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Electronic Effects on Reductive Elimination To Form Carbon–Carbon and Carbon–Heteroatom Bonds from Palladium(II) Complexes

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The electronic properties of reactive and ancillary ligands have a large impact on the rate and scope of reductive elimination reactions. The purpose of this review is to compare and discuss published data on the effect of ligand electronic properties on the rates and scope of reductive eliminations from palladium(II). An understanding of these effects is important because reductive elimination from palladium(II) is the product-forming step of a variety of catalytic processes. The scope of this review will encompass the effect of the electron-donating abilities of alkyl, aryl, amido, alkoxo, thiolato, and phosphido groups on the rate of reductive elimination, the relative importance of inductive and resonance effects on the rate of reductive elimination, the relative sensitivity of the different classes of reductive eliminations to electronic perturbations, and the effect of the differences in electronic properties between the two aryl groups of biaryl complexes undergoing reductive elimination. In addition, this review will include the effects of electronic properties of the ancillary ligands on the rate of reductive eliminations from palladium(II). The effect of the overall electron-donating ability of ancillary ligands and the effect of the relative orientation of ancillary ligands to the two reactive ligands on the rate of reductive elimination will be discussed. Where appropriate, electronic effects on reductive elimination from complexes of other metals are described.

A. Introduction

Palladium-catalyzed cross-coupling reactions have become some of the most-utilized transition-metal-catalyzed reactions in organic synthesis. In 1972 Kumada et al.[1] and Corriu and Masse[2] independently reported transition-metal-catalyzed coupling to form C−C bonds. In the past decade, efforts to develop new catalysts and procedures to couple aromatic and aliphatic electrophiles with increased scope, faster rates, and longer catalyst lifetimes have grown more intense. In addition to cross-coupling reactions that form C−C bonds, cross-coupling reactions that form C−N, C−O, C−S, and C−P bonds with aromatic electrophiles have been developed.[3,4] Reactions that form arylamines[4−15] are the most synthetically valuable of these processes.

Reductive elimination (eq 1) is responsible for the formation of the new bond in the product of these catalytic coupling processes. This reaction involves the coupling of two

$$L_nM\begin{matrix}\diagup A\\ \diagdown B\end{matrix}\ \underset{\text{oxidative addition}}{\overset{\text{reductive elimination}}{\rightleftharpoons}}\ L_nM + A{-}B \qquad (1)$$

covalent ligands and the formal reduction by 2 of the oxidation state of the metal. In many cases, the scope of

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cross-coupling is controlled by the rate and scope of the reductive elimination process. For example, palladium-catalyzed couplings to form C−N and C−O bonds were challenging to develop because palladium amido and palladium alkoxo complexes were reluctant to undergo reductive elimination.[5] However, the recent direct observation of these reductive eliminations, and the development of a body of catalytic chemistry based on them, makes it clear that reductive eliminations to form arylamines and aryl ethers can occur.

The existence of new catalytic processes based on reductive elimination reactions raises a series of questions about factors controlling the rates of reductive elimination. Although both steric and electronic properties of ancillary and reactive ligands certainly modulate the rates of these processes, the relative contributions of these effects and the sensitivity of the rates of reductive elimination to perturbations of the steric and electronic properties of the ligands were not well understood until recently.

The author's group has been particularly interested in understanding the electronic factors controlling the rates of reductive elimination to form C−C and C−X bonds and the relative magnitudes of the effects of steric and electronic perturbations on those rates.[5] Until recently, it was unclear whether all classes of C−X bond-forming reductive elimination processes would depend equally on the overall electron density at the metal center or whether each process would be controlled by its own set of electronic effects. Specific questions pertaining to the effect of electronic properties of ancillary and reactive ligands on the rates of reductive elimination include whether electronic effects of symmetrical and unsymmetrical ancillary ligands are the same, whether complexes containing more or less electron-donating reactive groups undergo faster reductive elimination, and whether similar changes to the electronic properties of heteroatom ligands and of hydrocarbonyl ligands would have the same or different effects on the rates of reductive elimination. The purpose of this minireview is to systematically present information gathered over the past decade that addresses these questions as they relate to reductive eliminations from palladium(II) complexes.

B. Brief Comments about Steric Effects on the Rate of Reductive Elimination from Palladium(II) and Electronic Effects on the Rate of Reductive Elimination from Other Metals

Although this paper will focus on the electronic effects on reductive elimination from palladium(II) complexes, some brief comments about how steric properties affect the rates of these reductive eliminations, and how the electronic effects of ancillary and reactive ligands affect reductive elimination from other metals, will provide a context for the results presented in this review. It is generally true that complexes with more hindered ancillary ligands undergo reductive elimination faster than complexes with less hindered ancillary ligands. This effect presumably arises from a relief in steric congestion upon generation of the free organic product and a resulting metal center with a reduced coordination number. Recent primary literature has shown that the steric effect on reductive elimination can be large,[16,17] and some of this literature is used later in this review to make comparisons between the magnitude of steric and electronic effects on the rates of reductive elimination.

During the past decade, data on the factors that control reductive elimination from complexes of other metals have also been obtained.[18,19] First, the effects of the overall electron density at the metal center can be overridden by the effects of orbital symmetry and π bonding in complexes with geometries that differ from the square-planar and T-shaped geometries of palladium(II) complexes.[18,19] Second, the effects of electronic properties of the reactive ligands on the rate of reductive elimination by stepwise pathways through ionic intermediates[20,21] are often distinct from the effects of the electronic properties of these ligands on reductive elimination by concerted mechanisms. The electronic effects on reductive elimination from palladium(II) most likely follow consistent trends because the reactions occur by concerted pathways and π effects are not pronounced in square-planar and T-shaped palladium(II) complexes. π effects are not pronounced in these complexes because they lack a low-lying unoccupied orbital of π symmetry. Thus, the electronic effects described in this minireview can be interpreted primarily as resulting from changes in the electron distribution within σ bonds.

C. Background about Electronic Effects on Reductive Elimination from Palladium(II) and Related Compounds

Two electronic effects have commonly been observed for reductive elimination from palladium(II) and platinum(II) complexes. First, reductive elimination is usually slower from more electron-rich complexes than from more electron-poor complexes.[22] Second, theoretical and early experimental studies suggested that complexes with more strongly electron-donating reacting ligands undergo concerted reductive eliminations faster than do complexes with more weakly electron-donating reacting ligands.[22−24] For example, many reductive eliminations occur from palladium methyl complexes, but reductive eliminations from analogous trifluoromethyl complexes usually do not occur (eq 2). In fact, only one example of reductive elimination from palladium trifluoromethyl complexes has been reported (eq 3).[25,26]

These two baseline effects of electronics on concerted reductive eliminations from palladium(II) complexes can be

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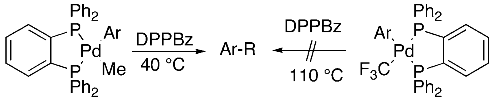
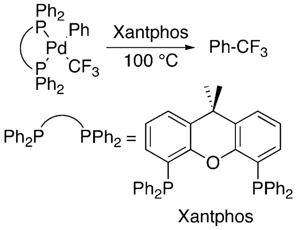


(2)



(3)

attributed to the effect of electronics on the ground state. First, strongly donating ancillary ligands make the metal center electron-rich, and electron-rich metal centers tend to undergo reductive processes more slowly than electron-poor metal centers. Second electron-withdrawing groups on the reactive ligand lead to an increase in the strength of the M−C or M−X bond.[27] These electron-withdrawing groups make the M−C or M−X bond more ionic, and this ionic character increases the thermodynamic bond strength. These changes in the electronic properties of anionic ligands tend to affect the strength of an M−X bond more than they affect the strength of a H−X (and presumably C−X) bond.[27,28] Thus, groups whose electronic properties increase the strength of the M−X bonds tend to decrease the thermodynamic driving force for reductive elimination.

