Carbon−Heteroatom Bond-Forming Reductive Eliminations of Amines, Ethers, and Sulfides

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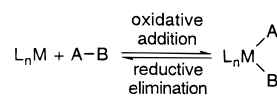*Department of Chemistry, Yale University, P.O. Box 208107, New Haven, Connecticut 06520-8107*

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Scheme 1

Scheme 2

Elementary transition metal-mediated reactions that form and cleave the bonds of organic molecules are the foundation of homogeneous catalysis. Such bond cleavage and formation often occurs by oxidative addition and reductive elimination. As shown in Scheme 1, these two reactions are essentially the same process in opposite directions: oxidative addition increases the oxidation state of the metal by two, decreases the d-electron count by two, and increases the overall number of valence electrons by two, while reductive elimination inflicts the opposite two-electron changes. Thermodynamic factors dictate whether a complex will undergo elimination or addition.
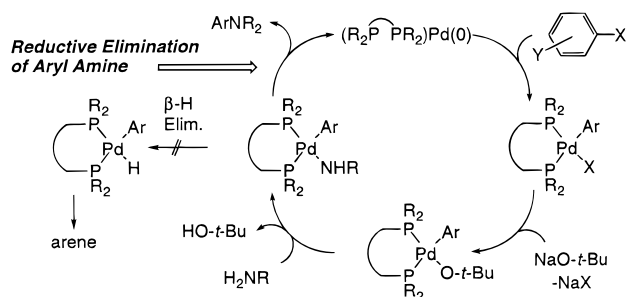
The formation of carbon−hydrogen and carbon−carbon bonds by reductive elimination is now common. Catalytic hydrogenation of alkenes, hydroformylation, alkene arylation (Heck reaction), and cross-coupling processes all involve C−H and C−C bond-forming reductive eliminations. The formation of carbon−heteroatom bonds by reductive elimination is less common, and just five years ago reductive elimination reactions that form C−O, C−N, and C−S bonds in ethers, amines, and sulfides had not been observed directly. It was unclear whether a kinetic barrier prevented these classes of reductive elimination, whether these eliminations were disfavored thermodynamically, or whether appropriate compounds to observe these reactions simply had not been prepared.

During the past five years, palladium-catalyzed chemistry that produces arylamines from aryl halides and either primary or secondary amines has been developed,[1−4] and a catalytic cycle that is supported by detailed mechanistic studies[5] is provided in Scheme 2. It seemed likely that the amination process, first reported with tin amides by Kosugi and Migita over 10 years ago,[6,7] involved reductive elimination of amine. It, therefore, seemed to the mem-

bers of my research group that the generation of stable palladium amido aryl complexes would allow for the direct observation of C−N bond-forming reductive elimination of amines.

In addition, similar palladium- and nickel-catalyzed reactions that form aryl sulfides have been reported,[8−14] and again, generation of stable thiolato aryl complexes would allow for the direct observation of C−S bond-forming reductive elimination of sulfides. Information on how these reactions occur might lead to improvements upon the catalytic formation of amines and sulfides. Finally, these studies may reveal systems that would undergo reductive elimination chemistry to form the C−O bonds in aryl ethers. As a result of this work, palladium- and nickel-catalyzed amination of aryl halides has become a general process[1−4] and new chemistry that forms aryl ethers has been developed recently.[15−19] Reviews of the catalytic carbon−heteroatom bond-forming coupling processes have been published recently.[20−22]

This Account describes work in my laboratory, along with related work from other groups, on the discovery of complexes that reductively eliminate amines, ethers, and sulfides and on the detailed mechanism of these reactions. In doing so I hope to provide correlations between C−N, C−O, and C−S bond-forming reductive eliminations that provide a coherent description of the factors that control the rates and mechanisms of these classes of reactions.

