. Am. Chem. Soc.* **1996**, *118*, 9295.
[55] F. Pohlki, S. Doye, *Chem. Soc. Rev.* **2003**, *32*, 104.
[56] S. Hong, T. J. Marks, *Acc. Chem. Res.* **2004**, *37*, 673.
[57] D. V. Gribkov, K. C. Hultzsch, F. Hampel, *J. Am. Chem. Soc.* **2006**, *128*, 3748.
[58] A. Motta, G. Lanza, I. L. Fragala, T. J. Marks, *Organometallics* **2004**, *23*, 4097.
[59] B. D. Stubbert, C. L. Stern, T. J. Marks, *Organometallics* **2003**, *22*, 4836.
[60] B. D. Stubbert, T. J. Marks, *J. Am. Chem. Soc.* **2007**, *129*, 4253.
[61] A. M. Baranger, P. J. Walsh, R. G. Bergman, *J. Am. Chem. Soc.* **1993**, *115*, 2753.
[62] P. J. Walsh, A. M. Baranger, R. G. Bergman, *J. Am. Chem. Soc.* **1992**, *114*, 1708.
[63] D. V. Gribkov, K. C. Hultzsch, *Angew. Chem.* **2004**, *116*, 5659; *Angew. Chem. Int. Ed.* **2004**, *43*, 5542.
[64] B. D. Stubbert, T. J. Marks, *J. Am. Chem. Soc.* **2007**, *129*, 6149.
[65] S. Majumder, A. L. Odom, *Organometallics* **2008**, *27*, 1174.
[66] M. R. Crimmin, I. J. Casely, M. S. Hill, *J. Am. Chem. Soc.* **2005**, *127*, 2042.
[67] M. R. Crimmin, M. Arrowsmith, A. G. M. Barrett, I. J. Casely, M. S. Hill, P. A. Procopiou, *J. Am. Chem. Soc.* **2009**, *131*, 9670.
[68] J. F. Dunne, D. B. Fulton, A. Ellern, A. D. Sadow, *J. Am. Chem. Soc.* **2010**, *132*, 17680.
[69] K. Manna, S. C. Xu, A. D. Sadow, *Angew. Chem.* **2011**, *123*, 1905; *Angew. Chem. Int. Ed.* **2011**, *50*, 1865.
[70] K. Manna, M. L. Kruse, A. D. Sadow, *Acs. Catal.* **2011**, *1*, 1637.
[71] a) D. C. Leitch, P. R. Payne, C. R. Dunbar, L. L. Schafer, *J. Am. Chem. Soc.* **2009**, *131*, 18246; b) D. C. Leitch, R. H. Platel, L. L. Schafer, *J. Am. Chem. Soc.* **2011**, *133*, 15453.
[72] Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **1998**, *120*, 1757.
[73] L. E. N. Allan, G. J. Clarkson, D. J. Fox, A. L. Gott, P. Scott, *J. Am. Chem. Soc.* **2010**, *132*, 15308.
[74] P. D. Knight, I. Munslow, P. N. O'Shaughnessy, P. Scott, *Chem. Commun.* **2004**, 894.
[75] B. Åkermark, J. E. Backvall, L. S. Hegedus, K. Zetterbe, K. Siiralah, K. Sjoberg, *J. Organomet. Chem.* **1974**, *72*, 127.
[76] J. E. Bäckvall, *Tetrahedron Lett.* **1978**, *19*, 163.
[77] B. Äkermark, K. Zetterberg, *J. Am. Chem. Soc.* **1984**, *106*, 5560.
[78] L. S. Hegedus, J. M. Mckearin, *J. Am. Chem. Soc.* **1982**, *104*, 2444.
[79] G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285.
[80] M. P. Watson, L. E. Overman, R. G. Bergman, *J. Am. Chem. Soc.* **2007**, *129*, 5031.
[81] B. M. Cochran, F. E. Michael, *J. Am. Chem. Soc.* **2008**, *130*, 2786.
[82] P. A. Sibbald, C. F. Rosewall, R. D. Swartz, F. E. Michael, *J. Am. Chem. Soc.* **2009**, *131*, 15945.
[83] J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893.
[84] J. E. Ney, J. P. Wolfe, *J. Am. Chem. Soc.* **2005**, *127*, 8644.
[85] D. N. Mai, J. P. Wolfe, *J. Am. Chem. Soc.* **2010**, *132*, 12157.
[86] D. M. Schultz, J. P. Wolfe, *Org. Lett.* **2011**, *13*, 2962.
[87] V. Kotov, C. C. Scarborough, S. S. Stahl, *Inorg. Chem.* **2007**, *46*, 1910.
[88] G. S. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2007**, *129*, 6328.
[89] G. S. Liu, G. Y. Yin, L. Wu, *Angew. Chem.* **2008**, *120*, 4811; *Angew. Chem. Int. Ed.* **2008**, *47*, 4733.
[90] J. Helaja, R. Gottlich, *Chem. Commun.* **2002**, 720.
[91] G. S. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2006**, *128*, 7179.
[92] K. Muniz, C. H. Hovelmann, J. Streuff, *J. Am. Chem. Soc.* **2008**, *130*, 763.
[93] H. Tsutsui, K. Narasaka, *Chem. Lett.* **1999**, 45.
[94] A. Minatti, K. Muniz, *Chem. Soc. Rev.* **2007**, *36*, 1142.
[95] J. P. Wolfe, *Synlett* **2008**, 2913.
[96] J. L. Brice, J. E. Harang, V. I. Timokhin, N. R. Anastasi, S. S. Stahl, *J. Am. Chem. Soc.* **2005**, *127*, 2868.
[97] X. Ye, P. B. White, S. S. Stahl, *J. Org. Chem.* **2012**, ASAP.
[98] A. B. Weinstein, S. S. Stahl, *Angew. Chem. Int. Ed.* **2012**, *51*, 11505.
[99] J. E. Ney, J. P. Wolfe, *Angew. Chem.* **2004**, *116*, 3689; *Angew. Chem. Int. Ed.* **2004**, *43*, 3605.
[100] R. L. Cowan, W. C. Trogler, *Organometallics* **1987**, *6*, 2451.
[101] A. L. Casalnuovo, J. C. Calabrese, D. Milstein, *J. Am. Chem. Soc.* **1988**, *110*, 6738.
[102] R. Dorta, P. Egli, F. Zurcher, A. Togni, *J. Am. Chem. Soc.* **1997**, *119*, 10857.
[103] J. R. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 12220.
[104] S. G. Pan, K. Endo, T. Shibata, *Org. Lett.* **2012**, *14*, 780.
[105] C. S. Sevov, J. R. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2012**, *134*, 11960.
[106] P. J. Zhao, C. Krug, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 12066.
[107] J. D. Neukom, N. S. Perch, J. P. Wolfe, *J. Am. Chem. Soc.* **2010**, *132*, 6276.
[108] P. S. Hanley, D. Markovic, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 6302.
[109] P. S. Hanley, J. F. Hartwig, *J. Am. Chem. Soc.* **2011**, *133*, 15661.
[110] J. D. Neukom, N. S. Perch, J. P. Wolfe, *Organometallics* **2011**, *30*, 1269.
[111] P. B. White, S. S. Stahl, *J. Am. Chem. Soc.* **2011**, *133*, 18594.

