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Reductive Elimination of Aryl Halides from Palladium(II)

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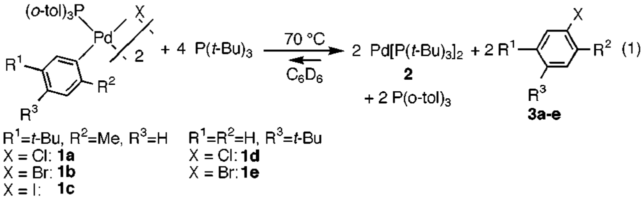
The oxidative addition of aryl halides to palladium(0) complexes[1,2] is the initial step of catalytic processes such as Heck,[3−5] Stille,[6,7] and Suzuki coupling,[8] as well as the recently developed arylation of amines,[9−12] ethers,[13,14] and carbonyl compounds.[15,16] Essentially any phosphine-ligated palladium(0) complex studied previously undergoes oxidative addition of aryl bromides and iodides. The opposite reaction, reductive elimination of aryl halides, is rare because addition is favored thermodynamically. A single example of aryl halide reductive elimination was observed from a higher valent Pt(IV) species many years ago,[17] but reductive elimination from low-valent centers has not been observed directly.[18]

In general, complexes with increasingly electron-donating ligands undergo faster oxidative addition because of the greater driving force for oxidation of a more electron-rich metal.[19] Indeed, trialkylphosphine complexes add even chloroarenes,[20] and some of these and related ligands provide fast rates for coupling processes.[21−23] P(t-Bu)$_3$ is the quintessential strongly electron donating ligand. Its ν_{CO} value for {Ni[P(t-Bu)$_3$](CO)$_3$} is the lowest of any phosphine ligand in Tolman's classic study.[24] Yet, we report the surprising result that reductive elimination of aryl halide is induced by addition of tri-*tert*-butylphosphine to arylpalladium(II) halide complexes (eq 1) and is favored thermodynamically over oxidative addition. We provide equilibrium constants for the addition and elimination processes in eq 1 and show that an unusual mechanism for ligand exchange occurs to initiate the reductive elimination.

Table 1. The Yield of ArX and the Calculated K_{eq}[a] Value for the Reactions in Eq 1

X	yield of ArX (%)	K_{eq}
1a (X=Cl)	70	$9(3) \times 10^{-2}$
1b (X=Br)	70	$2.3(3) \times 10^{-3}$
1c (X=I)	39	$3.7(2) \times 10^{-5}$
1d (X=Cl)	30	not measured[b]
1e (X=Br)	75	$3.3(6) \times 10^{-4}$

[a] K_{eq} values are referenced to a 1 M standard state. [b] This reaction appeared to consume all of the aryl chloride complex, but low yields for the formation of free aryl chloride may prevent reversibility.



Equation 1 and Table 1 summarize our data on the reductive elimination of aryl halide from complexes **1a**−**e**[25] upon addition of P(t-Bu)$_3$. All of the P(o-tolyl)$_3$-ligated arylpalladium halides formed {Pd[P(t-Bu)$_3$]$_2$} (**2**)[26] upon addition of an excess of P(t-Bu)$_3$. *Ortho*-substituted aryl halide complexes **1a**−**c** provided higher yields of free aryl halide product than did complexes **1d**−**e** containing unhindered palladium-bound aryl groups. Biaryl and arene were the predominant side products. The *tert*-butyl group in **1a**−**c** was employed to provide solubility. The amount of added P(t-Bu)$_3$ was crucial to obtain high yields of free aryl halide. The highest yields were obtained when approximately 15 equiv of P(t-Bu)$_3$ per dimer were used. Although not limited by the values of K_{eq} when 15 equiv of P(t-Bu)$_3$ were used, the yields for the reductive elimination of compounds **1a**−**c** paralleled the thermodynamic driving force. Yet, the rates did not. Reductive elimination from chloride **1a** was slower than that from bromide **1b**, even though reductive elimination from **1a** was more favored thermodynamically. The low yield of chloroarene from reaction of **1d** is consistent with the slow rates for reaction of the more hindered chloride **1a** and with generally slow rates for the microscopic reverse, oxidative addition of aryl chloride.

