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Mechanistic Significance of the Si–O–Pd Bond in the Palladium-Catalyzed Cross-Coupling Reactions of Alkenylsilanolates

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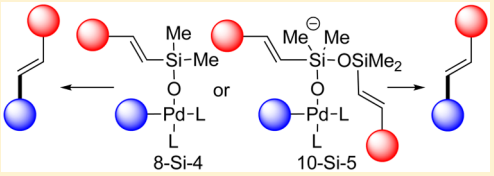
Supporting Information

ABSTRACT: Through the combination of reaction kinetics (both catalytic and stoichiometric) and solid-state characterization of arylpalladium(II) alkenylsilanolate complexes, the intermediacy of covalent adducts containing Si–O–Pd linkages in the cross-coupling reactions of organosilanolates has been unambiguously established. Two mechanistically distinct pathways have been demonstrated: (1) transmetalation via a neutral 8-Si-4 intermediate that dominates in the cross-coupling of potassium alkenylsilanolates, and (2) transmetalation via an anionic 10-Si-5 intermediate that dominates in the cross-coupling of cesium alkenylsilanolates. Arylpalladium(II) alkenylsilanolate complexes bearing various phosphine ligands (both bidentate and monodentate) have been isolated, fully characterized, and evaluated for their kinetic competence under thermal (stoichiometric) and anionic (catalytic) conditions. Comparison of the rates for thermal and anionic activation demonstrates that intermediates containing the Si–O–Pd linkage are involved in the cross-coupling process.



1. INTRODUCTION

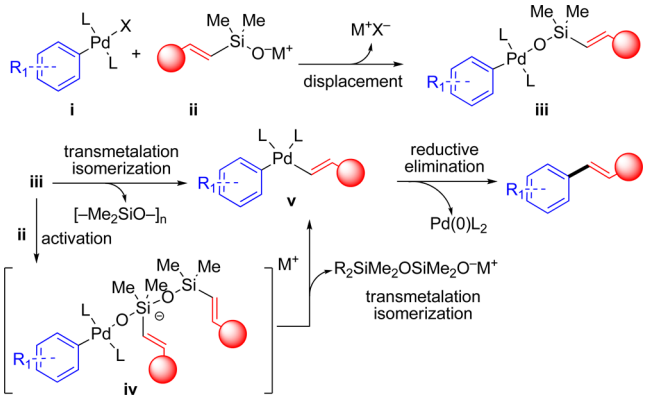
The isolation and study of reactive intermediates provides a wealth of insights into the mechanism and stereochemical course of synthetically useful reactions. Of course, many intermediates are not amenable to isolation because of their instability, reactivity or other complicating factors. In these cases, the synthesis of more stable model compounds can often provide useful information about critical structure and reactivity attributes. The isolation of intermediates from catalyzed reactions presents the additional challenges of low concentration and short half-life of relevant species that contain the catalytically active moiety complexed with one or more substrates. Here again, the synthesis and study of putative intermediates in stoichiometric reactions representing elementary steps in the catalytic cycle can afford valuable insights provided that proper care is taken to establish the species is on the reaction pathway and is kinetically competent.

Extensive studies of the kind described above for reactive intermediates in metal-catalyzed cross-coupling reactions have played a significant role in formulating the current understanding of the mechanistic detail of those processes. For two of the elementary steps in the now well-accepted catalytic cycle, oxidative addition and reductive elimination, wide-ranging investigations involving kinetic, spectroscopic, crystallographic, and computational analyses have revealed a clear, consistent picture of the structure of the intermediates and the structural attributes of substrate and reagents that influence the rate of these elementary steps.[1]

The third elementary step in the cross-coupling catalytic cycle, namely transmetalation, involves the organometallic donor, and thus, this step both unifies and differentiates the manifold variants of this process. With the exception of the Stille reaction, fewer decisive mechanistic studies are extant for this critical step in the catalytic cycle, most likely for several reasons: (1) its location in the middle of the catalytic cycle makes it difficult to study in isolation, (2) the nature of the pre-transmetalation intermediates is not well established, and/or (3) the pre-transmetalation intermediates are highly reactive.

As part of our ongoing preparative and mechanistic studies on the palladium-catalyzed cross-coupling of alkenylsilanolate salts[2] (**ii**), we obtained compelling kinetic evidence for the intermediacy of a discrete pre-transmetalation intermediate **iii**, a palladium complex containing the silanolate, the electrophile (from **i**), and ligands (Scheme 1).[3] Moreover, our kinetic analysis concluded that the transmetalation step from this neutral (8-Si-4)[4] intermediate was extremely rapid and did not require additional activation via a hypercoordinate siliconate species

Scheme 1



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such as **iv**. Thus, the reigning dogma that mandated a hypercoordinate silicon species (10-Si-5) for transmetalation was challenged.[5]

This critical conclusion, based solely on kinetic analysis, demanded additional concrete validation, ideally through isolation of the putative pre-transmetalation intermediate, arylpalladium alkenylsilanolate species **iii**, followed by a full structural and kinetic characterization. In addition, a thorough understanding of the controlling elements that influence the rate of transmetalation was desired. It is feasible that the nature of the transferable group plays a significant role in determining whether anionic activation is needed. Another reasonable hypothesis is that ligands contribute significantly to the course of transmetalation. The challenge to answer these questions was that **iii** undergoes spontaneous transmetalation at room temperature, thus precluding straightforward isolation and characterization.