These explanations can provide a first approximation of the electronic effects on rate. However, this description is clearly too simple and uses thermodynamic arguments to rationalize and predict trends in rates. As expected from the simplicity of this argument, some of these predicted electronic effects have been contradicted by more recent experimental data described in this review.

Experimental and theoretical studies also imply that the hybridization of the carbon bound to the metal has a large effect on the reaction rate. For example, triphenylphosphine-ligated palladium dimethyl complexes are stable, but the analogous diphenyl complexes are not.[29,30] Reductive eliminations to form C−C and C−heteroatom bonds from aryl complexes are typically faster than reductive eliminations to form the same bonds from alkyl complexes. Vinyl complexes are similarly more reactive than alkyl complexes, and some theoretical studies have implied that participation of the π system creates a lower-energy pathway for reductive elimination than is available for complexes of ligands lacking a π system.[31]

The following sections of this minireview will present recent data that clarify the electronic effects on C−X and C−C bond-forming reductive elimination from palladium(II). The discussion will focus predominantly on reductive eliminations involving aryl groups because these data are most extensive; however, reductive eliminations to form aliphatic products will also be presented when possible.

D. Electronic Effects of Ligands Undergoing Reductive Elimination

1. Electronic Effects on C−N Bond-Forming Reductive Elimination. Studies of reductive eliminations to form C−X bonds from isolated arylmetal or alkylmetal species began more recently than studies of reductive eliminations to form C−C or C−H bonds. Prior to initial observations of reductive eliminations to form C−N bonds in amines,[32,33] reductive eliminations to form amines from metal amido complexes were expected to be slower than alternative pathways for the reaction of amido complexes, such as β-hydrogen elimination. This expectation was based on the difficulties encountered in isolating late-transition-metal amido and alkoxo complexes containing β hydrogens[34,35] and on the lack of catalytic and stoichiometric processes that occur by reductive elimination from amido and alkoxo complexes. Prior to the early 1990s, reductive eliminations from isolated amido or alkoxo complexes were limited to reductive eliminations from iridium(III) and platinum(II) amido and alkoxo complexes to form N−H and O−H bonds.[36−39] Moreover, the mechanism of reductive elimination from the platinum(II) complexes was poorly understood.[38,39]

Review articles had[34,35] articulated the general belief that a mismatch of a hard amido ligand with a soft metal would create reactive compounds. However, the electronegativity of the N and O atoms in amido and alkoxo ligands could also make these ligands less reactive in organometallic processes such as reductive elimination. The greater ionic character of the M−N and M−O bonds could increase the thermodynamic stability of the complexes[27,40] and decrease the reactivity.[41] The effect of the polarity of the M−X bond in the reactant and the degree of polarity in the transition state for reductive eliminations to form C−X bonds were not known.

Experimental data are now available on the reductive elimination of arylamine derivatives from a series of complexes containing amido groups possessing varied electronic properties. These data show that reductive eliminations to form the C−N bond in arylamines are faster from

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(26) The electronic properties of reactive ligands in stepwise reactions that occur through ionic intermediates, such as those from platinum(IV) complexes, are often distinct from the electronic properties of the reactive ligands, and these reactions are faster when the reactive ligand is more electron-poor. For examples, see refs 27 and 28.

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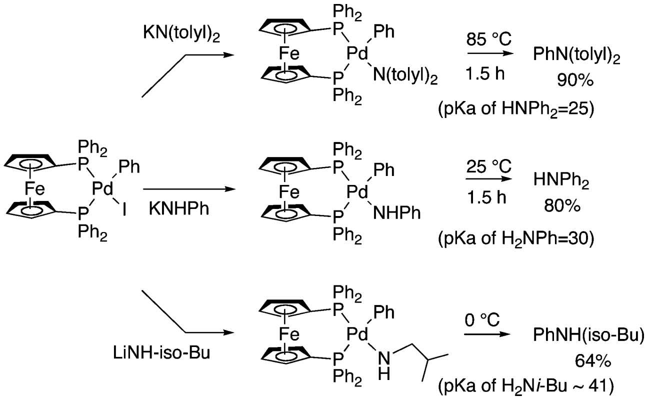
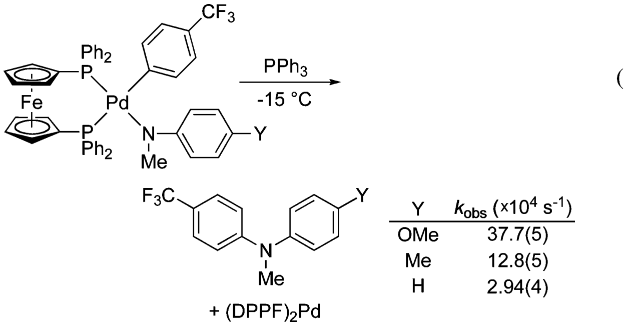
Scheme 1



complexes with more electron-rich amido ligands than from complexes with more electron-poor amido ligands. These data were first revealed by the studies of 1,1′-bis(diphenylphosphino)ferrocene (DPPF)-ligated arylpalladium amido complexes summarized in Scheme 1[33,42] and in eq 4.[43] The



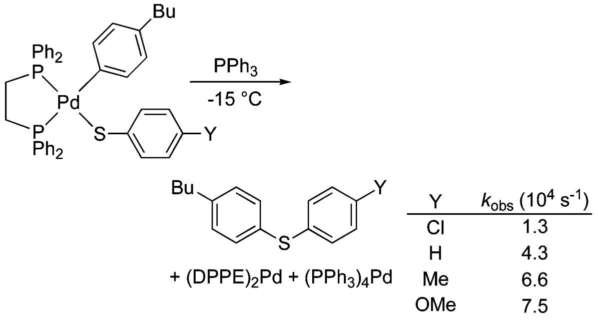
Y	k_{obs} (×10^4 s^{-1})
OMe	37.7(5)
Me	12.8(5)
H	2.94(4)

(4)

diarylamido complexes underwent reductive elimination at elevated temperatures over the course of 1−2 h. The analogous anilide complex underwent reductive elimination at room temperature over a similar time period, and the alkylamide underwent reductive elimination at 0 °C over this time. Thus, the complex with the more electron-rich amido group reacted faster than the complex with the less electron-rich amido group.[44]