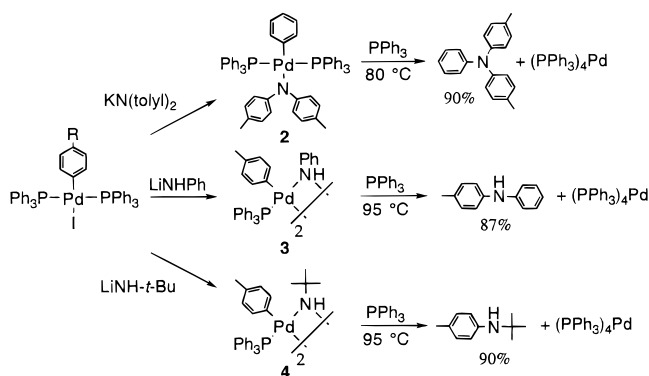## I. Reductive Elimination of Amines

My group chose palladium(II) amido complexes as candidates for reductive elimination because palladium aryl alkyl complexes were known to undergo C−C bond-forming reductive elimination[23−27] and because Kosugi had published a palladium-catalyzed conversion of aryl halides to arylamines that might have involved arylamine reductive elimination as the final elementary step.[6] Initially, we sought routes to tri-*o*-tolylphosphine-ligated palladium amido aryl complexes that would be the intermediate in the catalysis that underwent this reductive elimination. As shown in Scheme 3, experiments that formed these complexes indicated that tri-*o*-tolylphos-
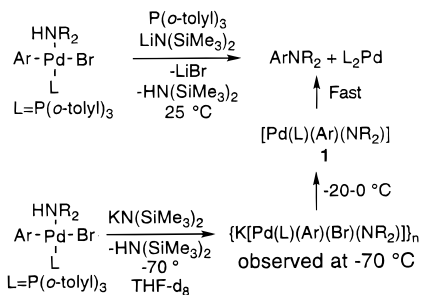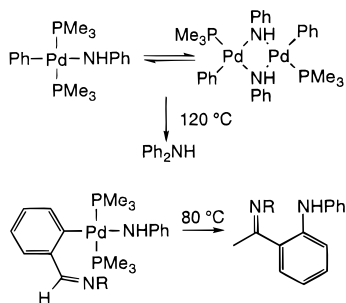
Scheme 3

Scheme 4

Scheme 5

phine-ligated amido aryl complexes, such as **1**, were too reactive to isolate, but did undergo reductive elimination of amine.[5,28]

Thus, we sought more stable amido aryl complexes, and found that complexes containing PPh₃ as the dative ligand were stable enough to isolate.[2,29,30] The synthesis and reactivity of these complexes is shown in Scheme 4. Most important, each class of amido aryl complex underwent reductive elimination of arylamine in high yields and at temperatures that were convenient for mechanistic analysis. Monomeric diarylamide **2**, as well as dimeric aryl- and alkylamido complexes **3** and **4** gave the coupled product in high yield, as long as PPh₃ as trap for the palladium(0) product was present in solution.

Boncella's group reported the synthesis of PMe₃-ligated palladium anilido complexes shown in Scheme 5 that could be isolated as monomers.[31] These complexes slowly dissociated phosphine to form dimers. Concurrent with this dimerization process, diarylamine was formed by reductive elimination. One complex contained an imino-substituted aryl group, and this complex underwent more facile elimination than did the simple phenyl complex.

This effect could be attributed to the electron-withdrawing nature of the imine group (vide infra), or its ability to accelerate cleavage of the dimers to monomers by an associative mechanism.
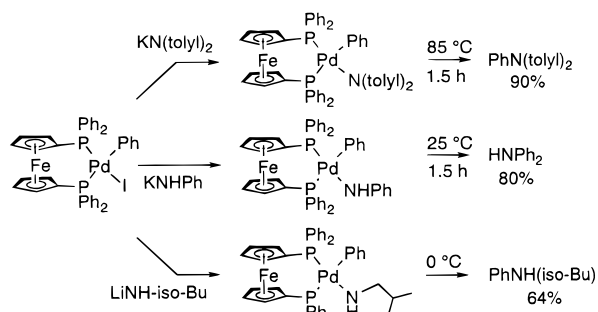
Important mechanistic information was gained from kinetic studies on complexes **2**–**4** prepared in our laboratory.[29,30] Reductive elimination reactions of palladium and nickel complexes to form C—C bonds occur by preliminary association[32] or dissociation[23,24] of dative ligand, or by direct reductive elimination.[27] The same pathways are available for C—N bond-forming elimination and can be distinguished by the reaction order in added ligand.

Reactions of **2** in the presence of PPh₃ were consistently first order in [**2**]. Reactions of **2** containing varied concentrations of added PPh₃ showed that a pathway involving initial dissociation of phosphine and reductive elimination from a three-coordinate complex occurred simultaneously with a pathway involving elimination from a four-coordinate complex, which is presumably the cis isomer of the trans starting complex. This information was deduced from a linear plot of k_{obs} vs 1/[PPh₃]. This plot displayed a positive slope corresponding to the observed rate constant for reductive elimination from a three-coordinate intermediate formed by phosphine dissociation. However, the plot also displayed a nonzero y-intercept corresponding to the observed rate constant for reductive elimination from a four-coordinate complex that is presumably the cis isomer of **2**.