However, if species such as **iii** could be isolated and studied, they would provide an unprecedented opportunity to directly interrogate the critical transmetalation step in the catalytic cycle. A program of research was thus formulated to synthesize, isolate, and characterize (both structurally and kinetically) arylpalladium(II) alkenylsilanolate complexes, stabilized by phosphine ligands of disparate denticity. Using these complexes, a detailed comparison of the effects of both phosphine ligands and silanolate structure on the transmetalation pathway could then be realized. More importantly, the kinetic competence of these complexes could be established under various conditions and the comparison of these rates to the preparatively significant catalytic processes studied previously could be made. A complete understanding of the catalytic cycle can guide improvements in substrate selection, reaction design and other crucial parameters for these synthetically useful transformations.

2. BACKGROUND

2.1. Influence of Ligands. Any investigation of the mechanistic features of the catalytic cycle in metal-catalyzed cross-coupling reactions must take careful account of the role of the ligands involved. Throughout the evolution of metal-catalyzed cross-coupling reactions, ligands have had an enormous impact on many aspects of this process, such as the ability to facilitate the various steps in the catalytic cycle, prolong catalyst lifetime, influence site selectivity, or induce enantioselectivity.[6] However, the means by which each ligand accomplishes these feats is associated with the molecular detail of the mechanistic pathways. As many preparative optimization studies have clearly demonstrated, not all ligands provide an effective catalytic process.[7] Ligands can impact multiple steps of a catalytic cycle, and thus the need to isolate the influence on each elementary step becomes paramount. Whereas data on the influence of ligands and mechanistic studies on oxidative addition[8] and reductive elimination[9] abound, much less is known about the effects on the transmetalation step. Thus, the following section will focus on the current state of understanding of this critical elementary step in various cross-coupling processes.

2.2. Mechanism of Cross-Coupling Reactions. As depicted in Figure 1, the currently accepted mechanism of palladium-catalyzed cross-coupling reaction begins with oxidative addition of the carbon−halide bond of the electrophile to the Pd(0) catalyst.[1] Following oxidative addition, the organometallic nucleophile approaches the palladium center to which the alkenyl or aryl group is transferred, creating a carbon−palladium bond. This process occurs through either coordination to the palladium center or direct attack of a nucleophile on the metal center. The carbon−carbon bond is formed through reductive elimination from the palladium center with simultaneous regeneration of the Pd(0) catalyst. The rate-determining step in many of these cross-coupling reactions is believed to be transmetalation, but other factors may influence which step becomes rate determining. The catalytic cycle involves a Pd(0)/Pd(II) cycle; however, many of the precatalysts used in these cross-coupling are Pd(II) precursors, which must be reduced to enter the catalytic cycle.

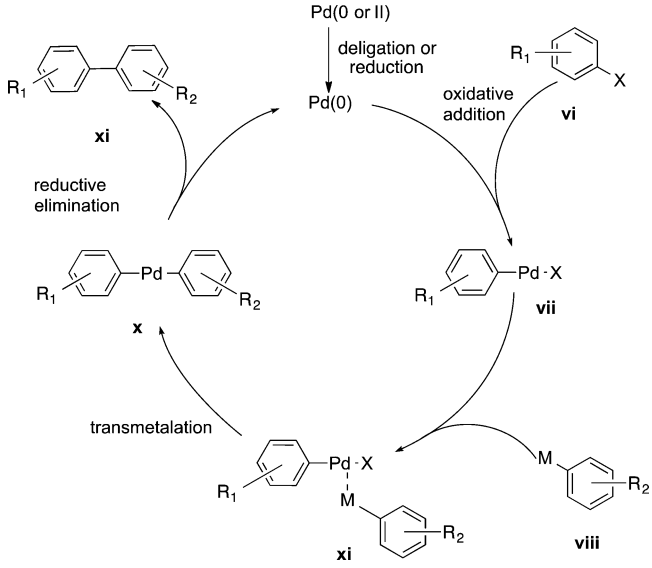

Figure 1. Consensus mechanism for the palladium-catalyzed cross-coupling reaction.

2.3. Studies of Transmetalation in the Cross-Coupling of Organosilanols. *2.3.1. Fluoride Activation.* Previous investigations in these laboratories have identified the detailed mechanism by which *alkenyl*silanols undergo fluoride-promoted cross-coupling reactions.[10] A bimolecular transmetalation of a fluoride-activated disiloxane **1** with an arylpalladium(II) halide has been identified by both kinetic and spectroscopic methods (Scheme 2). The transmetalation step has been identified as the turnover-limiting step, given the second-order dependence on silanol, the first-order dependence on arylpalladium halide, and the inability to saturate the silane cross-coupling partner as the activated disiloxane.[11]

2.3.2. Brønsted Base Activation. Early hypotheses on the mechanism of the cross-coupling of alkenylsilanols under activation by Brønsted bases proposed that a deprotonated silanolate plays a role similar to that of fluoride by activating silicon toward transmetalation (**iv**, Scheme 1). However, detailed kinetic analysis revealed the following characteristics: (1) zeroth-order dependence on silanolate at high concentrations, which provides support for the existence of an intermediate containing a silicon−oxygen−palladium bond; (2) the participation of an activated complex, **iv** (Scheme 1), is excluded as a result of the first-order dependence on silanolate when [silanolate]/[Pd] < 1; and (3) rate-determining formation of **iii** at [silanolate]/[Pd] < 20, and a rate-determining intramolecular transmetalation from **iii** at [silanolate]/[Pd] > 20.[3,12]