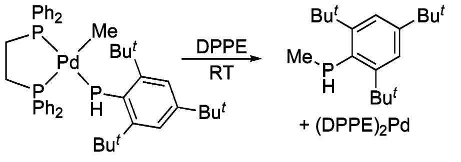
The data in eq 4 are more systematic and support the above conclusion. These data reveal the rates of reductive elimination from a series of para-substituted *N*-methylanilide complexes and demonstrate that the more electron-rich amido complex undergoes reductive elimination significantly faster than the less electron-rich amido complex.[43]

2. Electronic Effects on Reductive Elimination To Form Other C−X Bonds. Analogous electronic effects were observed for reductive elimination to form C−S bonds. Selected data are summarized in eq 5 and show that the rate of reductive elimination from arylpalladium arenethiolate complexes is faster from complexes containing more electron-rich thiolate ligands than from complexes containing more electron-poor thiolate ligands.[45] Studies on reductive eliminations from arylpalladium alkoxo complexes suggest that reductive elimination is also faster from more electron-rich alkoxides, although these conclusions were drawn from a set of complexes in which the steric and electronic properties of the alkoxide were varied simultaneously.[46]



Y	k_{obs} (10^4 s^{-1})
Cl	1.3
H	4.3
Me	6.6
OMe	7.5

(5)



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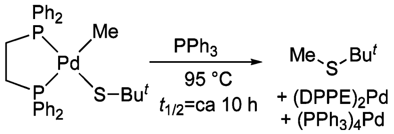

(7)

One can also compare the relative rates for reductive elimination from related arylpalladium complexes containing amido, alkoxo, thiolato, and phosphido ligands. Reductive eliminations to form C−X bonds from arylpalladium amido, alkoxo, thiolato, and phosphido complexes containing similar substituents on the heteroatom occur in the order C−P > C−S > C−N > C−O. This order of reactivity can be deduced from the following set of experimental results.

Two different sets of reactions reveal the relative rates for C−P and C−S bond-forming reductive eliminations. First, reductive elimination from a methylpalladium phosphide complex (eq 6)[47−50] occurs faster than reductive elimination of methyl sulfide from the methylpalladium thiolate complex in eq 7 containing the same ancillary ligand.[45] Second, reductive eliminations of arylphosphines from arylpalladium phosphido complexes have been too fast to observe directly, indicating that these reductive eliminations are faster than reductive eliminations of arylamines from arylpalladium amides.

A comparison of two other sets of reactions reveals the relative rates for C−S and C−N bond-forming reductive eliminations. First, reductive eliminations of alkylamines

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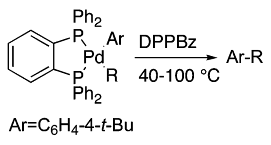
from alkylpalladium amido complexes are slower than reductive eliminations of alkyl sulfides. In fact, methylpalladium amido complexes containing standard bis(phosphines) have been stable to reductive elimination.[51] Second, reductive eliminations of aryl sulfides from palladium complexes containing 1,2-bis(diphenylphosphino)benzene (DPPBz) as an ancillary ligand occur in high yield under mild conditions, but reductive eliminations of arylamines from arylpalladium amido complexes containing this ancillary ligand occur slowly or not at all.[52]

The reactions of DPPF-ligated arylpalladium anilide and phenoxide complexes reveal the relative rates for C−N and C−O bond-forming reductive elimination. Reductive eliminations from DPPF-ligated arylpalladium anilide complexes containing electron-neutral, palladium-bound aryl groups occurred under mild conditions, but reductive eliminations of biaryl ethers from DPPF-ligated arylpalladium phenoxide complexes containing electron-neutral aryl groups did not occur. Reductive elimination of biaryl ethers from DPPF-ligated arylpalladium phenoxide complexes required that the palladium-bound aryl group be electron-poor.[17]

3. Effects of Electronic Properties of Alkyl Ligands on Reductive Elimination. Electronic properties of alkyl ligands can vary widely depending on the functional group attached to the α carbon, and reductive eliminations of alkylarenes from a series of arylpalladium alkyl complexes containing alkyl ligands with varied electronic properties have been studied.[53] The electronic effect on C−C bond-forming reductive elimination of alkylarenes can then be compared to the electronic effect on C−X bond-forming reductive eliminations of aromatic amines, ethers, phosphines, and sulfides. These studies addressed whether trends in electronic effects on reductive elimination to form carbon−heteroatom bonds applied equally to the reductive eliminations to form carbon−carbon bonds. Perhaps most significant, this comparison would reveal whether the electronic effects on reductive eliminations to form carbon−heteroatom bonds are transmitted primarily through the σ-bonding system or through bonding interactions involving the electron pair on the heteroatom.

The data in eq 8 show that similar effects are observed for reductive eliminations from alkyl groups as are observed for reductive eliminations from amido, alkoxo, phosphido, and thiolato complexes. These data on reductive elimination from DPPBz-ligated arylpalladium complexes containing methyl and functionalized alkyl ligands[53] show that reductive elimination is faster from the complexes containing the more electron-donating alkyl ligands than from the complexes containing the more electron-poor alkyl ligands. Moreover, the data in eq 8 reveal that the rate constants for reductive elimination from alkyl complexes, at least qualitatively, track inversely with the Taft aliphatic substituent parameter.



R	σ^{*a}	k_{rel}
Me	0	>600
CH_2Ph	0.22	>250
$CH_2C(O)Ph$	0.60	31
CH_2CF_3	0.92	1.7
CH_2CN	1.30	1
CF_3	2.60	no reaction

(8)

[a] Taft σ^*-values fromTaft, R.W. "Steric Effects in Organic Chemistry"; Newman, M.S., Ed., Wiley: New York, 1956; Chapter 13 and Kanerva, L.T.; Euranto, E.K. *J. Chem. Soc., Perkin Trans.* 2 **1987**, *1*, 7.

These data provide information on the origin of electronic effects on reductive eliminations to form carbon−heteroatom bonds. Reductive elimination could be faster from complexes containing more electron-rich amido, alkoxo, phosphido, and thiolato complexes because the nonbonded electron pair attacks the accompanying organic ligand during the reductive elimination process. If this were the primary reason for the observed electronic effect, however, then reductive eliminations from arylpalladium alkyl complexes should lack a similar electronic effect on the reaction rate. Because the trend for reductive eliminations from arylpalladium alkyl complexes is similar to that for reductive eliminations from arylpalladium amido, alkoxo, phosphido, and thiolato complexes, we conclude that the electronic effect on reductive eliminations to form carbon−heteroatom bonds is transmitted predominantly through the σ system and not through the nonbonded electron pair on nitrogen, oxygen, phosphorus, or sulfur.

4. Sensitivity of the Different Classes of Reductive Elimination to the Electronic Properties of the Reactive Ligands. The data presented in the preceding sections allow one to deduce the relative sensitivity of the different types of reductive eliminations to electronic perturbations of the alkyl, amido, alkoxo, phosphido, and thiolato ligands. For example, the data in eqs 4 and 5 imply that the sensitivity of the reductive elimination of an arylamine toward the electronic properties of the amido group is greater than the sensitivity of the reductive elimination of an aryl sulfide toward the electronic properties of the thiolate group. The ratio of rate constants for reductive elimination from the *N*-methylanilide complex and the *p*-methoxy *N*-methylanilide complex is about 10, while the ratio of rate constants for reductive elimination from the analogously substituted thiolates is less than 2. Thus, the rates of reductive elimination from the complexes containing softer, more polarizable, reactive ligands appear to be less sensitive to the electronic properties of the substituents on the atom bound to the metal than are the rates of reductive elimination from complexes containing harder ligands.