Mechanistic studies on the reductive elimination from dimeric complexes **3** and **4** showed that reductive elimination occurred after cleavage of the monomer to form a three-coordinate, monophosphine amido complex. The dimer cleavage of **4** was irreversible. Reaction of a mixture of **4** and the analogue of **4** with *p*-tolyl groups bound to palladium showed no crossover during the course of thermolysis. Thus, reductive elimination from the three-coordinate intermediate was faster than recombination to re-form bridging amido complexes. In contrast to the irreversible dimer cleavage of **4**, the cleavage of **3** was reversible. Kinetic studies on the thermal chemistry of **3** showed a half-order dependence of reaction rate on the concentration of **3**, indicating that reversible formation of the three-coordinate anilido complex occurred before reductive elimination. Thus, re-formation of the bridging anilido complex was faster than reductive elimination.

The conclusion that two mechanisms for reductive elimination can occur simultaneously rested solely upon the nonzero y-intercept in the k_{obs} vs 1/[PPh₃] plot. Thus, we sought independent confirmation that reductive elimination could occur from a four-coordinate bisphosphine complex. To this end, we prepared amido aryl complexes with chelating phosphines that would strongly disfavor reductive elimination from a three-coordinate intermediate.[2,30] Scheme 6 shows three such complexes, and each complex does reductively eliminate under mild conditions. Not all chelating phosphines provided complexes that underwent reductive elimination. For example, the DPPE

Scheme 6

KN(tolyl)$_2$ → 85 °C 1.5 h → PhN(tolyl)$_2$ 90%

KNHPh → 25 °C 1.5 h → HNPh$_2$ 80%

LiNH-iso-Bu → 0 °C → PhNH(iso-Bu) 64%

complex **5** in eq 1 underwent backbone cleavage faster than reductive elimination.[2]

$$\text{PPh}_3 \longrightarrow \quad + \text{PPh}_3 + \text{HNPh}_2 + (\text{PPh}_3)_4\text{Pd}(0)$$
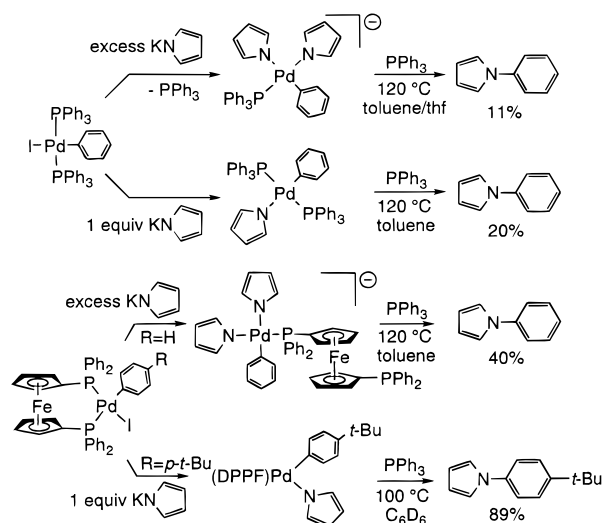
(1)
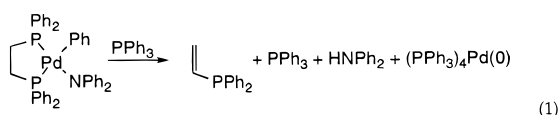
It is important for organic synthesis and interesting from a fundamental standpoint to determine the scope of anionic nitrogen ligands that will participate in C−N bond-forming reductive eliminations. For example, complexes that reductively eliminate *N*-aryl heterocycles and *N*-aryl imines would be analogous to those that form biaryls and styrenes by C−C bond formation. Studies on these types of reductive eliminations would provide fundamental information on the relative rates for different types of carbon−heteroatom bond-forming reductive elimination processes. *N*-Aryl heterocycles display a variety of biological activity, and both the heterocycles and imines can serve as protected anilines. In addition, reductive elimination of *N*-arylhydrazines and *N*-aryl-hydrazones would be the key bond-forming step of catalysis that could produce building blocks for the synthesis of *N*-arylpyrazole, -benzopyrazole, and -indole heterocycles.
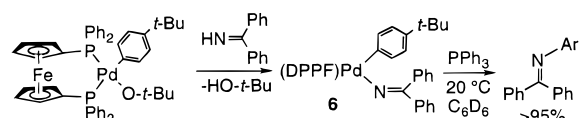
We found that reductive elimination of *N*-aryl hetero-cycles and *N*-arylhydrazones from palladium(II) phos-phine complexes can occur. However, this reaction occurred in higher yields for complexes containing chelat-ing ligands.[33,34] For example, Scheme 7 shows that reductive elimination of *N*-arylpyrrole from PPh$_3$ com-plexes occurred in modest yield and at high temperatures, while reductive elimination from DPPF-ligated palladium complexes occurred in high yields.

