Studies on the Mechanism of Allylic Coupling Reactions: A Hammett Analysis of the Coupling of Aryl Silicate Derivatives

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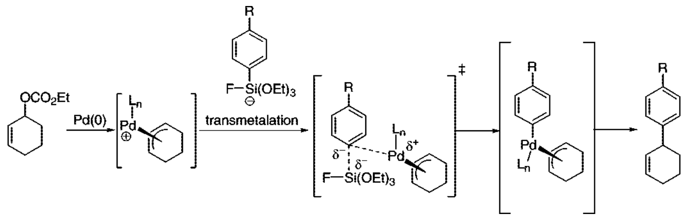

Hammett analysis of the palladium-catalyzed allyl−aryl coupling reaction has demonstrated that the rate of the coupling reaction is enhanced by electron-withdrawing groups on the aryl siloxane. The positive slope of the Hammett plot indicated involvement of a charged transition state in which negative charge on the aryl ring is stabilized inductively. This result is consistent with either transmetalation or reductive elimination being the rate-determining step in the coupling process. Furthermore, the influence of ligand on the metal site has been assessed from competition studies as a function of ligand type, cone angle, and electronic effects. From the relative ratios of coupling products produced in the Hammett study, it is possible to gather insight into the role of the electronic as well as the steric effects of ligands on the mechanism of the coupling reaction.

Introduction

Coupling reactions involving aryl- and alkyl silicon derivatives have a prominent position in modern synthetic chemistry.[1] We have developed the palladium-catalyzed arylation of allylic esters via coupling of aryl siloxanes.[2] This methodology has been shown to be both highly regio- and stereoselective and has been successfully applied to the synthesis of a (±)-7-deoxypancratistatin analogue **4** (Scheme 1).[3] However, repeated attempts to effect coupling between carbonate **5** and siloxane **1** for the synthesis of 7-deoxypancratistatin (**7**) were unsuccessful and no trace of the desired adduct **6** was detected.

It was hypothesized initially that failure of allyl carbonate **5** to undergo arylation was the result of the steric bulk of the isopropylidene group that blocked the β-face of the alkene and prevented formation of the requisite π-allyl intermediate **8** (Scheme 2). However, the successful coupling of allylic carbonate **5** with malonate anion **9** demonstrated that formation of π-allyl intermediate **8** had occurred.[4] This result led us to infer that either transmetalation or the subsequent reductive elimination step, latter steps in the mechanism, must be responsible for failure of the coupling reaction between aryl siloxane **1** and allyl carbonate **5** (Scheme 3). Since both transmetalation and reductive elimination involve transfer of an aryl group during the catalytic cycle, we anticipated that altering substituents on the aryl ring would affect the relative rates of these processes. Accordingly, we chose to investigate the role of substituents on aryl siloxane in controlling the rate of the coupling reaction via Hammett analysis.

Transmetalation of organometallic compounds with transition metal complexes is one of the key steps in carbon−carbon bond

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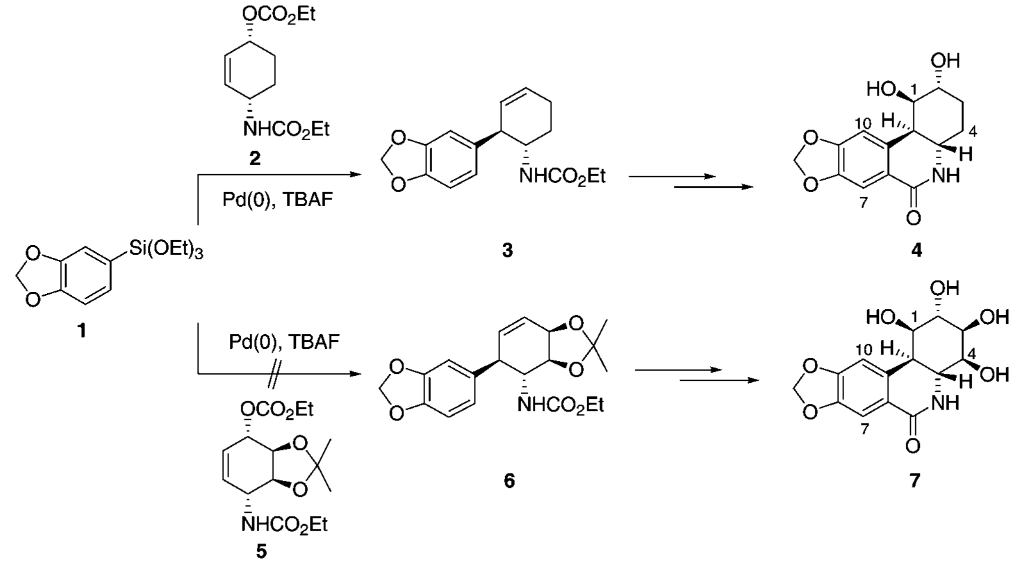
10.1021/jo8010254 CCC: $40.75