2.3.3. Models of Intramolecular Transmetalation. The preparations of complexes that *model* the intramolecular transmetalation of a number of organonucleophiles have been reported. Echavarren and co-workers described the isolation of a

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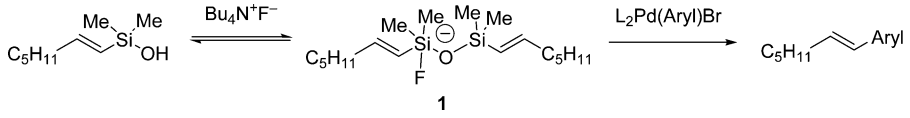
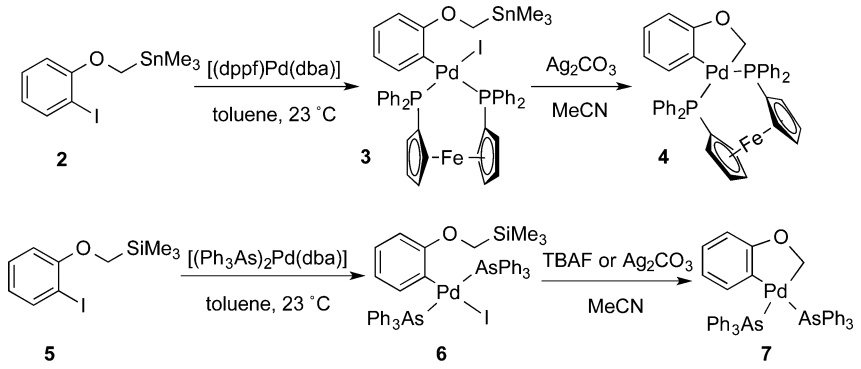
Scheme 2



Scheme 3



pre-transmetalation intermediate employing both an alkylstannane and an alkylsilane moiety (Scheme 3). Treatment of iodophenoxystannane **2** with [(dppf)Pd(dba)] complex results in oxidative addition of the aryl iodide to generate **3**.[13] Addition of Ag_2CO_3 promotes the intramolecular transmetalation step, and the resulting complex **4** can be isolated. Similarly, treatment of iodophenoxysilane **5** with $[(Ph_3As)_2Pd(dba)]$ affords the trans-ligated complex **6**.[13c] This complex undergoes transmetalation in the presence of either TBAF or Ag_2CO_3 to afford the palladacycle **7**. The isolation of another stable stannylpalladium complex has been achieved employing a pincer-type complex and 2-(tributylstannyl)furan.[14] These systems clearly demonstrate the isolation of competent transmetalation intermediates, but they are not specific to a catalytic process.

Platinum(II) and palladium(II) silanolates have been prepared and isolated and are potentially relevant to the cross-coupling of organosilanolates. Of these complexes, a majority are derived from triphenylsilanol.[15] The first of these complexes was prepared in 1994 by Fukuoka and co-workers by the equimolar reaction of COD-Pt(Et)Br (COD = 1,5-cyclooctadiene) and sodium triphenylsilanolate in THF at low temperature.[16a] The complexes were isolated from the reaction mixtures and purified by recrystallization, and their structures were confirmed by X-ray analysis.

The isolation of organoplatinum(II) silanolates from aryl(dimethyl)silanols provides a *model* for the cross-coupling of aryl(dimethyl)silanols. The reaction of (4-trifluoromethylphenyl)dimethylsilanol with phenylplatinum(II) iodide in the presence of 1.0 equiv of Ag_2O provides the corresponding phenylplatinum(II) silanolate complex.[16c] This species is thermally stable and does not undergo transmetalation to the diorganoplatinum(II) complex upon warming to 60 °C. This is in contrast to the reaction of a cationic platinum(II) complex with an arylsilanol, wherein only the post-transmetalation diorganoplatinum(II) complex could be isolated.[16d] These experiments highlight the effect of ligands and cationic platinum sources on the transmetalation of aryl(dimethyl)silanols.

The above cases represent the isolation of organoplatinum silanolates that are not relevant to the preparative cross-coupling reactions of interest. On the other hand, the isolation of organopalladium silanolates has been even more limited. The first complex was isolated in 1999 by Fukuoka and co-workers from the reaction of $(COD)Pd(CH_3)Br$ and sodium triphenylsilanolate.[16b] This complex was isolated and characterized but not investigated for its potential in cross-coupling.

2.4. Goals of This Study. The ability to independently prepare competent intermediates along the catalytic cycle for the cross-coupling reaction of alkenylsilanolates creates a unique opportunity to systematically study the features of the transmetalation step in detail. Instructive experiments designed to probe the molecular detail of this critical step can be devised, such as (1) verification of the mechanistic significance of the putative Si−O−Pd intermediate identified in previous kinetic studies, (2) independent isolation and characterization of arylpalladium alkenylsilanolate complexes, (3) determination of the kinetic competence of these isolable pre-transmetalation intermediates, and (4) comparison of the kinetic behavior of these complexes with the catalytic reactions. We report herein the successful achievement of these goals through the preparation of a number of arylpalladium(II) alkenylsilanolate complexes stabilized by phosphine ligands. These species have been thoroughly studied to elucidate the roles that ligands play in the key transmetalation step. Furthermore, these isolable intermediates and their kinetic behavior have further refined the controlling factors in the thermal and anionically activated pathways that have been proposed for the cross-coupling of this class of nucleophiles. The accompanying article details similar, albeit much more extensive studies on the cross-coupling of arylpalladium *aryl*silanolate complexes.[17]

