Communication
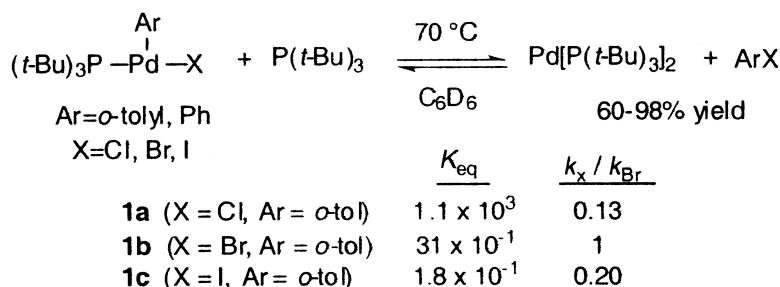
Directly Observed Reductive Elimination of Aryl Halides from Monomeric Arylpalladium(II) Halide Complexes

Amy H. Roy, and John F. Hartwig

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 15 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Directly Observed Reductive Elimination of Aryl Halides from Monomeric Arylpalladium(II) Halide Complexes

Amy H. Roy and John F. Hartwig*

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

Received August 15, 2003; E-mail: john.hartwig@yale.edu

Oxidative addition and reductive elimination are fundamental organometallic reactions and common steps in catalytic processes.[1] For example, the oxidative addition of aryl halides is the initial step in nearly all palladium-catalyzed cross-coupling reactions.[2−11] The oxidative addition of aryl halides to palladium(0) is common. Reductive elimination of aryl halides is rare because the free energy favors oxidative addition in most cases. A rare example of reductive elimination of an aryl halide was observed many years ago from the high-valent [Pt(PEt$_3$)$_2$(Ph)$_2$I$_2$].[12]

The oxidative addition of aryl iodides is faster than the oxidative addition of aryl bromides, and the oxidative addition of aryl chlorides is slower. These rates are usually attributed to the strengths of the Ar−X bonds.[1,13] However, no thermodynamic data on the overall oxidative addition process have been obtained, and the rates for elimination directly from the arylpalladium halide complexes have not been measured. These data would address fundamental questions. For example, reductive elimination from an arylpalladium chloride complex would be faster than elimination from the analogous bromide or iodide if ground-state effects, such as the carbon−halogen bond strengths, controlled relative reaction rates as proposed. However, reductive elimination from an arylpalladium chloride complex would be the slower than elimination from the bromide and iodide complexes if bonding and electronic properties of the halogen on the transition state controlled the relative rates for addition and elimination.
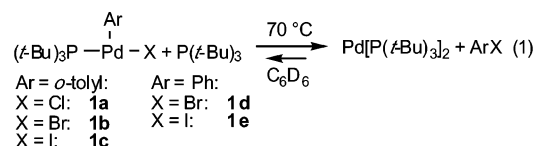
Recently, the oxidative addition of aryl halides to palladium(0) complexes of P(t-Bu)$_3$ or 1-AdP(t-Bu)$_2$ ligands to form three-coordinate monomers stabilized by an agostic interaction has been reported.[14] These compounds are likely intermediates in metal-catalyzed cross-coupling reactions. We also reported reductive elimination of aryl halides upon addition of the same type of alkylphosphine to {Pd[P(o-tolyl)$_3$](Ar)(X)}$_2$ complexes. In this case the species undergoing reductive elimination was not observed directly.[15] We now report the direct observation of the reductive elimination of aryl halide from a three-coordinate arylpalladium halide complex (eq 1) and equilibrium data for the addition and elimination of aryl halides from tri-*tert*-butylphosphine-ligated palladium complexes. These studies reveal the thermodynamic parameters for oxidative addition and reductive elimination, a high kinetic barrier for both addition and elimination of ArCl, and evidence for reversible ArX cleavage on the path to reductive elimination of haloarene.

Equation 1 and Table 1 summarize data on the reductive elimination of haloarene from arylpalladium halide complexes **1a−e**

Table 1. Yields of ArX and Values of K_{eq}[a] for the Reactions in Eq 1

| X	yield of ArX (%)[b]	K_{eq}
1a (X = Cl, Ar = o-tol)	76	10.9×10^2
1b (X = Br, Ar = o-tol)	98	32.7×10^{-1}
1c (X = I, Ar = o-tol)	79	1.79×10^{-1}
1d (X = Br, Ar = Ph)	68	13.4×10^{-1}
1e (X = I, Ar = Ph)	60	0.51×10^{-1}

[a] K_{eq} values are referenced to a 1 M standard state. [b] 10 mM **1a−e**, 20 equiv of added P(t-Bu)$_3$, 70 °C.

upon addition of P(t-Bu)$_3$. Yields for the direct reductive elimination in eq 1 were higher than the yields for the reductive elimination of aryl halide from the two-step ligand substitution and reductive elimination process initiated with dimeric, P(o-tolyl)$_3$-ligated arylpalladium halide complexes reported previously.[15] The yields were affected in some cases by the instability of the 14-electron products to the thermal conditions. No side products were observed by ^{1}H NMR spectroscopy at short times, but some decomposition products were observed as the reactions progressed. Arene and biaryl were the predominant side products.

