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Autocatalytic Oxidative Addition of PhBr to $Pd(P^tBu_3)_2$ via $Pd(P^tBu_3)_2(H)(Br)$

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The oxidative addition of aryl halides or sulfonates to Pd(0) complexes is the first step in classic and recently developed cross-coupling reactions. Among the most active catalysts for many coupling reactions are complexes of P^tBu_3.[1] Recently, we reported the isolation of unusual three-coordinate products from oxidative addition of bromoarenes to Pd(0) complexes of P^tBu_3.[2] We have now studied the mechanism of the oxidative addition of bromoarenes to $Pd(P^tBu_3)_2$, and this mechanism is equally unusual. The reaction in the absence of a strong base is autocatalytic, and a side product, $Pd(P^tBu_3)_2(H)(Br)$, is capable of acting as the catalyst. In contrast to the typically higher reactivity of haloarenes with Pd(0) species than with Pd(II), the reaction of bromobenzene with $Pd(P^tBu_3)_2(H)(Br)$ occurs faster than with $Pd(P^tBu_3)_2$ to form $Pd(P^tBu_3)(Ph)(Br)$. Studies that support these conclusions are reported here.

$$\begin{array}{llll} & & \text{toluene} & \text{MEK} \\ & (P^tBu_3)Pd(Ph)(Br)\ (\mathbf{2}) & 60\% & 98\% \\ (P^tBu_3)_2Pd\ (\mathbf{1}) \xrightarrow[\text{toluene or MEK}]{70\ ^{o}C} & (P^tBu_3)_2Pd(H)(Br)\ (\mathbf{3}) & 10\% & <2\% \\ \quad + PhBr & [(P^tBu_3)Pd(\mu\text{-}Br)]_2\ (\mathbf{4}) & 13\% & <2\% \\ & [\overline{Pd(P^tBu_2C(CH_3)_2CH_2})(\mu\text{-}Br)]_2\ (\mathbf{5}) & 16\% & <2\% \end{array} \quad (1)$$

The oxidative addition of PhBr to $Pd(P^tBu_3)_2$ (**1**) produces the three-coordinate $(P^tBu_3)Pd(Ph)(Br)$ (**2**).[2] The yields of **2** and side products in polar and nonpolar solvents are shown in eq 1. The reaction in polar solvents, such as methyl ethyl ketone (MEK), formed **2** in high yield. Reactions in toluene were slower, and this slower rate allowed decomposition of the product (vide infra) to occur in parallel with the oxidative addition. Thus, a typical product distribution in toluene was **2** (60%), $(P^tBu_3)_2Pd(H)(Br)$[3] (**3**) (10%), $[(P^tBu_3)Pd(\mu\text{-}Br)]_2$[4] (**4**) (13%), and $[Pd(P^tBu_2C(CH_3)_2CH_2)(\mu\text{-}Br)]_2$[5] (**5**) (16%). Protonated phosphine $[HP^tBu_3]^+$ (**6**) (12%) was also detected by ^{31}P NMR spectroscopy; the anion in this salt lacks an NMR active nucleus and is likely to be bromide. Each of the side products[3–5] was identified by independent synthesis and comparison of ^{31}P NMR chemical shifts to those of the reaction mixture.

The rate of reaction of the Pd(0) complex **1** with bromobenzene was measured by ^{31}P NMR spectroscopy with $[\mathbf{1}] = 0.040$ M and $[PhBr] = 1.9$ M in toluene, THF, and 2-butanone solvent at 70 °C. The reaction of **1** in toluene in the absence of any additive (open squares, Figure 1) was clearly not exponential and was characteristic of an autocatalytic reaction. To determine the origin of this kinetic behavior, the rate of the reaction of PhBr with **1** was conducted with 5 mol % of $(P^tBu_3)Pd(Ph)(Br)$ (**2**) and 5 mol % of the individual, independently synthesized side products. Each of these species accelerated the oxidative addition process but to different extents. The degree of acceleration by the different additives followed the trend $(P^tBu_3)Pd(Ph)(Br) \approx (HP^tBu_3)Br < [(P^tBu_3)Pd(\mu\text{-}Br)]_2 < (P^tBu_3)_2Pd(H)(Br)$. Added cyclometalated **5** did not affect the reaction of **1** with PhBr. Reactions in toluene in the presence of 5 mol % added $(P^tBu_3)_2Pd(H)(Br)$ occurred in less than half of the roughly 3.5 h required in the absence of additive.

