Transmetalation Involving Organotin Aryl, Thiolate, and Amide Compounds. An Unusual Type of Dissociative Ligand Substitution Reaction

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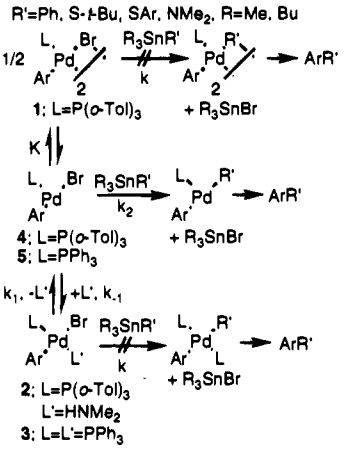
Organotin compounds are invaluable sources of carbon-centered nucleophiles in transition metal-catalyzed chemistry. Their specificity for halide replacement on transition metals in the presence of organic functional groups has led to their supplanting Grignard and organolithium reagents in cross-coupling chemistry. Heteroatom nucleophiles can also participate in catalytic cross-coupling chemistry to form arylamines,[1−4] thiolates,[5,6] and phosphines.[7,8] Typically, transmetalation, the ligand exchange between the transition metal and tin, is the rate-determining step of catalytic carbon−carbon bond-forming cross-couplings.[9,10]

We have been interested in developing a general understanding of how these important transmetalations occur. There is little mechanistic data concerning transfer of carbon-centered nucleophiles from tin to transition metals, and most of these data were obtained from catalytic studies.[11] Furthermore, there are no mechanistic data concerning transfer of heteroatom nucleophiles. We report the stoichiometric addition of organotin reagents to isolated aryl halide complexes, since the stoichiometric reactions of isolated reaction intermediates provide the most conclusive mechanistic information.[12] Our data demonstrate that these ligand exchanges between the square-planar, 16-electron palladium(II) and tin constitute an unusual type of dissociative ligand substitution.[13,14]

We have found that the stoichiometric reactions of isolated aryl halide complexes with trialkyltin aryls, thiolates, and amides provide biaryls, aryl sulfides, and arylamine products. Tri-*o*-tolylphosphine-ligated aryl halide complexes of palladium, {Pd[P(*o*-tolyl)$_3$](*p*-Tol)(Br)}$_2$ (**1**), are dimeric,[15,16] but monometallic derivatives {Pd[P(*o*-tolyl)$_3$](*p*-Tol)(Br)(NHMe$_2$)} (**2**) are formed upon addition of secondary amines.[16] In contrast, the aryl halide complexes of triphenylphosphine-ligated palladium(II) are monomeric with two phosphine ligands, [Pd(PPh$_3$)$_2$(*p*-Tol)(Br)] (**3**).[17] Either **1** or **3** reacts with trialkyltin aryls or thiolates to form coupled products, but only P(*o*-tolyl)$_3$-ligated complexes **1** and **2** provide arylamines upon reaction with tin amides. We have conducted kinetic studies on the reactions of Me$_3$SnPh with **1** and **3** that provide 4-methylbiphenyl in 95% and 55−75% yields, the reaction of Me$_3$SnS-*t*-Bu[18,19] with **3** that provides *p*-tolyl *tert*-butyl sulfide in 95% yield, and the reaction of Bu$_3$SnNMe$_2$[18] with **2** that provides *N*,*N*-dimethyltoluidene in 85% yield. Reactions with the P(*o*-tolyl)$_3$-ligated palladium complexes gave the Pd(0) product Pd[P(*o*-tolyl)$_3$]$_2$[4] in 85−100% yields. Reactions with the PPh$_3$-ligated palladium complexes gave Pd(PPh$_3$)$_4$ as the only palladium complex by ^{1}H and ^{31}P NMR spectroscopy in the homogeneous solution. Our mechanistic studies show that in all cases, reaction of the organotin compounds with the starting aryl halide complex occurred after formation of a three-coordinate monophosphine aryl halide intermediate.