SCHEME 1



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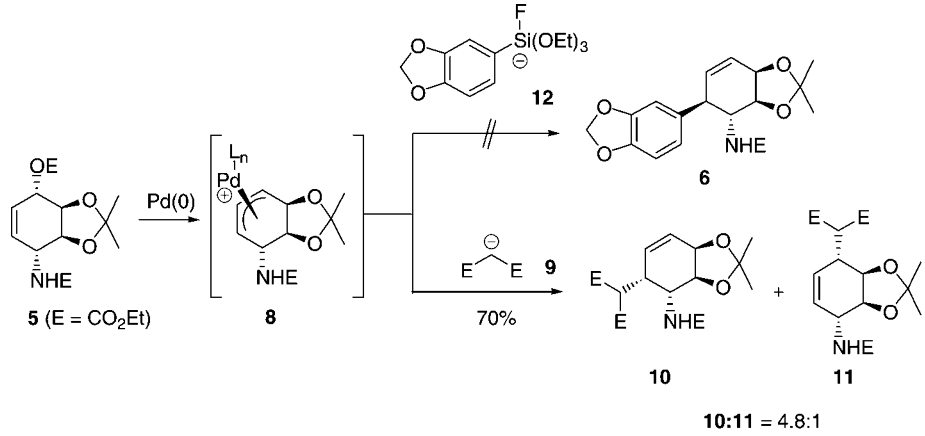

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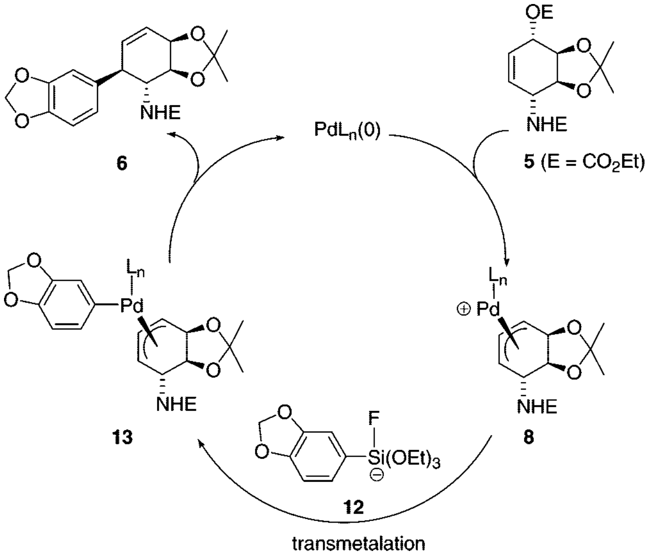

formation.[5] However, mechanistic details of the transmetalation process are not well understood for most of these catalytic processes. Among many useful coupling variants, the Stille reaction is the most extensively studied system with regard to the mechanism of transmetalation. One of the earliest studies is that of palladium-catalyzed coupling of benzoyl chloride with benzyltin reagents by Stille.[6] Subsequently, Farina reported a kinetic analysis of the effect of palladium ligands on Stille reaction[7] and Hartwig investigated the mechanism of transmetalation of tin amides and tin thiolates.[8] More recently, Amatore and Jutand have studied the mechanism of Stille reaction in the presence of AsPh$_3$ ligated palladium catalyst, and confirmed Farina's proposal that AsPh$_3$ increased the efficiency of the Stille reaction compared to PPh$_3$.[9] An extensive kinetic study of the transmetalation reaction in Stille coupling has been carried out recently by Espinet, who has proposed an