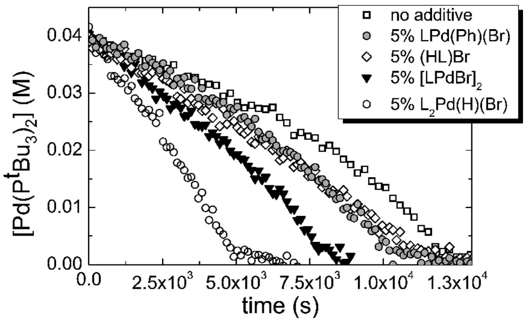

Figure 1. Decay of $Pd(P^tBu_3)_2$ (**1**) during the oxidative addition of PhBr in toluene at 70 °C in the presence of additives ($L = P^tBu_3$).

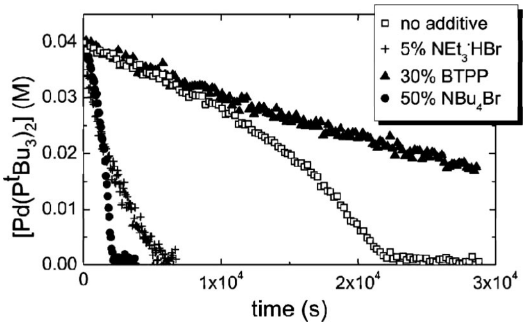

Figure 2. Decay of $Pd(P^tBu_3)$ (**1**), during the oxidative addition of PhBr in THF at 70 °C in the presence of 5 mol % of $NEt_3\cdot HBr$, 30 mol % of phosphazene base *tert*-butyliminotrispyrrolidino phosphorane (BTPP), or 50 mol % of NBu_4Br.

Because several of the compounds that affected the oxidative addition contained HBr, we sought to determine if the accelerating effect of these additives resulted from H^+, Br^-, or a combination of the two. The oxidative addition of PhBr to **1** in the presence of 5 mol % NBu_4Br[6] (0.020 M) occurred much faster than in the absence of an additive and was complete in about 30 min (Figure 2). The reaction in the presence of only 5 mol % $NEt_3\cdot HBr$ occurred faster than in the absence of an additive, in this case with an exponential decay possessing a half-life of about 30 min. Oxidative addition of PhBr to **1** in the presence of the strong, neutral phosphazene base *tert*-butyliminotrispyrrolidino phosphorane (BTPP)[7,8] also occurred with an exponential decay, in this case with a much longer half-life of 6.5 h. Reactions conducted with weaker bases, such as NEt_3, did not quench the autocatalysis.[9] These data show that both Br^- and H^+ contribute to the autocatalysis, and that a strong base is needed to quench the autocatalysis.

Because HBr adds to $Pd(P^tBu_3)_2$ to form hydridopalladium bromide **3**, and because complex **3** had the largest accelerating

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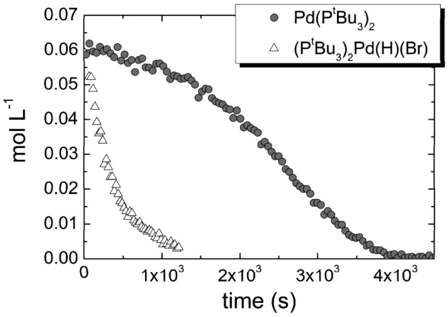


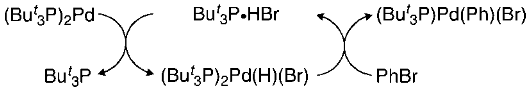
Figure 3. Relative decay of $\mathrm{Pd(P^{t}Bu_3)_2}$ (**1**) and $\mathrm{(P^{t}Bu_3)_2Pd(H)(Br)}$ (**3**) during the oxidative addition of PhBr in 2-butanone at 70 °C.

effect on the oxidative addition, we focused on how this complex could affect the reactions of PhBr with $\mathrm{Pd(P^{t}Bu_3)_2}$. Profiles of the reaction of PhBr with a 1:1 mixture of Pd(0) complex **1** and the hydrido bromide **3** at 70 °C in toluene (see Supporting Information for data) show that the concentration of **3** decreased only after Pd(0) complex **1** had been consumed. Because the oxidative addition to **1** was faster in the presence of **3**, but the concentration of **3** did not change during the consumption of **1**, complex **3** plays the unexpected role of a catalyst for this addition of PhBr to **1**.