The importance of the chelating ligand for these couplings is not well understood. Although a chelating ligand forces the two groups undergoing reductive elimi-nation to be located cis to each other, our results on the formation of *N*-arylamines by reductive elimination showed that phosphine dissociation leads to a three-coordinate amido complex with stereochemistry that allows elimina-tion of arylamine to be faster than elimination from four-coordinate complexes, perhaps the equilibrium between cis and trans T-shaped three-coordinate[35] complexes. The low concentration of the cis geometry would reduce the concentration of the species that forms the C−N bond,
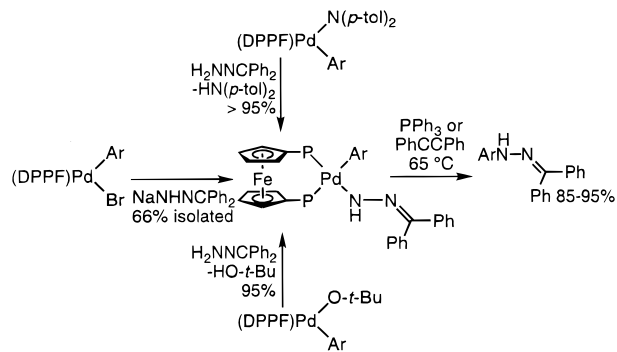
Scheme 7

excess KN → − PPh$_3$ → PPh$_3$ 120 °C toluene/thf → *N*-phenylpyrrole 11%

1 equiv KN → PPh$_3$ 120 °C toluene → 20%

excess KN → R=H → PPh$_3$ 120 °C toluene → 40%

R=*p-t*-Bu → (DPPF)Pd → PPh$_3$ 100 °C C$_6$D$_6$ → 89%

1 equiv KN

Scheme 8

HN=CPh$_2$, −HO-*t*-Bu → (DPPF)Pd **6** → PPh$_3$ 20 °C C$_6$D$_6$ → >95%

Scheme 9

(DPPF)Pd N(*p*-tol)$_2$ / Ar

H$_2$NNCPh$_2$ −HN(*p*-tol)$_2$ >95%

(DPPF)Pd Ar / Br NaNHNCPh$_2$ 66% isolated → Pd

PPh$_3$ or PhCCPh 65 °C → ArN=N−CPh$_2$ / H Ph 85−95%

H$_2$NNCPh$_2$ −HO-*t*-Bu 95%
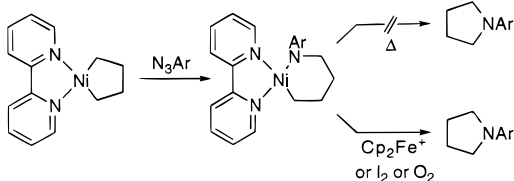
(DPPF)Pd O-*t*-Bu / Ar

reduce the rate of the overall reaction, and consequently allow alternative reactions to dominate.
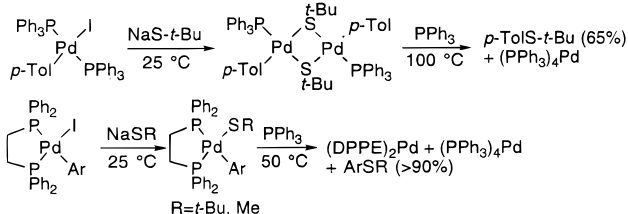
Reductive elimination to form *N*-aryl imines would also form a product with sp^2-hybridized nitrogen, and this reaction would be the analogue of coupling reactions that create the C−C bond in styrenes. In contrast to the eliminations that formed *N*-aryl azoles, the reactions that yielded *N*-aryl imines were fast.[33] We generated the aryl methylenimido complex **6** as shown in Scheme 8 and characterized this complex by low-temperature solution NMR and IR techniques. This complex eliminated *N*-aryl imine in quantitative yield after 30 min at room temper-ature.

Initial attempts to prepare palladium hydrazido com-plexes in our laboratory were unsuccessful, but our subsequent efforts to prepare η^1-hydrazonato complexes were successful. Scheme 9 shows the synthesis of this complex by both proton transfer and metathesis with alkali metal hydrazonato reagents. Scheme 9 also shows that these complexes undergo reductive elimination in yields and at rates comparable to those of the related DPPF-ligated palladium aryl- or diarylamido complexes.