5. Effect of Electronic Properties of the Aryl Group on the Rate of Reductive Elimination. The effect of electronic properties of the aryl group on the rate of reductive elimination is distinct from the effect of electronic properties of the alkyl, amido, alkoxo, thiolato, and phosphido ligands. Reductive elimination occurs *faster* from complexes with *less* electron-donating aryl groups than from complexes with more electron-donating aryl groups. This trend has now been observed for reductive eliminations from arylpalladium alkyl,[53] amido,[42] thiolato,[45] and alkoxo[54] complexes. The

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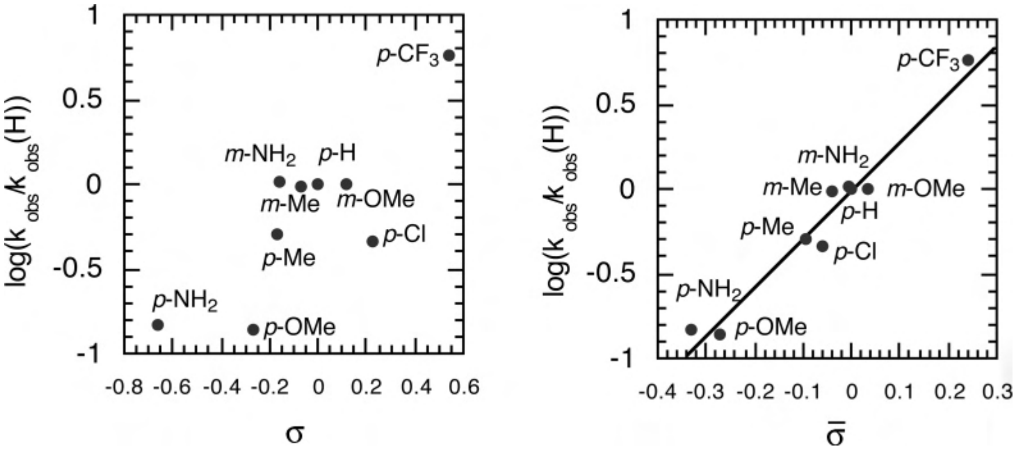

Figure 1. Standard Hammett plots for reductive elimination of sulfides from [Pd(DPPE)(Ar)(S*t*Bu)]. The separation of inductive and resonance effects leads to the values $\rho_I = 1.7$ and $\rho_R = 5.0$. Reproduced from ref 45 with permission from the American Chemical Society.

details of this electronic effect will be presented below, but one can first rank-order the sensitivity of these classes of reductive eliminations to the electronic properties of the metal-bound aryl group. In general, the electronic properties of the aryl group appear to affect the rate of reductive elimination of aryl ethers the most, followed by the effect on the rate of reductive elimination of arylamines, and then the effect on the rate of elimination of aryl sulfides. The least sensitive of these reactions appears to be reductive elimination to form C−C bonds from arylpalladium alkyl complexes.

Complementary studies of the electronic effects of the alkyl, amido, alkoxo, phosphido, and thiolato groups on the rates of reductive elimination suggest that the rates are controlled by a combination of inductive and resonance effects and that resonance effects are particularly pronounced. For example, classic Hammett plots for reductive elimination from arylpalladium thiolato complexes (Figure 1, left) were not linear.[45,55] To address the nonlinearity of these plots, data for reductive elimination from the arylpalladium thiolate and amido complexes were analyzed using dual-substituent parameters for inductive and resonance effects developed many years ago.[56] Weighting of the inductive and resonance effects on reductive elimination of aryl sulfides leads to the more linear free-energy relationship at the right of Figure 1. This analysis (and a similar anslysis of the data for reductive eliminations from arylpalladium amido and alkoxo complexes) suggested that the rate of reductive elimination from arylpalladium complexes is controlled more by the resonance effects of the substituents on the aryl group than by the inductive effects. For example, the ρ value for the inductive effect ρ_I on the reductive elimination of aryl sulfides was 1.7, and the ρ value for the resonance effect ρ_R was 5.0. A similar ratio between the ρ values for resonance and inductive effects was subsequently observed for the reductive elimination of arylamines from arylpalladium amido complexes,[42] and a strong resonance effect was observed for reductive elimination of aryl ethers from arylpalladium alkoxo complexes.[54] The importance of resonance effects on the reductive elimination of aryl sulfides led to the conclusion that the metal center interacted with the π system of the aryl group during the reductive elimination process and that an η^2-arene complex is the initial product of the reductive elimination.[45]

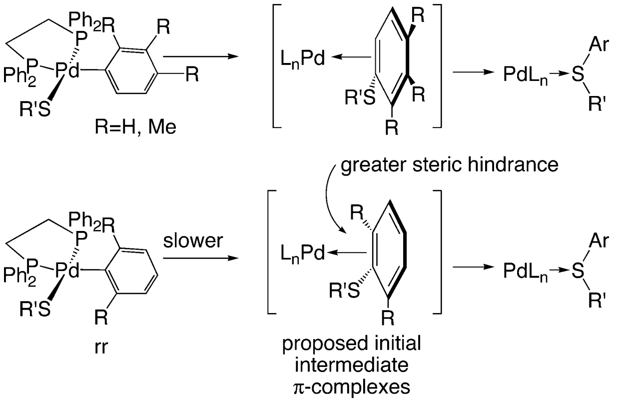

Figure 2. Proposed π complexes formed during reductive elimination from arylpalladium complexes.

The proposal that the pathway for reductive elimination involves interaction of the metal with the π system of the arene was supported by studies with arylpalladium thiolate complexes containing ortho substituents and has been implicitly supported by subsequent computational studies on the oxidative addition of haloarenes.[57−60] 1,2-Bis(diphenylphosphino)ethane (DPPE)-ligated *o*-tolylpalladium thiolate and phenylpalladium thiolate complexes (Figure 2) reacted with similar rate constants, but the 2,6-dimethylphenylpalladium thiolate complex reacted more slowly. As shown in Figure 2, the 2,6-disubstituted arylpalladium thiolate complex would suffer steric interactions during the formation of the initial complex to the arene π system at either of the two ortho carbons, but the 2-substituted and

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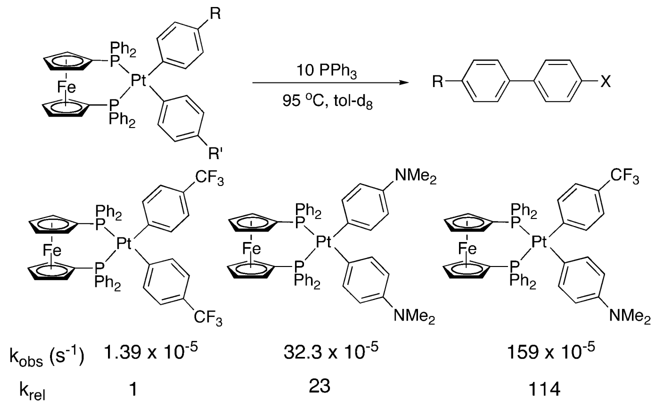
Scheme 2



unsubstituted aryl complexes would not encounter such strong steric effects during the formation of the initial complex to the arene π system at the unsubstituted ortho carbon.[45] More recent computational studies have suggested that the aryl group coordinates through the π system and that the metal migrates to the π system between the ipso and ortho carbons prior to carbon−halogen bond cleavage. Coordination of the metal to the π system between the ipso and ortho carbons after C−S, C−N, or C−O bond formation would, therefore, occur on the reaction coordinate in the reverse direction of reductive elimination.