Scheme 1



Potential pathways for reactions of **1**−**3** with tin reagents are outlined in Scheme 1. A general pathway could involve direct reaction of the tin reagent with the starting complex, and the rate behavior of this path would be described by eq 1. Alternative routes may involve phosphine dissociation or dimer cleavage, and their rate behavior would be described by eqs 2 and 3. Clearly, these mechanisms can be distinguished by the

$$\text{rate} = k[\mathbf{1}, \mathbf{2}, \text{ or } \mathbf{3}][R_3SnR'] \quad (1)$$

$$\text{rate} = \frac{k_1k_2[R_3SnR'][\mathbf{2} \text{ or } \mathbf{3}]}{k_{-1}[PPh_3] + k_2[R_3SnR']} \quad (2)$$

$$\text{rate} = Kk_2[\mathbf{1}]^{1/2}[R_3SnR'] \quad (3)$$

reaction order in the palladium starting material and in added phosphine. Kinetic studies were conducted by ^{1}H NMR spectroscopic monitoring of the palladium aryl halide complex in the presence of phosphine ligand and excess tin reagent in perdeuterated arene solvents.

Reactions of dimeric **1** with Me$_3$SnPh provided linear plots of [**1**]$^{1/2}$ vs time, whereas plots of ln [**1**] vs time were markedly curved. A plot of ln k_{obs} vs ln [Me$_3$SnPh] at phenyltrimethyltin concentrations ranging from 0.171 to 0.473 M indicated first-order behavior in tin reagent (slope = 1.1). Reactions were zero-order in [P(*o*-tolyl)$_3$] through the concentration range of 0.0342−0.1368 M ($k_{obs} = 5 \times 10^{-5}$ M$^{1/2}$ s^{-1}). Importantly, the presence of added Me$_3$SnBr, which is one of the reaction products, did not affect reaction rates. These data are consistent with reversible dimer cleavage to produce monomeric {Pd[P(*o*-Tolyl)$_3$](*p*-Tol)(Br)} (**4**) that reacts irreversibly with Me$_3$SnPh.

A three-coordinate triphenylphosphine-ligated intermediate **5** that is analogous to **4** could form from **3** by phosphine dissociation. Reactions of **3** with Me$_3$SnPh were monitored at 110 °C in C$_7$D$_8$[20] while [PPh$_3$] was varied from 0.0330 to 0.181 M. Linear first-order plots were obtained for each of these reactions, and plots of ln k_{obs} vs ln [PPh$_3$] provided an inverse

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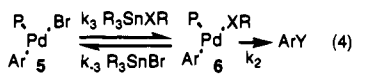
first-order dependence (slope = −0.98) on added PPh_3. These results are consistent with the formation of **5**.

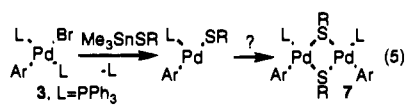
The requirement for three-coordinate intermediates proved to be general, even for reaction of heteroatom nucleophiles bound to tin. Reaction between Me_3SnS-*t*-Bu and **3** at 60 °C in C_6D_6 solvent in the presence of different concentrations of PPh_3 gave linear first-order plots. As observed for reaction of **3** with phenyltrimethyltin, an inverse reaction order in added phosphine was determined from plotting ln k_{obs} vs ln [PPh_3] (slope = −1.0).

In this case, transmetalation became reversible upon addition of excess Me_3SnBr to initial reaction mixtures. In the absence of added Me_3SnBr, ln [**3**] vs time plots were linear, but addition of Me_3SnBr at concentrations between 0.0316 and 0.0787 M gave incrementally decreasing reaction rates. It appears that throughout reactions in the absence of added tin bromide, the rate of sulfide reductive elimination (k_3 in eq 4) remained greater than the rate of reversion to **3** and tin thiolate (k_{-3}). A larger

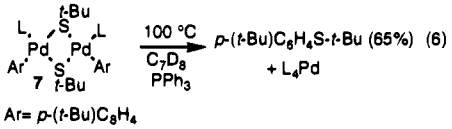


range of Me_3SnBr concentrations was employed in attempts to precisely evaluate the reaction order in this product, but decomposition of **3** and poor yields of sulfide product (~50%) at high [Me_3SnBr] precluded our obtaining an accurate reaction order. However, the clear product inhibition of these stoichiometric reactions by tin halide strongly suggested that transmetalation was endothermic[21] and was reversible under some reaction conditions.