3. RESULTS

3.1. Preparation and Structural Analysis of Arylpalladium(II) Alkenylsilanolate Complexes. *3.1.1. Synthesis.* In view of the extensive kinetic analysis already in hand on the cross-coupling of alkenylsilanols,[3] the isolation of a putative transmetalation intermediate involving *alkenyl*silanolates was investigated first. As was alluded to above, the rapid rate of reaction for these coupling partners presented a serious challenge to the isolation of a pre-transmetalation intermediate.[18] The reaction conditions for the catalytic process employed no ligands (only iodides had been coupled at that time), so the use of strongly coordinating phosphine ligands was investigated to slow

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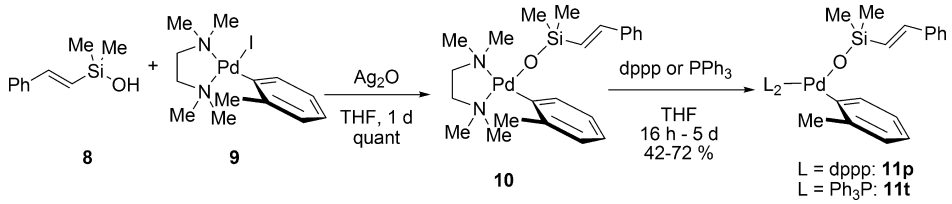
Scheme 4



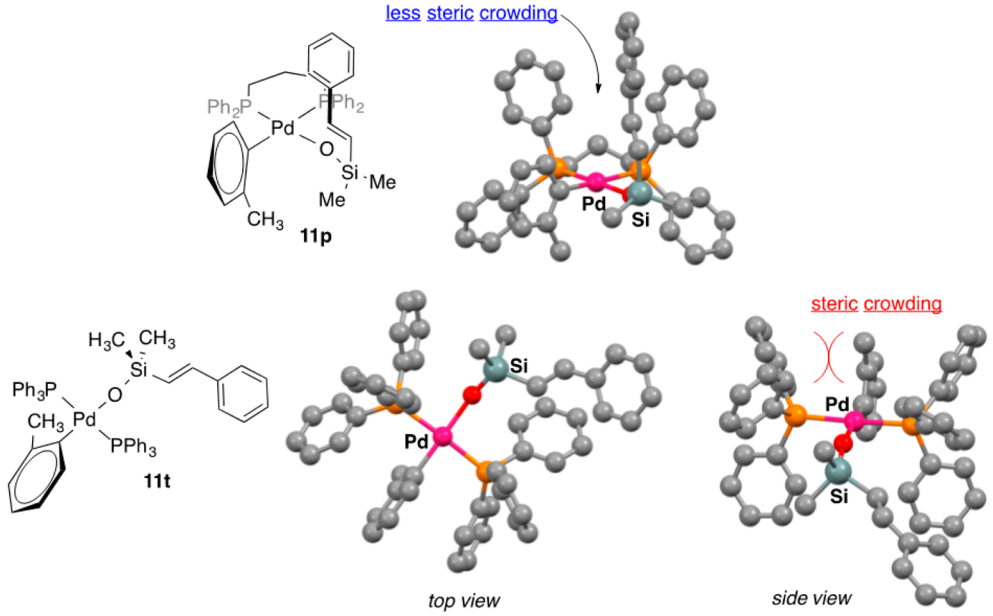


Figure 2. Structural representations of dppp (**11p**) and Ph_3P (**11t**) ligated 2-tolylpalladium(II) (*E*)-styrylsilanolate complexes (hydrogens omitted for clarity).

the key transmetalation step and allow the intermediate to be intercepted. Thus, the independent synthesis of an alkenylsilanolate complex was initially pursued through the introduction of 1,3-(diphenylphosphino)propane (dppp) and triphenylphosphine as stabilizing ligands. Combination of (TMEDA)(2-tolyl)palladium(II) iodide complex **9**[19] with styrylsilanol **8** in the presence of silver oxide afforded the (TMEDA)(2-tolyl)-palladium(II) silanolate **10** in quantitative yield (Scheme 4). Treatment of **10** with dppp afforded (dppp)(2-tolyl)palladium-(II) silanolate **11p** in 72% yield, whereas treatment with 2.0 equiv of triphenylphosphine afforded the *trans*-$(Ph_3P)_2$(2-tolyl)-palladium(II) silanolate **11t** in 42% yield.[20] Both complexes were stable at room temperature when maintained under an inert atmosphere.

3.1.2. Structural Features. ^{1}H NMR spectroscopic analysis of complex **11p** showed the loss of the TMEDA ligand and the characteristic pattern for the styrylsilanol moiety. Moreover, the ^{31}P NMR spectrum of **11p** displayed two non-equivalent phosphorus nuclei (δ = +20.1 and −11.7 ppm, doublets, J = 49 Hz), whereas the ^{31}P NMR spectrum of **11t** showed a single phosphorus resonance (28.0 ppm). The structures of complexes **11p** and **11t** were confirmed by single-crystal X-ray analysis, which unambiguously established the presence of a Si−O−Pd linkage (Figure 2).[21] The Pd(1)−O(1) bond lengths for **11p** (2.050 Å) and **11t** (2.053 Å) are slightly longer than those for other palladium(II) silanolates.[15] The Si(1)−O(1) bond length is typical for organosilanolates, which suggests that the lengthened Pd(1)−O(1) bond may be due to a ligand effect at the palladium center. The trans influence of the 2-tolyl group in **11p** is significant, as the P(2)−Pd(1) bond (2.348 Å) is much longer than the P(1)−Pd(1) bond (2.218 Å) trans to the silanolate oxygen in **11t**. However, the major difference in these structures lies in the orientation of the styryl group. The two phosphine atoms are 177° disposed, which causes some steric crowding about the palladium center. As shown in Figure 2, the dppp-derived styryl complex places the olefin of the styrene above the square plane of the complex, whereas the steric environment created by the six phenyl rings of **11t** prevents the alkene from approaching the palladium center. The ligand directs the styryl substituent to point away from the metal coordination sphere in the solid state. The ligand effects seen in the solid state may also manifest themselves in changes in the chemical reactivity of these intermediates in solution and play a role in the transmetalation step.