6. Reductive Elimination from Biarylpalladium Complexes. The distinct electronic properties of the aryl ligand and of the alkyl, amido, alkoxo, phosphido, and thiolato ligands led the author's group to design a study of electronic effects on reductive elimination that would allow for systematic variation of two similar reactive ligands. Reductive elimination from biaryl complexes afforded an opportunity to conduct such a systematic study. Because biarylpalladium complexes are unstable, except in special cases,[61,62] these studies were conducted with biarylplatinum complexes.[63] The results from these studies implied that two electronic effects on the rate of reductive elimination occurred simultaneously. First, these studies implied that reductive elimination is faster from biarylplatinum complexes containing more electron-donating aryl groups. This trend is the opposite of the effect of the aryl group on reductive eliminations to form C−X bonds from arylpalladium amides, alkoxides, phosphides, and thiolates and to form C−C bonds from arylpalladium alkyls. Second, these results imply that reductive elimination is faster from biarylpalladium complexes possessing a greater difference between the electronic properties of the two ligands undergoing reductive elimination than from biaryl complexes containing two electronically similar aryl groups.

The data supporting these conclusions include the rates of reductive elimination from the three complexes in Scheme 2 and the Hammett plots of Figures 3−5. The three complexes in Scheme 2 show that the complex containing the two most electron-rich aryl groups eliminates faster than the complex containing the most electron-poor aryl groups but that the complex with one electron-rich group and one electron-poor aryl group eliminates the fastest. This trend is shown in more detail by the data in Figures 3−5. The two Hammett plots in Figures 4 and 5 show that the absolute value of ρ is significantly greater for reactions of the complexes containing one trifluoromethyl group than for the series of complexes containing one (dimethylamino)phenyl group. The larger absolute value of ρ for the series of complexes with one (trifluoromethyl)phenyl group is proposed to result from a larger difference between the electronic properties of the two aryl groups when the variable aryl group is more electron-rich and the constant group is more electron-poor. The small ρ value, at least for the set of data excluding the compound containing a (trifluoromethyl)phenyl group, is proposed to result from a smaller difference between the

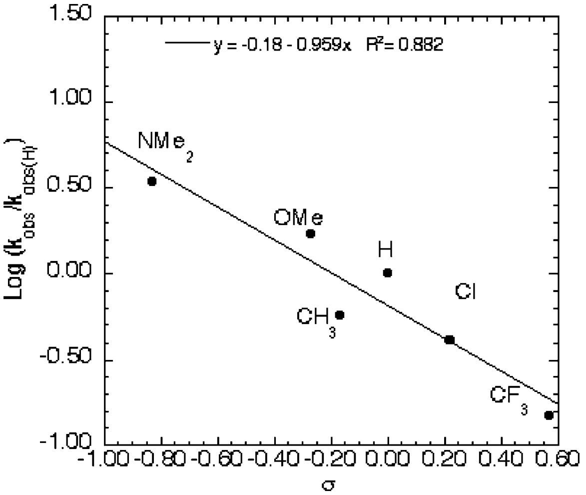


Figure 3. Hammett plot of the rates of reductive elimination from symmetrical biaryl complexes (DPPF)Pt(C_6H_4-4-X)$_2$. Adopted from ref 74 with permission from the American Chemical Society.

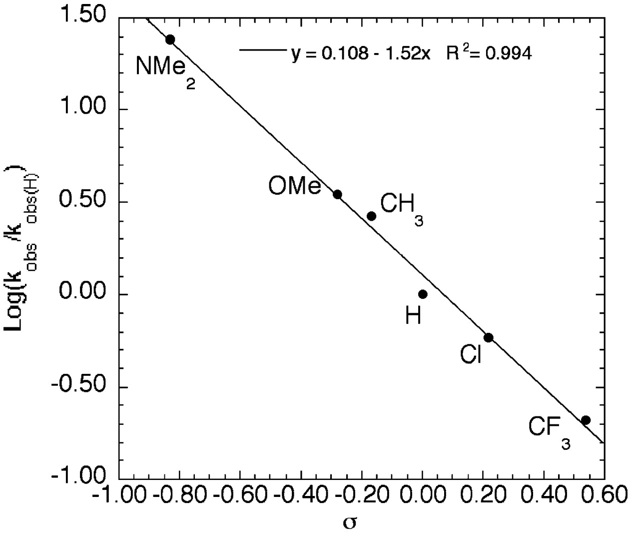


Figure 4. Hammett plot of the rates of reductive elimination from unsymmetrical biaryl complexes containing one electron-poor aryl group: (DPPF)Pt(C_6H_4-4-CF_3)(C_6H_4-4-X). Adopted from ref 74 with permission from the American Chemical Society.

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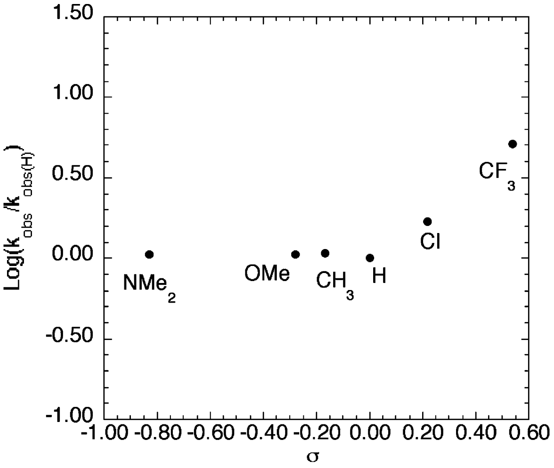


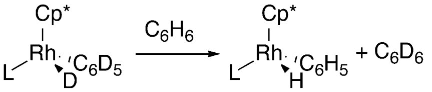
Figure 5. Hammett plot of the rates of reductive elimination from unsymmetrical biaryl complexes containing one electron-rich aryl group: (DPPF)Pt(C_6H_4-4-NMe_2)(C_6H_4-4-X). Adopted from ref 74 with permission from the American Chemical Society.

electronic properties of the two aryl groups when the variablearyl group and the constant aryl group are more electron-rich. Thus, the two electronic effects are proposed to enhance each other in the set of compounds with a constant (trifluoromethyl)phenyl group, but they counterbalance each other in the set of compounds with a constant (dimethylamino)phenyl group.