To probe the origin of the accelerating affect of hydrido bromide complex **3** on the reaction of PhBr with Pd(0) complex **1**, we studied the reaction of **3** with PhBr and compared the rates of this reaction to that of **1** with PhBr. The reaction of PhBr with hydrido bromide complex **3** at 70 °C in toluene occurred faster than that with Pd(0) complex **1**. The yield of **2** was modest (32% at 77% conversion), just as it was for reaction of **1** with PhBr in toluene (vide supra) because the decomposition products **5** and $\mathrm{(HP^{t}Bu_3)_2[PdBr_4]}$ (**7**)[10] increased at higher conversion of **3**.[11]

However, the high yields of the reaction of **3** with bromoarenes at 70 °C in 2-butanone allowed a clear illustration of the difference between the rates of reactions of the Pd(II) complex **3** and the Pd(0) complex **1**.[12] Figure 3 shows the decay of **1** from reaction with PhBr and the decay of hydrido bromide **3**. The reaction of PhBr with **3** to form arylpalladium halide **2** occurred to 90% conversion after about 900 s with a decay profile that was similar to that in toluene. In contrast, the reaction of PhBr with **1** under the same conditions for the same time occurred to less than 10% conversion. We propose that $\mathrm{L_2Pd(H)(Br)}$ reacts with bromobenzene by reversible reductive elimination to generate the ionic species $\mathrm{[HP^{t}Bu_3][Pd(P^{t}Bu_3)(Br)]}$ containing a Pd(0) anion that would be expected to add bromoarenes rapidly.[13,14]

Scheme 1



These observations led to the basic steps of a catalytic cycle for oxidative addition of ArBr to Pd(0) complex **1** shown in Scheme 1. By this mechanism, reaction of the bromoarene with hydrido bromide complex **3** via the proposed unsaturated, anionic intermediate forms arylpalladium bromide complex **2** and $\mathrm{{}^{t}Bu_3P\cdot HBr}$ (**6**). Phosphonium salt **6** then transfers HBr to Pd(0) complex **1** to regenerate hydrido bromide **3** and free $\mathrm{P^{t}Bu_3}$.

This mechanism requires the generation of **6** or hydrido bromide complex **3** from the combination of Pd(0) complex **1** and PhBr to initiate the autocatalysis. To determine the origin of these species, we studied the relative stabilities of the initial products from reaction of PhBr with complex **1** at different temperatures. These studies showed that thermal decomposition of arylpalladium bromide **2** at 50 °C in toluene forms μ-Br complex **4**[15] and that complex **4** degrades at 80 °C in toluene to form hydridopalladium bromide **3** (5%), cyclometalated **5** (42%), and the phosphonium salt (53%). Thus, the decomposition of the simple oxidative addition product **2** to μ-Br complex **4** and then $\mathrm{{}^{t}Bu_3P\cdot HBr}$ appears to initiate the autocatalysis.

In conclusion, we have shown that the oxidative addition to $\mathrm{Pd(P^{t}Bu_3)_2}$ occurs, at least under certain conditions, by an unusual and complex autocatalytic mechanism, and these studies led to the counterintuitive observation that bromobenzene reacts faster with the palladium(II) complex $\mathrm{L_2Pd(H)(Br)}$ than with the related palladium(0) species $\mathrm{L_2Pd}$. The formation of $\mathrm{L_2Pd(H)(Br)}$ from a cascade beginning with the oxidative addition product, along with the faster reaction of the bromoarene with $\mathrm{L_2Pd(H)(Br)}$ than with $\mathrm{L_2Pd}$, can account for this autocatalysis. The fact that these processes occur in the absence of base or in the presence of bases of modest strength could make the autocatalytic pathway relevant to the mechanisms of Stille cross-couplings,[16] certain Suzuki couplings,[17] and Heck reactions.[18] In fact, complex **3** is the resting state of the Heck reaction catalyzed by Pd(0) complexes of $\mathrm{P^{t}Bu_3}$ under some conditions.[19]

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Supporting Information Available: Experimental procedures and characterization of reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) The products (normalized relative to **3**) observed by ^{31}P NMR spectroscopy at 91% conversion of **3** are: **2** (0.13), **5** (0.24), **4** (0.01), $\mathrm{P^{t}Bu_3}$ (0.37), and $\mathrm{HP^{t}Bu_3}$ (0.19).
(12) The reaction of **3** with PhBr in MEK occurred in 92% yield with 0.5 equiv of added $\mathrm{P^{t}Bu_3}$. The same reaction without added ligand gave 63% of **2** and 23% of **5** at 92% conversion of **3**.
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