Scheme 10

Scheme 11

Scheme 12

$R = CH_3, CHCH_2, C_6H_5, CC(CH_2)_3CH_3, CCPh$

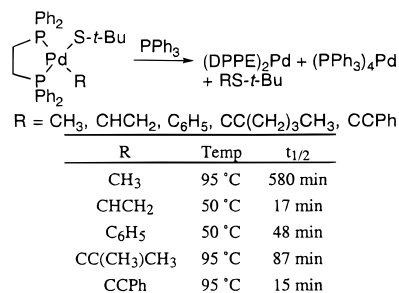| R	Temp	$t_{1/2}$
CH_3	95 °C	580 min
$CHCH_2$	50 °C	17 min
C_6H_5	50 °C	48 min
$CC(CH_3)CH_3$	95 °C	87 min
$CCPh$	95 °C	15 min

Hillhouse has prepared nickel complexes that undergo reductive elimination of *N*-alkylamines.[36,37] These complexes contain bipyridine ligands and were prepared as shown in Scheme 10 by insertion of "NR" groups from organoazides. Unlike the phosphine-ligated palladium arylamides, these complexes did not undergo thermal reductive elimination. From these results, it is unclear if the dative ligand prevents reductive elimination, if nickel complexes undergo reductive elimination of amines more slowly than palladium complexes, or if amido alkyl complexes will not thermally eliminate alkylamines. Buchwald has reported bipyridine-ligated nickel-catalyzed amination of aryl halides,[38] and Hillhouse has reported thermal elimination of alkylamines from phosphine-ligated nickel complexes after consumption of phosphine.[39] Thus, it appears at this time that the *combination* of bipyridine ligand and alkyl groups prevents thermal reductive elimination.

Interestingly, these metallacyclic amido alkyl complexes do undergo reductive elimination after oxidation to Ni-(III), as shown in Scheme 10. The order of events after oxidation is unclear, but it was proposed that an alkyl radical is generated. This proposal explained the low yields of alkylamine products for acyclic nickel complexes. These results raise the possibility that the reductive elimination reaction in nickel-catalyzed aryl halide amination occurs from nickel(III) amido aryl complexes rather than the nickel(II) amido complexes that would be the direct analogues of the palladium(II) amides that reductively eliminate amine.

II. Reductive Elimination of Sulfides

Palladium thiolate complexes that are closely related to the amido complexes discussed above have also been prepared, and they undergo reductive elimination of sulfides in high yields in many cases.[40] The synthesis and reductive elimination chemistry of these complexes is shown in Scheme 11. The PPh3-ligated systems form stable dimeric complexes with bridging thiolates that undergo reductive elimination in modest yields at 120 °C. In contrast, the DPPE-ligated complexes are stable at room temperature in most cases and undergo reductive elimination of sulfide in high yields under mild conditions. The ease of synthesis and generality of this reaction allowed for detailed analysis of steric and electronic factors that affect the rates of these reactions, as well as analysis of the relative rates for sulfide elimination involving different palladium-bound R-groups.[41] Important for interpretation of these results, reductive elimination occurred directly from the four-coordinate complex in all cases. Thus, electronic and steric perturbations alter the reductive elimination rate in the absence of phosphine dissociation or geometric rearrangements.

Scheme 12 shows the relative rates for formation of sulfides from thiolatopalladium alkyl, vinyl, aryl, and alkynyl complexes. The relative reactivity of these complexes was vinyl > aryl > alkynyl > alkyl. It is likely that coordination of the π-system of the unsaturated ligands accelerates the reductive elimination of the vinyl, aryl, and alkynyl complexes relative to that of the alkyl complex, as has been proposed previously for C−C bond-forming reductive eliminations.[42] The alkynyl complex may eliminate more slowly than the vinyl or aryl complexes because a large distortion would be necessary for this π-coordination to occur in the transition state. Alternatively, the slower rate could be explained in terms of thermodynamic driving forces; the ΔG for elimination of alkynyl sulfide is smaller than that for elimination of vinyl or aryl sulfide; an equilibrium mixture of the alkynylpalladium thiolate complex (ca. 5%) and the combination of Pd(0) and alkynyl sulfide was observed.

The top of Scheme 13 shows the effect of altering the palladium-bound aryl group steric properties on the sulfide elimination. Charge buildup at the aryl group in the transition state has been deduced by studies of substituent effects (see section IV). Perhaps alleviation of this charge buildup by coordination of the aryl group to the metal center accelerates the reaction. Consistent with this proposal, the presence of two *o*-methyl groups on the palladium-bound aryl group greatly decelerates the reductive elimination. As shown in Figure 1, coordination to the metal center would be greatly disfavored in the case of the complexes containing a palladium-bound 2,6-dimethylphenyl group.