E. Electronic Effects of Ancillary Ligands on the Rate of Reductive Elimination from Palladium(II)

1. Background on the Effect of Ancillary Ligands on the Rate of Reductive Elimination. Much of transition-metal chemistry is controlled by ancillary ligands, and the rates of reductive elimination are no exception. In the absence of large π effects, reductive elimination usually occurs faster from more electron-poor metal centers than from more electron-rich metal centers possessing similar steric properties. This effect can be rationalized using thermodynamic arguments. If the reaction is considered an overall reductive process at the metal, then the reaction will be more favored thermodynamically when the metal center of the reactant is more electron-poor. Because more electron-donating ancillary ligands make the metal center more electron-rich, complexes containing strongly electron-donating ancillary ligands tend to undergo reductive elimination more slowly than complexes containing weakly electron-donating ancillary ligands.

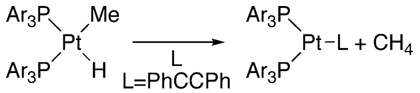
Two specific examples illustrate the effects of ancillary ligands on C−H bond-forming reductive eliminations. Jones and Kuykendall studied the reductive elimination of C_6D_6 from Cp*Rh(L)(C_6D_5)(D) complexes, certain pairs of which contained phosphine ligands that were not identical but possessed similar steric properties.[64] As summarized in eq 9, these studies showed that the reductive elimination of C_6D_6 was faster from complexes containing more strongly electron-donating ligands. Likewise, Halpern and co-workers showed



(9)

L=	cone angle	k_{obs}=
PMe_2Ph	122	1.08×10^{-6}
PMe_3	118	3.35×10^{-7}
PMe_2Ph	136	1.11×10^{-5}
PMe_2Bu^t	139	6.6×10^{-6}

that reductive elimination of methane from methyl hydride complexes of platinum-containing substituted triarylphosphine ligands occurs faster from complexes containing electron-withdrawing groups on the phosphine (eq 10).[65]



(10)

Ar=	k_{obs}(x 10^4)
C_6H_4Cl	9.2
C_6H_5	4.5
C_6H_4Me	1.4
C_6H_4OMe	0.47

However, this trend is not always followed. For example, the oxidative additions of MeI to the series of complexes $[Ir(CO)(PPh_3)_2X]$ (in which X = Cl, Br, or I) follow the relative reactivity Cl > Br > I, but the oxidative addition of dihydrogen to the same series of compounds follows the opposite relative reactivity of I > Br > Cl. Moreover, the oxidative addition of dihydrogen to a 16-electron iridium(III) fragment with an aryl group containing varied substituents is favored for the complex containing less electron-releasing substituents. Studies on the origin of this effect have been published.[18,66]

Naturally, the steric properties of ancillary ligands also affect the rate of reductive elimination. Complexes containing more sterically hindered ligands tend to undergo faster reductive elimination than complexes with less hindered ancillary ligands. This trend is observed for reductive eliminations to form C−H,[64] as well as C−X, bonds.[67,68] Because reductive elimination decreases the coordination number of the complex, steric hindrance will affect the energy of the reactant more than it will affect the energies of the transition state and product. Thus, reductive elimination from complexes containing more hindered ancillary ligands is more favorable thermodynamically and kinetically.

The effect of the coordination number on the rate of reductive elimination is less intuitively understood. Many studies have shown that reductive elimination to form C−C and C−X bonds occurs faster from three- and five-coordinate

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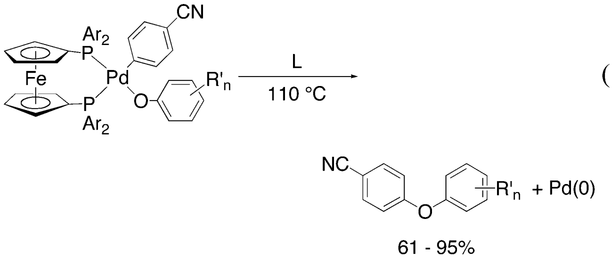
complexes than from four- or six-coordinate palladium and platinum complexes.[29,30,69−75] As a result, square-planar palladium(II) complexes containing monodentate ligands that generate three-coordinate intermediates by ligand dissociation typically undergo reductive elimination faster than complexes containing chelating ligands. Predictions of the rates of reaction as a function of steric and electronic properties should, therefore, be made for complexes with the same coordination number, and experiments to measure these effects should be conducted so that the electronic effects on dissociation or association of ligands are either avoided or taken into consideration.

2. Recent Studies of the Effect of Ancillary Ligands on Carbon−Heteroatom Bond-Forming Reductive Elimination. Many of the generalizations one can make about the electronic properties of ancillary ligands on C−H and C−C bond-forming reductive eliminations also apply to C−N, C−O, and C−S bond-forming reductive eliminations. Recent studies have provided information about the electronic effects of ancillary ligands on these reductive eliminations to form C−X bonds. These electronic effects are simplest for complexes of symmetric ancillary ligands. However, electronic effects on reductive elimination resulting from the orientation of unsymmetrical ancillary ligands have also been revealed, and these effects are comparable in magnitude to the effects from overall changes in the electron density at the metal center. The origins of the effects of unsymmetrical ancillary ligands are subtle.

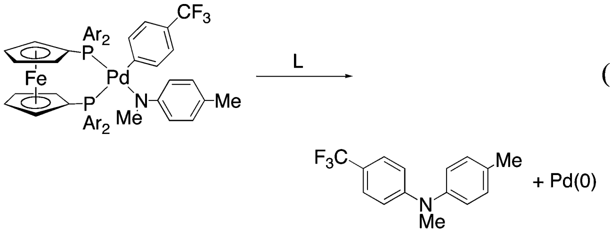
a. Electronic Effects of Symmetric Ancillary Ligands. The electronic effects of ancillary ligands on the rate of reductive elimination to form carbon−heteroatom bonds were first studied systematically by varying the electronic properties of the 1,1′-bis(diarylphosphino)ferrocene (DAPF) ligand in arylpalladium phenoxide complexes that form aryl ethers.[17] Not only did such a systematic variation reveal the effect of varying electronic properties of ancillary ligands on C−X bond-forming reductive elimination, but also this study provided a comparison of the relative sensitivities of the reaction toward electronic and steric effects. Equation 11 includes a summary of the complexes encompassed by this study. The arylpalladium aryloxide complexes containing *p*-anisyl groups on the phosphorus of the ancillary ligand underwent reductive elimination to form biaryl ether, but at a slower rate than the complex containing *p*-(trifluoromethyl)phenyl groups on phosphorus. However, the difference in the rate of reaction of the two complexes was only about a factor of 2.



(11)

Ar = Ph, C_6H_4-4-CF_3
R'_n=4-OMe, 4-OBu, 3,5-(t-Bu)$_2$
L = DPPF, CF_3DPPF, PhCCPh, PPh_3

Similar experiments were conducted on the reductive elimination of arylamines from arylpalladium amido complexes containing DAPF ligands.[43] These data are shown in eq 12. Again, reductive elimination was faster from the complex containing the less electron-donating ligand. A change in the aryl group from *p*-(trifluoromethyl)phenyl to *p*-anisyl led to a roughly 7-fold decrease in the rate of the reductive elimination of amine.