3.2. Reactivity and Kinetic Analysis of Arylpalladium(II) Alkenylsilanolate Complexes. The following studies were directed toward understanding how both the transferable group on silicon and the respective ligands affect the transmetalation step. Moreover, these investigations can help establish which mode of transmetalation (8-Si-4 versus 10-Si-5) occurs under various reaction conditions. With these overarching goals in mind, each of the complexes prepared in the foregoing section was evaluated for their independent reactivity as well as in quantitative comparisons to functioning catalytic systems.

*3.2.1. Catalytic Cross-Coupling of Alkenylsilanolates M^+**8**$^-$.* The rate equation for the catalytic cross-coupling of styryl-(dimethyl)silanolate under "ligandless" conditions was determined to establish if it was operating in the same kinetic regime as

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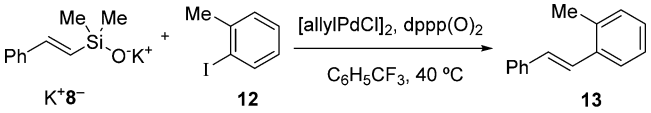
the previously studied alkenyl(dimethyl)silanolate, which employed dibenzylideneacetone (dba) as the ligand.[3] Previous studies had established that the use of allylpalladium chloride dimer (APC) affords ligandless palladium(0) because the reduction is effected by silanolate displacement of the allyl ligand to produce an allyl silyl ether and potassium chloride.[22] Moreover, it was discovered that phosphine oxides serve very effectively as weakly coordinating, stabilizing ligands for the palladium nanoparticles formed and increase the turnover number by preventing precipitation of palladium black.[23]

The partial order in each component in the reaction of potassium (*E*)-2-phenylethenyldimethylsilanolate ($K^+\mathbf{8}^-$) with 2-iodotoluene (**12**) catalyzed by APC in the presence of a phosphine oxide additive was determined individually at 40 °C in benzotrifluoride (Table 1).

Table 1. Initial Rates Using $K^+\mathbf{8}^-$



$K^+\mathbf{8}^-$ **12** **13**

entry	$K^+\mathbf{8}^-$ (mM)	**12** (mM)	dppp(O)$_2$ (mM)	Pd (mM)	initial rate[a] (10^{-2} mM/s)
1	60	80	3.6	3.6	3.49
2	80	80	3.6	3.6	3.05
3	160	80	3.6	3.6	3.23
4	80	40	3.6	3.6	2.72
5	80	160	3.6	3.6	3.03
6	80	80	5.4[b]	5.4	4.47
7	80	80	7.2[b]	7.2	6.40
8	80	80	10.6[b]	10.6	10.1
9	80	80	7.2	3.6	3.47

[a]Average of triplicate runs. [b]Equimolar amount of bis-oxide was used to ensure consistent palladium concentrations at lower temperatures.

The rate of the cross-coupling reaction is clearly independent of the concentration of $K^+\mathbf{8}^-$ and establishes zeroth-order behavior for this component (Table 1, entries 1−3). A slope of 0.019 was obtained for the order in 2-iodotoluene at 40, 80, and 160 mM, corresponding to no change in reaction rate and, again, established zeroth-order behavior for this component (entries 2, 4, and 5). Next, the dependence of the rate constant on the loading of the palladium catalyst was determined by comparison of the initial rates of product formation at 80 mM in 2-iodotoluene (entries 2, 6−8). A slope of 1.105, obtained from a log(rate) vs log(conc) plot of the data, is consistent with a first-order dependence of the observed rate constant on the concentration of palladium. To ensure that the phosphine oxide additive does not impact the reaction rate, the cross-coupling was repeated with increased dppp(O)$_2$ loadings (entries 1 and 9). No change in the reaction rate was observed, ruling out any kinetically significant role of the phosphine oxide. These data establish the overall rate equation for the reaction of $K^+\mathbf{8}^-$ with **18** catalyzed by [allylPdCl]$_2$, where $k = 8.83 \times 10^{-3}$ s^{-1}, as

$$\text{rate} = k_{obs}[K^+\mathbf{8}^-]^0[\mathbf{12}]^0[\text{dppp(O)}_2]^0 \quad \text{with } k_{obs} = k[\text{Pd}]^{1.1} \tag{1}$$

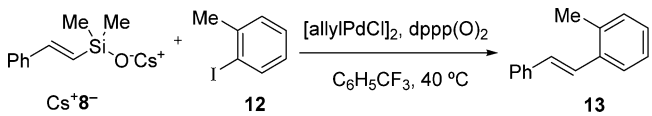
This rate equation matches that of the alkenylsilanolates reported previously, in which turnover-limiting, direct transmetalation from an arylpalladium(II) intermediate (**iii** to **v**) takes place without anionic activation via **iv** (Scheme 1).[3] However, this rate equation is also consistent with an activated mechanism where **iii** is completely saturated as **iv**. Indeed, turnover-limiting, activated transmetalation from $K^+\mathbf{8}^-$ will also result in a zeroth-order dependence on $K^+\mathbf{8}^-$.[24] The kinetic analysis of the catalytic reaction with $K^+\mathbf{8}^-$ alone does not unambiguously distinguish between the two possible mechanisms.