The bottom of Scheme 13 also shows the unusual effects of the thiolate steric properties on reductive elimination. As one might expect, an increase in size of an alkyl thiolate group led to increasing reaction rates. This trend would result from decreasing steric effects as
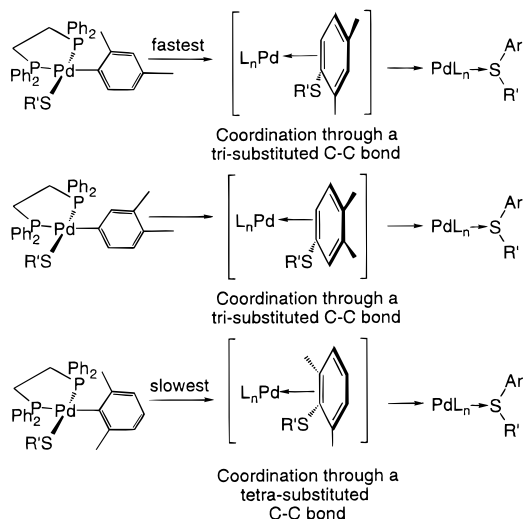
FIGURE 1. Potential explanation for effect of palladium-bound aryl group steric properties on reductive elimination rates.
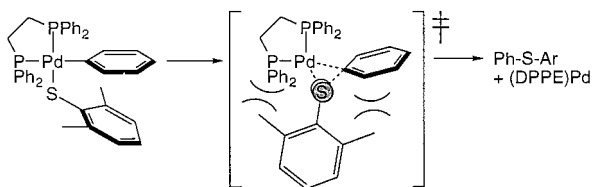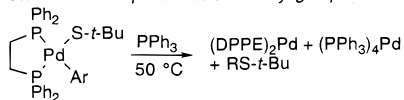

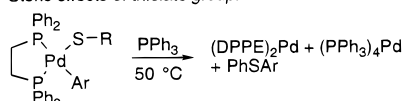**FIGURE 2.** Potential stereoelectronic effect on reductive elimiantion of diaryl sulfides.

Scheme 13

the sulfide product is eliminated. However, we were surprised to find that an increase in size of an aryl thiolate group led to decreasing reaction rates. This unexpected result may originate from a stereoelectronic effect wherein the geometry required for overlap of the thiolate aryl π-system with the sulfur electron pair leads to an increased steric interaction with the metal center or the palladium-bound aryl group (Figure 2).

Scheme 14
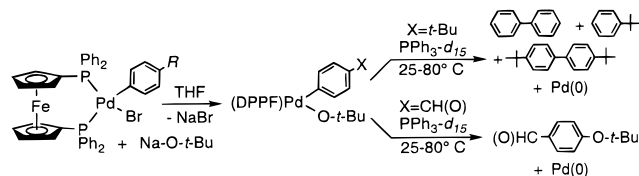
III. Reductive Elimination of Ethers

My group has prepared alkoxo aryl complexes to investigate their ability to undergo reductive elimination of ethers.[15] We prepared and fully characterized, including X-ray diffraction, an alkoxo aryl complex with an electron neutral aryl group. This complex did react under mild thermal conditions, but did not produce any aryl ether. Instead, a series of biaryls derived from the phosphine- and palladium-bound aryl groups were observed. Apparently the reductive elimination of ether from this complex was slower than competing, undesired aryl exchange chemistry. In fact, results on electronic properties of amine and sulfide eliminations discussed in section IV below suggest that the weaker the nucleophilicity of the heteroatom involved in the reductive elimination, the less favored is the reductive elimination process.

However, these electronic studies also showed that reductive eliminations of amines and sulfides are accelerated by electron-withdrawing substituents on the palladium-bound aryl group. In particular, electron-withdrawing substituents with large ρ_R values had the greatest accelerating effect. Thus, we prepared the *p*-CH(O) aryl alkoxo complex in Scheme 14. This complex, indeed, underwent reductive elimination of ether in high yield. This reaction was the first reductive elimination that formed the C—O bond in an aryl ether and was the first C—O bond-forming reductive elimination of any ether in high yield.

Buchwald and Widenhoefer studied the mechanism of the reductive elimination of aryl ethers from DPPF- and BINAP-ligated palladium complexes generated in situ with electron poor, palladium-bound aryl groups.[43] They found that BINAP arylpalladium alkoxo complexes underwent reductive elimination faster than analogous DPPF complexes and that more sterically hindered alkoxo groups led to faster elimination. The acceleration of reductive elimination by sterically hindered alkoxo groups is similar to the faster elimination of sulfide from S—*t*-Bu complexes than from S—Me complexes.[40] They also found a perplexing dependence of the reaction rate on alkali alkoxide concentration. Rate acceleration and higher yields were observed with excess of alkoxide. They attributed this effect to an alkoxide dependent pathway in which reductive elimination occurs from an electron rich anionic palladium bisalkoxide complex.