(12)

Ar	k_{obs} (10^4 s^{-1})
$C_6H_4CF_3$	27
C_6H_5	13
C_6H_4OMe	4.2

The small difference in the rate of reductive elimination from complexes with electronically distinct aryl groups on the phosphine ligand, and the accelerating effect of steric hindrance in the ancillary ligand, implies that complexes containing hindered alkylphosphines should undergo reductive elimination of aryl ethers. Indeed, complexes that are analogous to those in eq 11 but that contain the 1,1′-bis(di-*tert*-butyl)phosphine ligand underwent reductive elimination 2 orders of magnitude faster than complexes containing arylphosphine ligands.[17] To the extent that one can compare the magnitudes of the steric and electronic effects, this set of results implies that reductive elimination from square-planar palladium(II) complexes is more sensitive to steric effects than it is to electronic effects.

b. Electronic Effects of Unsymmetrical Chelating Ligands. Many palladium catalysts for reactions that occur by reductive elimination contain symmetric bidentate ligands. However, a number of such catalysts contain unsymmetrical bidentate ligands. Moreover, dissociation of a ligand from a four-coordinate palladium(II) complex generates a T-shaped intermediate that contains one ligand and one open-coordination site trans to the two reactive ligands. This lack of symmetry of the dative ligand set leads to two isomeric forms of the four- or three-coordinate arylpalladium complexes. These two isomers could undergo reductive elimination at different rates, and thus these relative rates would provide information as to how the orientation of two different electron donors affects the relative rates of reductive elimination.

In practice, arylpalladium amido complexes containing unsymmetrical DAPF ligands were prepared to determine if

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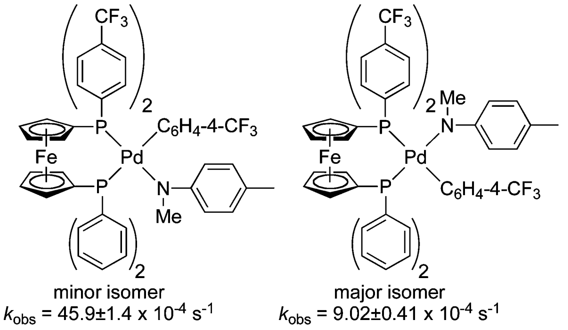

Figure 6. Rate constants for reductive elimination of *N*-methyldiarylamine from the major and minor isomers containing unsymmetrical DAPF ligands.

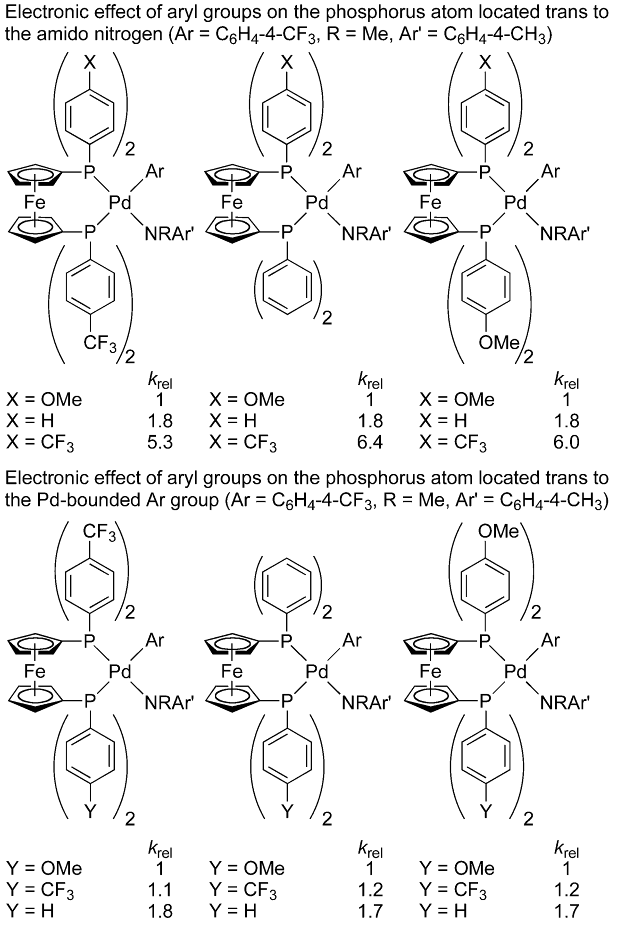

Figure 7. Data showing the relative magnitudes of the effect of varying the electron donor trans to the amido group and trans to the aryl group in the arylpalladium amido complexes containing electronically varied DAPF ligands. Adapted from ref 43 with permission from the American Chemical Society.

the orientation of two-electron donors with respect to the two groups undergoing reductive elimination affects the rate of reductive elimination.[43] These studies showed that reductive elimination from the less thermodynamically stable isomer was faster than reductive elimination from the more thermodynamically stable isomer. Two isomers of an arylpalladium halide complex containing an unsymmetrical ferrocenyl ligand are shown in Figure 6. As shown in this figure, the difference in the rate constants for the reaction of the two stereoisomers was about a factor of 5. The magnitude of this effect can be compared to the magnitude of the effect of changes to the overall electron density at the metal. As has been shown in eq 12, the difference in the rates of reductive elimination from the complex containing the two symmetrical DAPF ligands, DPPF and 1,1′-bis[[di-*p*-(trifluoromethyl)phenyl]phosphino]ferrocene, was only a factor of about 2. This comparison indicates that the effect of the orientation of the unsymmetrical ligand can be larger than the effect of the overall change in the electron density at the metal.

A more complete set of data on reductive elimination from complexes containing various DAPF ligands is provided in Figure 7.[43] The top of the figure shows three sets of complexes in which the phosphino group trans to the amido group is varied, and the bottom of the figure shows three sets of complexes in which the phosphino group trans to the palladium-bound aryl group ligand is varied. The data at the top of the figure illustrate that the electronic properties of the phosphino group trans to the amido ligand have a measurable effect on the rate of reductive elimination. This effect is similar in magnitude to the overall effect of varying the electronic properties of the symmetrical ligands. The data at the bottom of the figure show that variations in the electronic properties of the phosphino group trans to the aryl ligand have a much smaller effect on the rate of reductive elimination than do variations of the phosphino group trans to the amido ligand.

An understanding of the relative contributions of ground- and transition-state effects can be gained by considering the difference in the thermodynamic stabilities of two isomers containing different orientations of unsymmetrical bis(phosphine) ligands. Figure 8 summarizes the relative ground- and transition-state energies in a proposed reaction coordinate for reductive elimination from the two isomers. The difference in the thermodynamic stabilities is close to the difference in the rate constants. This similarity implies that the observed effect of the orientation of the unsymmetrical ligand on the rate of reductive elimination originates predominantly from an electronic effect on the relative energies of the ground states.