Support for the assertion that $K^+\mathbf{8}^-$ was reacting via a direct, thermal transmetalation of an 8-Si-4 species was obtained from the kinetic analysis of the reaction of the cesium salt (Table 2). Reaction of $Cs^+\mathbf{8}^-$ with 2-iodotoluene (**12**) (with APC and dppp(O)$_2$ in benzotrifluoride at 40 °C) changed the rate equation such that a fractional order (0.55) in $Cs^+\mathbf{8}^-$ was observed (eq 2). Apparently, the more nucleophilic $Cs^+\mathbf{8}^-$ is not

$$\text{rate} = k_{obs}[Cs^+\mathbf{8}^-]^{0.55}[\mathbf{12}]^0[\text{dppp(O)}_2]^0 \quad \text{with } k_{obs} = k[\text{Pd}] \tag{2}$$

operating in the same kinetic regime as $K^+\mathbf{8}^-$ and may open an activated pathway for transmetalation. The partial order indicates that two separate mechanistic pathways are operative, involving equilibration of the intermediates **xii** and **xiii** (Figure 3). Moreover, as the loading of $Cs^+\mathbf{8}^-$ increased, the rate leveled to a zeroth-order behavior for this component (Table 2, entries 6 and 7). This is consistent with a regime of complete saturation of **xii** as **xiii**, such that only an activated transmetalation pathway is operative.

Table 2. Initial Rates Using $Cs^+\mathbf{8}^-$



$Cs^+\mathbf{8}^-$ **12** **13**

entry	$Cs^+\mathbf{8}^-$ (mM)	**12** (mM)	dppp(O)$_2$ (mM)	Pd (mM)	initial rate[a] (10^{-2} mM/s)
1	60	80	3.6	3.6	4.28
2	80	80	3.6	3.6	5.23
3	120	80	3.6	3.6	6.37
4	160	80	3.6	3.6	7.96
5	240	80	3.6	3.6	9.05
6	320	80	3.6	3.6	11.1
7	400	80	3.6	3.6	11.2

[a]Average of triplicate runs.

3.2.2. Thermal Cross-Coupling of Arylpalladium(II) Alkenylsilanolates 11. When the preformed dppp complex **11p** was stirred in either THF or benzotrifluoride at room temperature, no product formation was observed, even after 24 h. *Remarkably, no product formation was observed until a temperature of >100 °C was reached.* In refluxing benzotrifluoride (bp 102 °C), the expected stilbene **13** was produced in 82% yield (GC) (Scheme 5).[25] Given the low temperature for the catalytic reaction, the elevated temperature needed for the isolated complex to undergo transmetalation must be associated with the requirement for dissociation of the strongly binding phosphine ligand.

To support this hypothesis, it was necessary to effect the chemical decomplexation of the ligand from **11p** and measure the rate of cross-coupling. Liebeskind, Farina, and co-workers have demonstrated the ability of copper(I) thiophene carboxylate (CuTC) to sequester phosphines in palladium-catalyzed cross-coupling reactions.[26] The addition of CuTC to an

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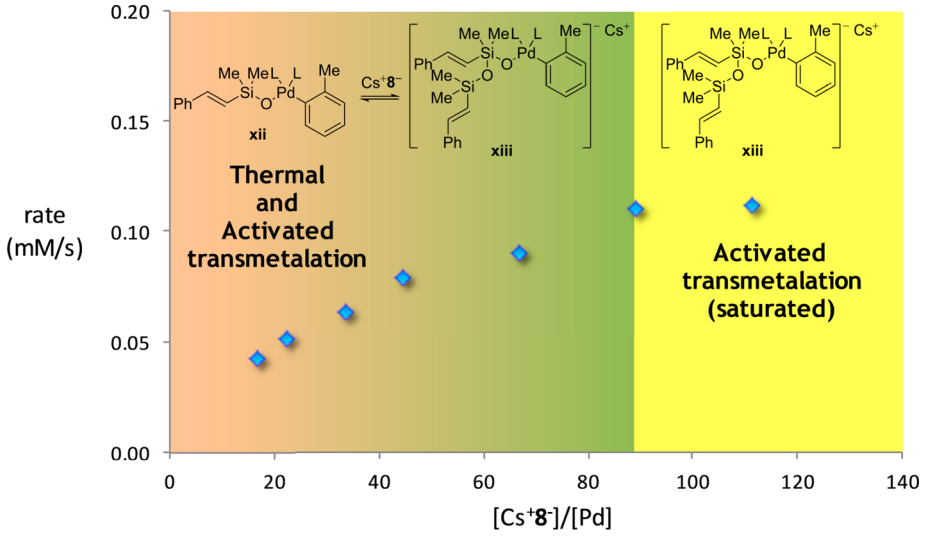
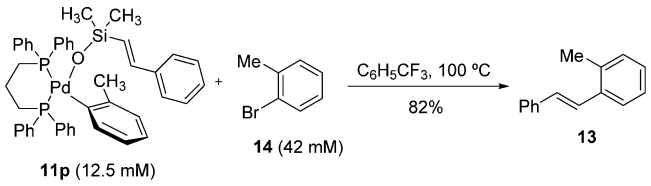


Figure 3. Summary of kinetic regimes for the transmetalation in the presence of $Cs^{+}\mathbf{8}^{-}$.