K_{eq} values (Table 1) were obtained for the process in eq 1 by initiating reactions from both sides of the equilibrium. All reaction components of the equilibrium were observed by NMR spectroscopy when less than 4 equiv of P(t-Bu)$_3$ were added to a 10 mM solution of chloride **1a**, less than 10 equiv to a 10 mM solution of bromide **1b**, and less than 15 equiv to the same solution of **1c**. Quantitative data are provided in Table 1. An o-methyl group on the aryl halide increased the value of K_{eq} for reductive elimination by a factor of roughly ten. Chloride **1a** displayed the largest driving force for reductive elimination and iodide **1c** had the smallest. The change in K_{eq} that accompanied each successive change of halide was roughly a factor of 100. Despite this trend, oxidative addition of aryl halides **3c** and **3e** to {Pd[P(t-Bu)$_3$]$_2$} was not observed in the absence of added P(o-tolyl)$_3$.

The reductive elimination most likely occurs from a monomeric complex, but the coordination sphere of this monomer and the mechanism for its formation were unclear. Moreover, we could not predict whether the generation or reaction of the monomer was rate determining. To address these questions, we measured the rate constants for reaction of **1b** by ^{1}H NMR spectroscopy at 55 °C. The concentration of P(t-Bu)$_3$ was varied from 0.10 to 0.84 M, [P(o-tol)$_3$] was varied from 0.030 to 0.35 M, and [**1b**] was varied from 5.2 to 21 mM. Because the P(o-tol)$_3$ product

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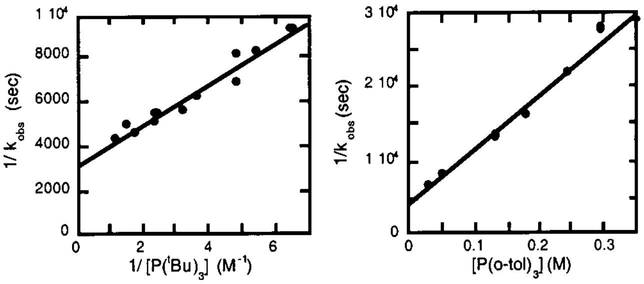
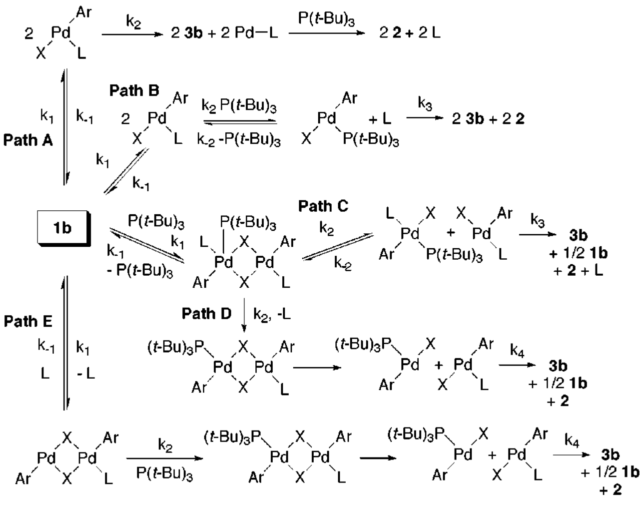
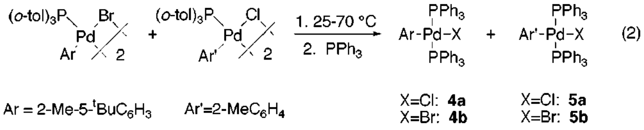


Figure 1. Plots of $1/k_{obs}$ vs $1/[P(t\text{-}Bu)_3]$ and $1/k_{obs}$ vs $[P(o\text{-}tol)_3]$.

Scheme 1



may be formed reversibly and can enter the rate equations, it was added to the reactions to maintain a constant concentration. Excellent fits to a first-order appearance of each product were obtained. Figure 1 shows the dependence of k_{obs} on the concentration of the two phosphines. A positive, linear dependence of $1/k_{obs}$ vs $1/[P(t\text{-}Bu)_3]$ was observed, along with a nonzero *y*-intercept. The inverse dependence of k_{obs} on $[P(o\text{-}tolyl)_3]$ in Figure 1 also showed a nonzero *y*-intercept.



Qualitative mechanistic studies showed that the reaction was not affected by light, and that anthracene was not formed as product when the reactions were run in the presence of 9,10-dihydroanthracene. Moreover, the rate constants were highly reproducible. Thus, further studies to detect a radical pathway were not conducted as part of our mechanistic evaluation.