Values of K_{eq} were obtained for the process in eq 1 by initiating reactions in both directions. Qualitatively, an equilibrium was established when less than 8 equiv of P(t-Bu)$_3$ were added to a 10 mM solution of bromide **1b** and less than 20 equiv to a 10 mM solution of iodide **1c**. The reductive elimination of chloroarene from aryl chloride complex **1a** occurred to high conversion, even with only 1 equiv of added P(t-Bu)$_3$. Conditions to measure K_{eq} for the addition and elimination of chloroarene were established with 100 equiv of added chloroarene.
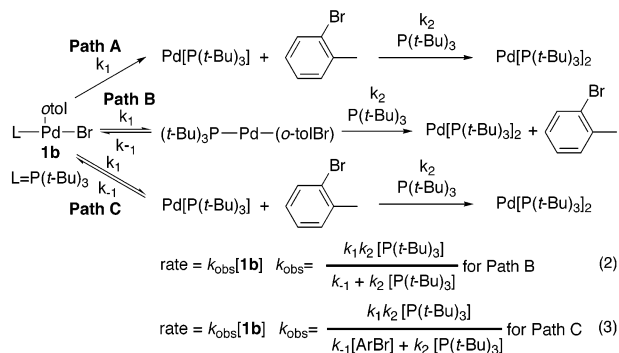
Quantitative data for the addition and elimination equilibria are provided in Table 1. The identity of the halide affected the value of K_{eq} by several orders of magnitude. Reductive elimination from chloride **1a** was more favorable than elimination from bromide **1b** by a factor of 3000. Reductive elimination from iodide **1c** was less favorable than elimination from **1b** by a factor of roughly 20. This trend parallels the strengths of the PhX bonds,[13] implying that the carbon−halogen bond strength dominates the reaction thermodynamics. The presence of an ortho methyl group on the aryl halide increased the value of K_{eq} for reductive elimination only by a factor of about 3.

However, the reaction kinetics did not track with thermodynamics. The rate of reductive elimination from chloride **1a** was slower than that from bromide **1b**, even though this reductive elimination was more favorable thermodynamically. The rate of reductive elimination from iodide **1c** lay between that for reaction of **1b** and for reaction of **1a**. The comparison of rates of reaction of **1a** and **1b** show that the relative rates for reaction of chloro- and bromoarenes are controlled by transition-state energies, not by ground-state thermodynamics. The strength of the C−X bond that is claimed to be responsible for the slow rate for addition does not
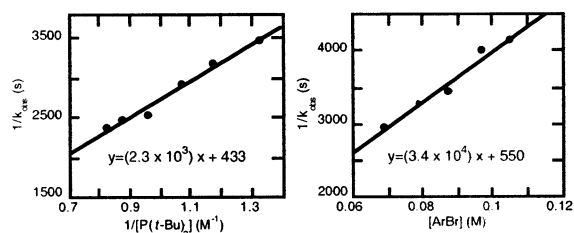
Figure 1. Plot of $1/k_{obs}$ vs $1/[P(t\text{-Bu})_3]$ and $1/k_{obs}$ vs $[ArBr]$ for the reductive elimination of aryl bromide from complex **1b**.

Scheme 1

$$\text{rate} = k_{obs}[\mathbf{1b}] \quad k_{obs} = \frac{k_1 k_2 [P(t\text{-Bu})_3]}{k_{-1} + k_2 [P(t\text{-Bu})_3]} \text{ for Path B} \quad (2)$$

$$\text{rate} = k_{obs}[\mathbf{1b}] \quad k_{obs} = \frac{k_1 k_2 [P(t\text{-Bu})_3]}{k_{-1}[ArBr] + k_2 [P(t\text{-Bu})_3]} \text{ for Path C} \quad (3)$$

create a low-energy transition state. Instead, the softness or nucleophilicity of the halogen in the transition state for addition and elimination is likely to be more important. The rate of reaction of the iodide **1c** appears to result from a combination of ground- and transition-state effects.

Reductive elimination is typically faster from three-coordinate than related four-coordinate complexes,[1,16] and the steric hindrance of $P(t\text{-Bu})_3$ makes elimination from a four-coordinate species after ligand association unlikely. Thus, reductive elimination of bromoarene from the starting arylpalladium bromide complex seemed the most likely mechanism.[17] This mechanism is shown as Path A in Scheme 1. Under conditions in which the reaction is driven far to the side of reductive elimination, formation of bromoarene from the three-coordinate complex would correspond to a rate equation that is zero order in the concentration of ligand and aryl bromide.