Hillhouse has also reported examples of reductive elimination of ether.[44-46] In his examples, the reactions form cyclic dialkyl ethers, or cyclic alkyl aryl ethers as shown in Scheme 15. These reactions occurred in low yields, even after oxidation to Ni(III). The mechanism that forms the dialkyl ethers is likely to be similar to the one
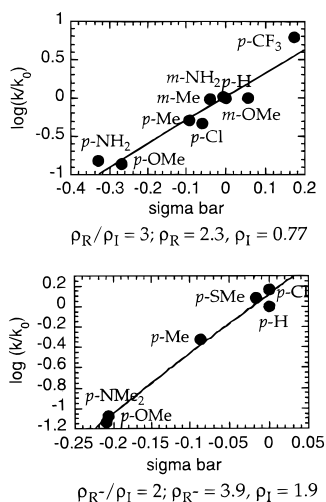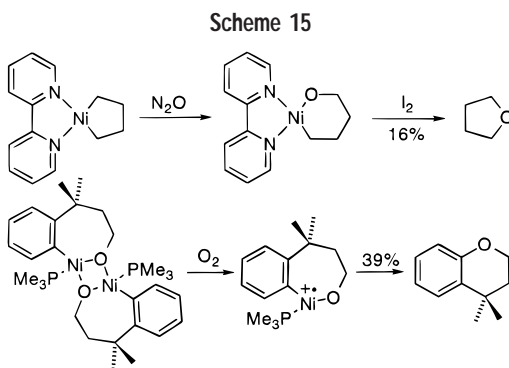
$\rho_R/\rho_I = 3$; $\rho_R = 2.3$, $\rho_I = 0.77$

$\rho_{R^-}/\rho_I = 2$; $\rho_{R^-} = 3.9$, $\rho_I = 1.9$

FIGURE 3. Electronic analysis using a combination of σ_I and σ_{R0} for the reductive elimination of aryl sulfides (top) and arylamines (bottom).

Scheme 15

that formed alkylamines after oxidation of Ni(II) to Ni(III). Although these reactions were proposed to occur by a radical mechanism, which is distinct from the mechanism for reductive elimination of ethers from palladium, the fact that elimination of ether is more difficult than elimination of amine from nickel parallels reactivity trends for eliminations from palladium.

IV. Electronic Effects on Amine, Sulfide, and Ether Eliminations

The electronic effects on reductive elimination rates have been studied quantitatively for examples that form amines, sulfides, and ethers.[30,40,41,47] The electronic effects on sulfide reductive elimination are the most thoroughly studied case.[40] Ten complexes with varying electronic properties of the palladium-bound aryl group were prepared, and the rates for their reductive elimination were measured. These results showed that reductive elimination was accelerated by electron-withdrawing groups, but that the relationship between log k_{obs} and σ was poorly correlated. However, the relationship between log k_{obs} and $\bar{\sigma}$, a synthetic σ-value created from the resonance and inductive parameters σ_{R^-} and σ_I,[48,49] was linear, as shown at the top of Figure 3. This analysis generates ρ_{R^-}, which reflects the correlation between log k_{obs} and σ_{R^-}, and ρ_I, which reflects the correlation between log k_{obs} and σ_I. In

the case of sulfide reductive elimination, ρ_{R^-} and ρ_I were both positive and ρ_{R^-} was larger than ρ_I.

A similar electronic effect on reductive elimination rate was observed for amine elimination.[30] Again, a poor correlation between k_{obs} and σ was observed, but a good correlation was observed between k_{obs} and a $\bar{\sigma}$ created from σ_R and σ_I as shown at the bottom of Figure 3. Again, ρ_R was larger than ρ_I. Because both amine and sulfide eliminations showed a $\rho_R > \rho_I$, this unusual electronic effect appears to be a meaningful characteristic of these reductive eliminations. In fact, analysis of data from Yamamoto's laboratory on reductive elimination from alkyl aryl complexes shows a similar trend, although the number of complexes studied was small.[27]

Finally, Widenhoefer and Buchwald studied the electronics of ether elimination.[47] Again, electron-withdrawing substituents on the aryl group accelerated reductive elimination. In this case, only aryl groups with strong electron-withdrawing substituents gave any ether product, limiting the number of examples that could be included in a Hammett plot. The slope of a Hammett plot for ether elimination was much larger than in the sulfide and amine cases, and the authors concluded that the positive slope was purely due to resonance effects.