Figure 9 summarizes several gross changes that would occur during the reductive elimination process. This figure highlights several reasons why the effect of the orientation of the ligand might be expected to originate from the orientation's effect on the stability of the ground states. First, this drawing reveals that the products from the reaction of both isomers are the same. Second, the drawing shows that the coordination sphere of the metal becomes less unsymmetrical as the reaction progresses. Thus, the observed effect of the geometry on the reaction rate can be attributed more to a ground-state “trans influence” than to a kinetic “trans effect”.[76]

F. Comparison of Relative Rates to Early Predictions

The large amount of data gathered recently on electronic effects on the rates of reductive elimination allow for a meaningful discussion of how well these data fit early predictions[22−24,77] about the nature of electronic effects on the rates of reductive elimination. Some of the data on the

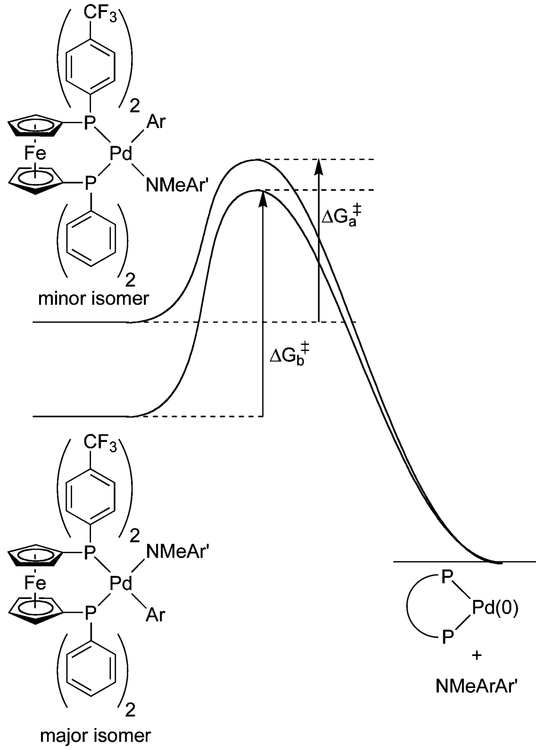

Figure 8. Qualitative energy diagram for reductive elimination from two isomeric arylpalladium amido complexes containing an unsymmetrical bis(phosphine) ligand. Adapted from ref 43 with permission from the American Chemical Society.

relative rates for reductive elimination from palladium alkyl, amido, alkoxo, thiolato, and phosphido complexes follow predictions made many years ago about the effect of electronics on reductive elimination, but other data contradict these predictions or require modifications of them. As noted in the Introduction, complexes containing more electron-donating reactive ligands were predicted to undergo reductive elimination faster than complexes with less electron-donating reactive ligands. Consistent with this prediction, arylpalladium amido complexes tend to undergo reductive elimination faster than arylpalladium alkoxo complexes, and arylpalladium amido complexes undergo reductive elimination faster than arylpalladium amidate complexes.[78] Moreover, complexes containing less electron-donating ancillary ligands were predicted to undergo reductive elimination faster than complexes with more electron-donating ancillary ligands. Many results with palladium(II) complexes are also consistent with this basic trend.

However, several pieces of data do not fit this simple trend. First, organopalladium thiolato complexes undergo reductive elimination[45,55] faster than organopalladium amido complexes,[42] even though a thiolate ligand is less basic than an amido ligand. Because the thiolate ligand is much more polarizable than the amido ligand, we propose that the polarizability of the heteroatom or the nucleophilicity of the ligand is as important in controlling the rate of reductive elimination as the overall electron-donating ability.

Second, data from studies on electronic effects of the aryl group on reductive elimination[42,45,53−55,63] directly conflict with the assertion that reductive elimination should be faster from complexes containing more electron-donating reactive ligands. Instead, reductive elimination from arylpalladium complexes containing more electron-poor aryl groups occurs faster than reductive elimination from arylpalladium complexes containing more electron-rich aryl groups. This effect has not been explained by modern computational studies. A close view of this electronic effect from experimental studies did shed some light on this issue, however. Analysis of the electronic effects of the aryl group implied (1) that the effect of electronic properties of the aryl group results from both inductive and resonance effects, (2) that the inductive effect is smaller than the resonance effect,[42,54,55] and (3) that the resonance effect results from binding of the metal to the arene π system of the initially formed product of reductive elimination.[55]

Third, these studies of electronic effects led to the conclusion that the rate of reductive elimination depended on a synergistic relationship between the electronic properties of the two reactive ligands rather than depending the electronic properties of the individual ligands.[63] Reductive elimination was faster from complexes possessing a larger difference in the electronic properties of the two reactive ligands than from complexes possessing a smaller difference in the electronic properties of the reactive ligands. Further, the sensitivity of reductive elimination processes to differences in the electronic properties of the aryl group depended on the type of heteroatom ligand with which the aryl group was coupling.

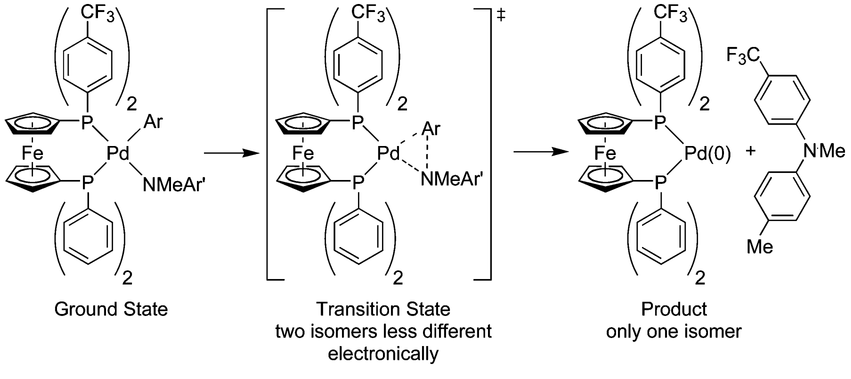

Figure 9. Depiction of the geometric changes that occur during reductive elimination from an arylpalladium amido complex containing an unsymmetrical bidentate ligand. Adapted from ref 43 with permission from the American Chemical Society.

Fourth, data on complexes containing unsymmetrical dative ligands showed that the orientation of the electron donors can influence the rate of the reaction as much as the overall electron-donating ability of the dative ligands.[43] This effect of the orientation of such a ligand had not previously been addressed. This effect proved important to consider because the difference in the rate of reductive elimination from two stereoisomeric arylpalladium amido complexes was as large as differences in the rates of reductive elimination from complexes containing ancillary ligands that impart significant changes in the overall electron density at the metal.

Thus, many of the inconsistencies between previous predictions and recent data arose when reductive elimination occurred from unsymmetrical complexes. Of course, reductive elimination to form carbon−heteroatom bonds must occur from unsymmetrical complexes through unsymmetrical transition states. Athough reductive elimination to form C−C bonds can occur from symmetrical complexes in special cases, in catalytic processes it occurs more often from unsymmetrical complexes. Therefore, an understanding of the electronic effects on reductive elimination in the general case, when two different ligands undergo coupling, is crucial to understanding and predicting the rates and scope of catalytic processes, including commonly practiced cross-couplings. A theoretical explanation for these electronic effects awaits additional modern computational work.

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