To evaluate this mechanistic assumption, rate constants for the reductive elimination of bromoarene from {Pd[P(t-Bu)$_3$](o-tolyl)-(Br)} (**1b**) at 17 mM initial concentrations were measured over 5 half-lives by ^{1}H NMR spectroscopy at 65 °C. Excellent fits to a first-order appearance of product were obtained. The concentration of $P(t\text{-Bu})_3$ was varied from 0.13 to 0.61 M while maintaining a constant concentration of added bromoarene by addition of 0.069 M bromotoluene to the initial reaction, and the concentration of 2-bromotoluene was varied from 0 to 0.11 M with a constant 0.87 M concentration of $P(t\text{-Bu})_3$. In contrast to the predictions of Path A, the observed rate constants depended on the concentration of both ligand and bromoarene. Figure 1 shows that the reaction displayed a positive, linear dependence of $1/k_{obs}$ on $1/[P(t\text{-Bu})_3]$ and $[ArBr]$, with a nonzero y-intercept that was similar in both plots.

Thus, two mechanisms, Paths B and C in Scheme 1, were considered as alternatives to Path A. Path B involves reversible reductive elimination of aryl bromide from **1b** to produce a $P(t\text{-Bu})_3$-ligated palladium complex with an intact, coordinated bromoarene. Associative ligand substitution of phosphine for the coordinated

bromoarene would then form Pd[P(t-Bu)$_3$]$_2$ and free aryl bromide. As shown in eq 2, this pathway predicts first-order behavior in **1b**, zero-order behavior in bromoarene, first-order behavior in $P(t\text{-Bu})_3$ at low $[P(t\text{-Bu})_3]$, and zero-order behavior at high $[P(t\text{-Bu})_3]$. Path C involves reversible reductive elimination of aryl bromide from **1b** with or without an intermediate haloarene complex,[18] followed by trapping of the palladium(0) intermediate by $P(t\text{-Bu})_3$. As shown in eq 3, this pathway predicts the same behavior in the concentration of **1b** and $P(t\text{-Bu})_3$ as path B. However, path C predicts that the observed rate constant will depend inversely on $[ArBr]$ when the k_2 step competes with the k_{-1} step. The inverse dependence of the rate constant on the concentration of $[ArBr]$ shows that the reaction occurs by path C.

The y-intercept of the plot of $1/k_{obs}$ vs $[ArBr]$ corresponds to $1/k_1$. The value k_1 is the rate constant for reductive elimination of 2-bromotoluene from **1b**. The ratio of k_{-1}/k_2, describes the relative rate constants for the oxidative addition of this bromoarene to Pd[P(t-Bu)$_3$] and the coordination of $P(t\text{-Bu})_3$ to Pd[P(t-Bu)$_3$]. The data in Figure 1 show that the rate constant for oxidative addition of bromoarene exceeds the rate constant for ligand association by a factor of 65 ± 25. Thus, oxidative addition to Pd[P(t-Bu)$_3$] is even faster than simple coordination of ligand to this highly unsaturated intermediate.

In summary, we have shown that slow activation of chloroarenes results from a transition state that is high in energy for reasons beyond the strength of the ArCl bond and that oxidative addition of aryl halides to Pd[P(t-Bu)$_3$] is faster than simple ligand coordination. Further studies with other hindered alkylphosphines and the effects of haloarene electronics on the rates and equilibria for addition and elimination will comprise future studies.

Supporting Information Available: Experimental methods and spectral data for **1a–d** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed.; University Science Books: Mill Valley, CA, 1987; pp 322−333.
(2) Heck, R. F. *Org. React.* **1982**, *27*, 345−390.
(3) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009−3066.
(4) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524.
(5) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1−652.
(6) Kosugi, M.; Fugami, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: Hoboken, NJ, 2002; Vol. 1; pp 263−283.
(7) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483.
(8) Hartwig, J. F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; E. I. Negishi, Ed.; Wiley-Interscience: New York, 2002; Vol. 1; pp 1051, 1097.
(9) Hartwig, J. F. In *Modern Arene Chemistry*; Astruc, C., Ed.; Wiley-VCH: Weinheim, 2002; p 107.
(10) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131.
(11) Culkin, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234−245.
(12) Ettorre, R. *Inorg. Nucl. Chem. Lett.* **1969**, *5*, 45−49.
(13) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 7−1062.
(14) Stambuli, J. P.; Buhl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 9346−9347.
(15) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, 1232−1233.
(16) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*, 3rd ed.; John Wiley & Sons: New York, 2001; pp 162−166.
(17) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 8232−8245.
(18) Kulawiec, R. J.; Crabtree, R. H. *Coord. Chem. Rev.* **1990**, *99*, 89−115.

JA037959H