Scheme 6 had shown that alkylamido complexes reacted faster than arylamido complexes, which reacted faster than diarylamido complexes. Further, pyrrolyl complexes reductively eliminated more slowly than any of the amido complexes. This information suggests that more nucleophilic anionic ligands bound to palladium through a heteroatom react faster than do more weakly nucleophilic groups. Further consistent with this hypothesis, alkyl thiolate complexes eliminated sulfides faster than did aryl thiolate complexes, and the more basic the alkoxide the faster was elimination of ether. A careful analysis of diaryl sulfide elimination from aryl thiolate aryl complexes containing electronically varied S-bound aryl groups verified this hypothesis.[41] A linear correlation between k_{obs} and σ was observed. The ρ-value was negative, indicating that increasing electron density on the thiolate led to increasing reaction rates.

It is commonly believed that decreasing electron density at the metal accelerates reductive elimination.[51] This hypothesis, which is clearly true in many cases involving variation in dative ligand electron donation, would predict that more donating aryl and amido or thiolato groups would lead to decreasing rates for reductive elimination because they would increase electron density at the metal. In contrast, theoretical work has shown that more weakly donating dative ligands, but more donating covalent ligands, accelerate reductive elimination from Pd(II) by destabilizing the metal d-orbitals on the starting metal complex.[25] Thus, the result that more nucleophilic amido ligands and more electrophilic aryl ligands led to the fastest elimination rates cannot be explained by simple arguments focusing on overall metal electron density, or more complex arguments based on metal d-orbital energies. These results suggest that the complementary pairing of a nucleophilic heteroatom-

containing ligand and an electrophilic aryl ligand dominates any perturbations in metal electron density. In fact, a similar effect on the stability of platinum diaryl complexes has been observed qualitatively. Pt(II) complexes with two electron rich or two electron poor aryl groups were stable, but complexes with one electron rich and one electron poor aryl group could not be isolated.[51]

Of course, ground state energetics can influence the reaction rates, and one might attempt to explain the observed trends in the context of thermodynamics. One could argue that the more exothermic reductive eliminations will occur faster than the less exothermic ones. However, reductive elimination of aryl sulfides is significantly less favorable thermodynamically than is the reductive elimination of arylamines. The C–N bond in an arylamine is 15–20 kcal/mol stronger than a C–S bond in an aryl sulfide. For example, the C–N bond in aniline is 104.3 kcal/mol,[52] while the C–S bond in thiophenol is 86.5 kcal/mol.[53] Platinum and ruthenium M–S bonds are stronger than the corresponding M–N bonds, and Pd–S bonds are, therefore, almost certainly stronger than analogous Pd–N bonds.[54] Yet, sulfide reductive elimination is faster. Thus, the favorable matching of an electrophilic aryl group with a nucleophilic anionic nitrogen, sulfur, or oxygen ligand is a more valid rationalization for the reactivity trends than is a thermochemical argument.

It should be noted, however, that the influence of electronics on amine or sulfide reductive elimination rates is much less pronounced than electronic effects on direct nucleophilic aromatic substitution reactions.[49,55,56] Nucleophilic aromatic substitution rates are strongly influenced by the electrophilicity of the aryl halide. Mild nucleophilic aromatic substitutions require polar solvents and aromatic systems containing nitro activating groups.[57,58] The electronic effects on direct nucleophilic aromatic substitution reaction rates involving thiolate and amine nucleophiles have been evaluated, and these show linear free energy relationships with ρ-values that are significantly larger than those seen for the reductive eliminations of ethers or sulfides.[49] The smaller, albeit measurable, electronic influence on the reaction rates for the palladium chemistry allows this reaction to be general and to encompass electron poor and electron rich aryl halides and amines. The large ρ-value for the reductive elimination of ethers has limited the generality of this type of carbon–heteroatom bond-forming reductive elimination.

V. Summary

The discovery of a new class of chemical reaction is uncommon and often leads to new applications and new chemical principles. The formation of amines, ethers, and sulfides by carbon–heteroatom bond-forming reductive elimination has been instrumental in developing practical new routes to aromatic amines, ethers, and sulfides. This reaction is the final step of catalytic processes that can be used to form new pharmaceuticals, new ligands, new chemical libraries, as well as new conductive and magnetic

materials. The beginning of a mechanistic understanding of this reaction has emerged, and these mechanistic studies have revealed the coordination number of the species undergoing reductive elimination, the types of covalent ligands that will participate in this reaction, and the effects of electronic and steric perturbations on reaction rate. Studies involving alterations of the dative ligands are required to generate improved catalysts for C–X bond formation, as are examples of high-yielding thermal reductive eliminations from metals other than palladium. These studies will be a part of our future work.

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