Scheme 5



alkenylsilanolate complex should result in the decomplexation of dppp, thus creating a quantity of the 14-electron species from which transmetalation may proceed. Indeed, when complex **11p** was treated with 10 mol % of CuTC in benzotrifluoride at room temperature, **13** was generated in quantitative yield with an initial rate of 2.27×10^{-4} mM/s.[27] When the corresponding *trans*-Ph_3P complex **11t** was employed under identical conditions, the initial rate of product formation was slightly faster (2.75×10^{-4} mM/s).[28] *These results clearly demonstrate the ability for alkenylsilanolates to undergo transmetalation without the need for external activation at room temperature.*

To make a direct comparison to the kinetic rate constant for the catalytic reaction, the Cu-assisted thermal transmetalation was conducted at 40 °C, which resulted in a faster rate of transmetalation (**11p**, 2.71×10^{-3} mM/s; **11t**, 1.20×10^{-3} mM/s). However, the rates for these processes at 40 °C are slightly lower than those for the corresponding catalytic reaction (3.25×10^{-2} mM/s).[29] We assume that the stoichiometric reaction of **11p** is 1.25 mM in active Pd catalyst (because it is 1.25 mM in CuTC),[30] which gives the 2.71×10^{-3} mM/s rate. Simply dividing the initial rate by [Pd] gives the principal rate constant for this process, 2.17×10^{-3} s^{-1}. Accordingly, the kinetic rate constant for this process at 40 °C is lower than that for the corresponding catalytic reaction ($k = 9.04 \times 10^{-3}$ s^{-1}), thus precluding an unambiguous conclusion about the intermediacy

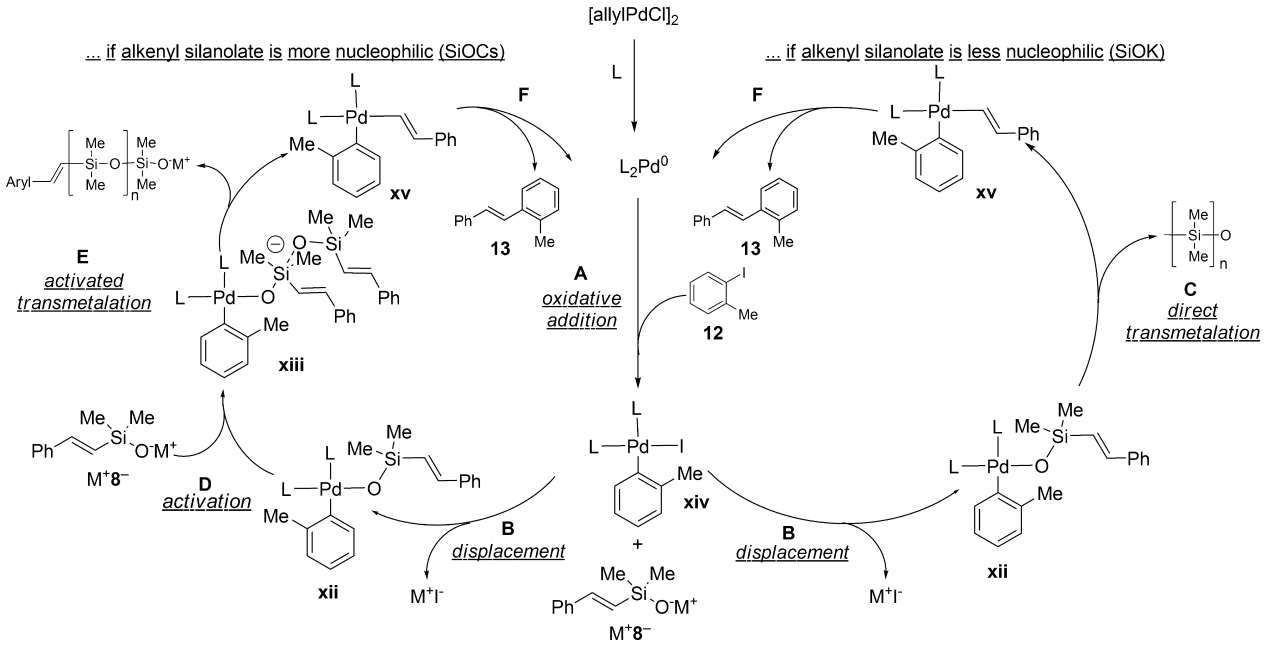


Figure 4. Proposed cross-coupling pathways for *alkenyl*silanolates.

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of **iii**. This disparity could arise from either incomplete or slow decomplexation of the ligand from the isolated complexes.

The unknown rate and extent of ligand dissociation at lower temperatures prevents the direct rate comparison of catalytic alkenylsilanolate cross-coupling reactions with their putative pre-transmetalation intermediates.

4. DISCUSSION: REACTIVITY OF ARYLPALLADIUM ALKENYLSILANOLATE COMPLEXES

The rate equation found from kinetic experiments involving $K^+\mathbf{8}^-$ and **12** employing APC and dppp(O)$_2$ $K^+\mathbf{8}^-$ at 40 °C in trifluorotoluene (eq 1) was identical to that for the cross-coupling of 1-heptenyl(dimethyl)silanolate, where no rate effect was observed with increasing the concentration of silanolate.[3] On the other hand, the use of $Cs^+\mathbf{8}^-$ (with **12**) led to a fractional dependence (0.55) on the concentration of the silanolate. Clearly these two salts are operating (for the most part) in different kinetic regimes.