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associative transmetalation model for the key step.[10] Also, theoretical calculations on transmetalation have been performed by Álvarez,[11] Ariafard,[12] and Farina.[13] Studies on internal-coordination driven transmetalation are also known in literature.[14] Transmetalation studies on palladium-catalyzed cross couplings of alkynyl stannanes with aryl iodides and that with metal-halides have been reported by Crociani[15] and Lo Sterzo,[16] respectively. Additionally, Wendt[17] and Clarke[18] have reported studies on transmetalation of organostannanes and organozincs, respectively, with platinum complexes. Transmetalation in the Suzuki-Miyaura and Hiyama protocols have been studied less extensively. Transmetalation processes for cross-coupling of organoboron compounds in alkaline solution have been studied by Miyaura.[19] Woerpel and Soderquist studied transmetalation of alkyl borane derivatives and proposed an S_E2 (cyclic) mechanism as the key mechanistic feature.[20] More recently, theoretical studies on mechanism of Suzuki-Miyaura reaction have been reported by Ujaque and Maseras.[21] Studies on coupling of aryl halides with a diboron species[22] and coupling of aryl boronic acids and carboxylic anhydrides are also known in literature.[23] Along with Hiyama's initial study on transmetalation of organosilanes,[24] Denmark has also performed mechanistic studies on organosilanes via kinetic analysis under both fluoride-mediated and fluoride-free conditions.[25,26] In an effort to study transmetalation process, stable transmetalation intermediates in Stille, Suzuki, and Hiyama cross-coupling have also been isolated.[27]

Mechanistic studies of transmetalation of an aryl group in metal-catalyzed couplings via Hammett analysis have been reported previously. For example, Hatanaka and Hiyama has shown that electron-donating groups (EDG) enhance the rate of transmetalation of diarylfluorosilicates with an aryl-palladium complex ($\rho = -1.5$).[28] On the other hand, nickel-catalyzed Suzuki coupling gave the opposite result: electron-withdrawing groups (EWG) on the aryl boronic acid facilitated transmetalation and gave a slope of $\rho = 0.81$.[29] Farina demonstrated that an EDG on the aryl stannane accelerated transmetalation ($\rho = -0.89$) when coupled to an olefinic triflate in absence of lithium chloride.[30] These mechanistic studies have indicated that transmetalation is a complex process in which the rates of coupling are strongly influenced by substituents on the ring as well as the catalyst and/or ligand.[31] In light of the failure of our *allyl−aryl coupling* reaction in the 7-deoxypancratistatin (**7**) synthesis (Scheme 1), we chose to investigate the mechanism of the siloxane-based coupling reaction in detail. The goal of this project was to perform a Hammett study of the coupling reaction utilizing palladium-catalyzed siloxane derivatives. The study reported below is the first mechanistic investigation of an *allyl−aryl coupling* process involving silicon-based reagents.

Results and Discussion

The proposed mechanism for the allyl−aryl coupling reaction is summarized in Scheme 4. The relative rates for each individual step of the coupling will be discussed below. Cyclohexenyl carbonate (**14**) was chosen as the coupling partner for the siloxane study because it was known to undergo facile allyl−aryl coupling with siloxane derivatives under established protocols. There is significant literature precedent for the *rapid and reversible* formation of π-allyl palladium complexes from allylic derivatives with both phosphine and dibenzylideneacetone (dba) ligands.[32–34] However, it was important to conclusively demonstrate that this step was not rate-determining in this