Instead, the five classes of mechanism for the reductive elimination in Scheme 1 were considered. Rate expressions are provided as supporting information. Path A is initiated by reversible or irreversible cleavage of the dimeric complex to form two monomers, which undergo reductive elimination to form a Pd(0) species that is trapped by $P(t\text{-}Bu)_3$ to form **2**. Although reductive elimination from **1** would be endothermic, the trapping of the Pd(0) intermediate by $P(t\text{-}Bu)_3$ to form **2** would provide the overall driving force. This mechanism predicts either half-order rate behavior in dimer and first-order behavior in $P(t\text{-}Bu)_3$ or first-order behavior in dimer and zero-order behavior in $P(t\text{-}Bu)_3$. Both of these predictions are inconsistent with our data. Moreover, these mechanisms predict that dimer cleavage requires 55 °C to occur or that reductive elimination of aryl halide occurs reversibly at 55 °C in the absence of $P(t\text{-}Bu)_3$. To probe for reversible dimer cleavage, we conducted the reaction in eq 2 and analyzed the products after addition of PPh_3 to simplify the product distribution. Although several potential pathways for exchange are possible, this experiment was consistent with our intuition that cleavage of the halogen bridges is more rapid than the overall reaction at 55 °C. To probe for reversible reductive elimination in the absence of added $P(t\text{-}Bu)_3$, we added 4-BrC_6H_4-*t*-Bu to **1b** and $\{Pd[P(o\text{-}tolyl)_3](p\text{-}tol)(Br)\}_2$. Only small amounts of exchange were observed after days at 55 °C.

Path B involves reversible or irreversible cleavage of the dimer, followed by ligand exchange and reductive elimination. This pathway again predicts a reaction that is either half order in dimer first order in $P(t\text{-}Bu)_3$ or, if first order in dimer, then zero order in both $P(t\text{-}Bu)_3$ and $P(o\text{-}tol)_3$. Again, these predictions are inconsistent with the kinetic data.

Path C involves initial coordination of $P(t\text{-}Bu)_3$ to palladium and either reversible or irreversible formation of a three-coordinate $P(o\text{-}tol)_3$ complex and a four-coordinate mixed-phosphine complex. The four-coordinate, $P(t\text{-}Bu)_3$-ligated complex would then reductively eliminate aryl halide either before or after dissociating $P(o\text{-}tolyl)_3$. This associative mechanism with reversible formation of mononuclear species predicts a simple half-order dependence of rate on $[P(t\text{-}Bu)_3]$, and this prediction is inconsistent with data in Figure 1 displaying a first-order dependence and *y*-intercept. Irreversible association of $P(t\text{-}Bu)_3$ or dimer cleavage would provide zero-order behavior in $P(o\text{-}tolyl)_3$. The nonzero *y*-intercept and the inverse rate dependence on $[P(o\text{-}tolyl)_3]$ in Figure 1 are clearly inconsistent with this prediction. Path D shows an initial, reversible associative phosphine substitution and irreversible cleavage of the resulting dinuclear species. This mechanism would show a simple first-order dependence on $[P(t\text{-}Bu)_3]$ and if the liquid substitution were reversible a simple inverse dependence on $[P(o\text{-}tolyl)_3]$. These predictions are inconsistent with the nonzero *y*-intercepts in Figure 1.

Instead, all of our data are consistent with Path E, involving an irreversible dissociative ligand substitution, which is presumably followed by cleavage of the dinuclear species prior to reductive elimination. Of course, dissociative substitution is unusual for square-planar geometries. The rate equation for dissociative substitution predicts positive slopes and nonzero *y*-intercepts for both plots in Figure 1. The first-order rate behavior in [**1b**] indicates an irreversible formation of monomers from the dinuclear species formed from ligand substitution. Moreover, the nonzero *y*-intercept requires that the k_2 step be irreversible. These data demonstrate that each ligand substitution event leads to reductive elimination. Thus, formation of monomers and reductive elimination is faster than dissociation of $P(t\text{-}Bu)_3$.

The reductive elimination reported here uncovers several fundamental principles. First, reductive elimination is often induced by coordination of electron-accepting ligands, but is induced here by coordination of a strongly electron-donating ligand. Thus, severe steric crowding not only can accelerate the rate for reductive elimination, but also can alter the thermodynamics so severely that reductive elimination of aryl halide is favored thermodynamically. Second, oxidative addition occurs rapidly to $P(t\text{-}Bu)_3$-ligated Pd(0) complexes in catalytic processes despite the weak driving force for this reaction. Third, ligand substitution in this square-planar system is dissociative, presumably because of the steric properties of the ligands involved. Finally, these studies suggest that a palladium-catalyzed aromatic halide exchange process is feasible. Further studies that target such a catalytic, aromatic Finkelstein reaction are in progress.

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Supporting Information Available: Spectroscopic and analytical data on new compounds, procedures for kinetic studies, and kinetic expressions for mechanisms A–E in Scheme 1 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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