The various steps of the catalytic cycle predict different concentration dependences on each component. The experimentally established rate law can eliminate a number of possibilities for the turnover-limiting steps (Figure 4 and Table 3). Starting from the palladium(II) precatalyst [allylPdCl]$_2$, reduction to the active Pd(0) catalyst involves the participation of the silanolate.[22] Oxidative addition to Pd(0) occurs with the aryl halide, producing a palladium(II) halide intermediate (first order in [**12**], step A). Displacement of the palladium iodide proceeds by a nucleophilic attack by an equivalent of $M^+\mathbf{8}^-$ and predicts a first-order dependence on $M^+\mathbf{8}^-$ (step B). Next, if the transmetalation is proceeding via a direct, unactivated process, then a zeroth-order behavior for $M^+\mathbf{8}^-$ should arise (step C). Alternatively, either a zeroth- or first-order behavior could result from an activation-limiting transmetalation step (step E). Finally, if reductive elimination is turnover limiting (step F), then zeroth order in both components, $M^+\mathbf{8}^-$ and **12**, will be observed.

Table 3. Expected Kinetic Consequences

turnover-limiting step	order for silanolate	order for aryl halide
A	zeroth	first
B	first	zeroth
C	zeroth	zeroth
D	first	zeroth
E	zeroth or first	zeroth
F	zeroth	zeroth

Thus, zeroth-order dependence on $M^+\mathbf{8}^-$ and **12** is consistent with step C, E, or F; however, step F has already been eliminated.[24] The most reasonable explanation is that the styrylsilanolate cross-coupling is proceeding via a rate-limiting transmetalation involving either neutral 8-Si-4 or 10-Si-5 intermediates, depending upon the nucleophilicity of the silanolate. Previous studies on the alkenylsilanolate cross-coupling using Pd(dba)$_2$ demonstrated zeroth-order dependence for [silanolate] once saturation of the intermediate **xiii** is achieved.[3] This intermediate undergoes transmetalation at 40 °C without activation in the presence of the potassium salt $K^+\mathbf{8}^-$. However, the increased nucleophilicity of the cesium silanolate $Cs^+\mathbf{8}^-$ opened the possibility for an activated transmetalation pathway via **xiii** not seen previously. As before, this pathway also reaches saturation at ca. 90 equiv of $M^+\mathbf{8}^-$ per Pd. At the saturation limit, the rate of cross-coupling represents the intrinsic rate of *intramolecular* transmetalation via **xiii**. The fractional order in $Cs^+\mathbf{8}^-$ most likely represents simultaneous operation of both pathways (Figure 3).

The rate of the catalytic reaction employing phosphine oxides was four times faster than the rate obtained by generation of a subligated palladium complex using CuTC. The lower temperatures employed for the CuTC-assisted transmetalation may decrease the rate of deligation; therefore, the nominal concentration of subligated palladium is smaller than expected. Nevertheless, the ability for the cross-coupling of alkenylsilanolates to proceed via an unactivated, direct transmetalation has been confirmed through both kinetic studies and the isolation of ligand-stabilized complexes.

5. CONCLUSIONS

The mechanistic formulation for the cross-coupling of alkenylsilanolates with aryl halides is now substantially understood. The isolation and characterization of two arylpalladium alkenylsilanolate complexes allowed for the unambiguous demonstration of both neutral (8-Si-4) and anionic (10-Si-5) mechanistic pathways for transmetalation from silicon to palladium. In general, potassium salts of alkenylsilanolates react via neutral (8-Si-4) intermediates, whereas the enhanced nucleophilicity of the cesium alkenylsilanolates allows for the reaction to access the 10-Si-5 intermediate and proceed via the anionically activated pathway. These conclusions mandate a revision of the paradigm that organosilicon compounds must be anionically activated to engage in transmetalation processes (Hiyama–Hatanaka paradigm). Through the agency of intramolecularity, direct transmetalation of silicon to palladium can be achieved under mild conditions. The mechanistic details of the related cross-coupling of arylsilanolates with aryl halides are addressed in detail in the accompanying paper.[17]

■ ASSOCIATED CONTENT

Supporting Information

Full experimental procedures and characterization data, X-ray coordinates for **11p** and **11t**, and ^{1}H and ^{13}C NMR spectra along with full kinetic data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b02515.

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Notes

The authors declare no competing financial interest.

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(21) The crystallographic coordinates of complexes **11p** and **11t** have been deposited with the Cambridge Crystallographic Data Centre, deposition nos. 606765 and 765349, respectively. These data can be obtained free of charge from the CCDC via www.ccdc.cam.ac.uk/conts/retreiving.html.

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(28) A number of control experiments were carried out to eliminate other possible roles of CuTC: (1) equimolar amounts of CuTC (with respect to Pd) have no accelerating effect on the rate of the catalytic reaction (2.68×10^{-2} mM/s vs 3.05×10^{-2} mM/s without CuTC) and (2) the room-temperature reaction of **11p** with 10 mol % of potassium thienylcarboxylate afforded no product, thus excluding an activating role of the carboxylate in CuTC.

(29) This rate is the average of entries 1−3 in Table 1.

(30) This experiment assumes that the affinity of Cu(I) for phosphine is sufficiently higher than that of Pd(II) to allow complete sequestering of the ligand by the Cu(I).

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