In the case of these reactions of tin thiolates with **3**, the three-coordinate palladium thiolate complex [Pd(PPh_3)(*p*-Tol)(S-*t*-Bu)] (**6**) that would be generated by transmetalation could undergo dimerization to form **7**, as in eq 5. In fact, we have indepen-



dently synthesized and isolated dimeric thiolate complex **7** by reaction of **3** with LiS-*t*-Bu. Surprisingly, this complex underwent reductive elimination of thiolate at much higher temperatures (100 °C) than those employed for reaction of **3** with Me_3SnS-*t*-Bu and with lower yields of aryl sulfide (65%) (eq 6). Thus, dimeric **7** cannot be formed during reactions that form aryl sulfide.



Apparent reversibility of transmetalation prevented our determining precise information on exchange reactions involving tin amides, but our results were again consistent with a dissociative mechanism. Reactions of **1** were complicated by reversible formation of tin amide adducts that are likely to be similar in structure to amine complex **2**. However, the use of monometallic amine complex **2** eliminated this complication. Addition of free amine to reactions of **2** and Bu_3SnNMe_2 inhibited reaction rates, suggesting the importance of amine dissociation. Thus, Bu_3SnNMe_2 does not undergo simple irreversible acid/base chemistry with the coordinated amine of **2**.

The plots of ln [**2**] vs time for reactions with Bu_3SnNMe_2 in the absence of added Bu_3SnBr were curved but were linear in the presence of 10 equiv of added Bu_3SnBr. These results were consistent with reversible transmetalation and subsequent irreversible reductive elimination. Thus, amine dissociation need not precede transmetalation but must precede the irreversible reductive elimination. Nevertheless, amine dissociation prior to transmetalation is consistent with these results and follows from our other transmetalation reactions that have required three-coordinate intermediates.

Square-planar, 16-electron metal complexes typically undergo ligand substitution by associative mechanisms.[13] As a simple ligand substitution, there is little reason to suggest that reaction of **1**, **2** or **3** could not occur directly with the organotin reagents. Moreover, dissociative ligand substitutions typically occur by initial loss of the covalent ligand that is being replaced. It is striking that transmetalation reactions involving organotin reagents are dissociative and even more unusual that it is a dative spectator ligand that undergoes dissociation.

Oxidative addition reactions to square-planar, 16-electron complexes sometimes require dative ligand dissociation.[12,22] Similarly, reductive elimination reactions from octahedral compounds typically occur by ligand dissociation.[23-25] Reductive elimination from the resulting 5-coordinate compounds then generate 3-coordinate intermediates before final ligand reassociation. We sought to probe electronic effects in order to distinguish between mechanisms involving a combination of such oxidative and reductive steps and those that might require ligand dissociation for steric reasons and would involve a more standard nucleophilic attack at palladium by the group being transferred from tin.

The electronic properties of the transition state relative to those of the starting materials will be different for such oxidative addition and either metathetical or electrophilic substitutions. Oxidative additions are typically faster with electron-poor substrates,[26] whereas nucleophilic attack by the sulfur atom of the tin thiolates would be expected to occur more readily as the nucleophilicity of the thiolate is increased.[27] The aromatic tin thiolates Me_3SnS-*p*-C_6H_4X (X = Cl, H, CH_3, and NH_2) were reacted with **3**. Increasing electron-donating ability led to decreasing reaction rates. Me_3SnS-*n*-Bu reacted slower than Me_3SnSPh, and varied aromatic groups gave a positive but small ρ value of 0.6.[28] This small ρ value indicated little differences in charge between the ground states and transition states, but its positive value was inconsistent with a nucleophilic attack by the tin thiolate.

A number of years ago, Cross suggested that a continuum between metathesis and oxidative/reductive substitutions may exist.[13] The possibility that these reactions of tin reagents have transition states resembling an oxidative addition as well as a typical metathetical replacement may account for the observed ligand dissociation.

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Supporting Information Available: Spectroscopic and analytical data for **7**, representative kinetic plots for the decays of **1**−**3** for their various reactions, and plots showing the reaction orders in various reagents (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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