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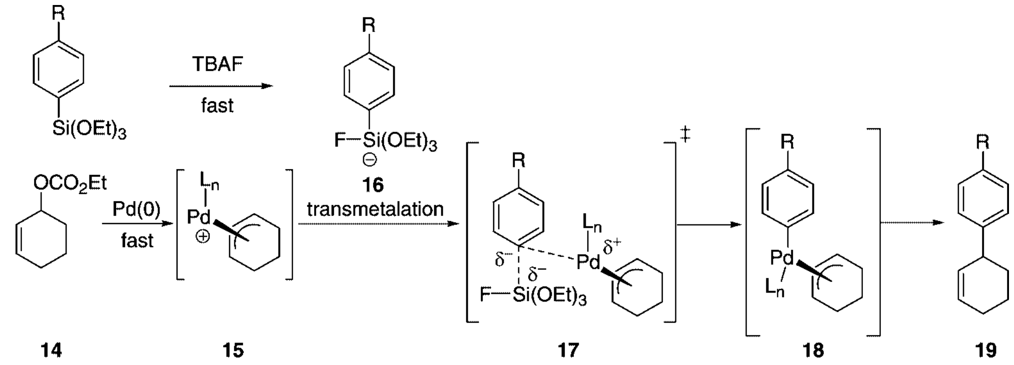
SCHEME 4



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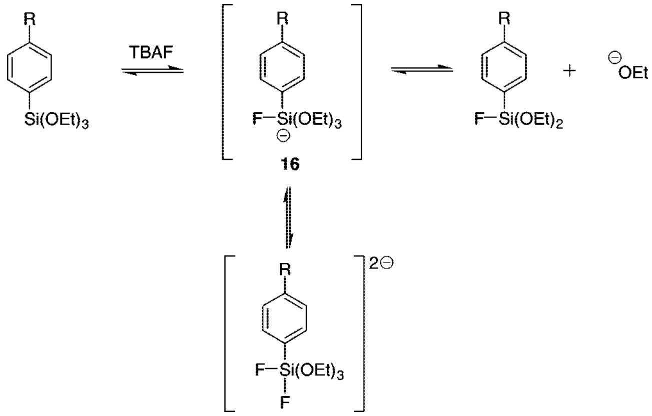

coupling system, and that can be inferred from the subsequent Hammett analysis reported below. If formation of the π-allyl intermediate **15** were rate-determining, then a correlation of rates with Hammett parameters on the siloxane moiety would not be observed because the siloxane would not appear in the rate equation for formation of the π-allyl complex. Accordingly, the Hammett correlation observed (*vide infra*) is consistent with the formation of the π-allyl palladium complex being a fast process.

Formation of the hypercoordinate silicate **16** from the reaction of fluoride anion (TBAF) with the siloxane derivative is not rate-determining either. This was demonstrated by ^{19}F NMR spectroscopy of the reaction of TBAF and phenylsiloxane derivatives. In the key experiment, a hypercoordinate silicate species (**16**, R = H) was generated *in situ* by reaction with fluoride source (TBAF) (Scheme 5 and Figure 1). The formation of hypercoordinate silicates was observed using ^{19}F NMR where the fluorine signal of TBAF[35] (δ −114) disappeared rapidly (10 min) *at room temperature* on addition of phenylsiloxane to give two new fluorine signals: a sharp singlet at δ −121, and a broad resonance centered at ca. δ −127, respectively, as shown in Figure 1. The signals at δ −121 and δ −127, respectively, are consistent with chemical shifts of hypercoordinate fluorosilicate species reported by this and other groups.[36] The broad signals in the ^{19}F NMR spectrum are consistent with formation of hypercoordinate complex(es) that undergo dynamic processes including ligand exchange and pseudorotation.[37] The conclusion drawn from this study is that at room temperature, the siloxane reacted with fluoride ion to provide a hypercoordinate silicate rapidly, much more rapidly than coupling occurred.

Analogously, when TBAF (2 equiv) was added to a mixture of phenylsiloxane (1 equiv) and its *p*-methoxy congener (1 equiv), the signal for TBAF rapidly disappeared and was replaced by a series of resonances indicative of hypercoordinate silicate formation. This experiment conclusively demonstrated that formation of the silicate from the reaction of fluoride ion and the siloxane derivatives was fast and could not be the rate-determining step in the coupling reaction.

We had proposed initially that either transmetalation of silicate **16** to π-allyl palladium complex **15** or subsequent reductive elimination was the rate-determining step in the coupling reaction (Scheme 4). If this assumption were correct, then the rate of the allyl−aryl coupling should be influenced by the electronic characteristics of the substituent present on the aryl ring of siloxane **16**, and substituents in the para-position would stabilize (or destabilize) transition state **17** resulting in a rate enhancement (or diminution). Competition experiments between phenyltriethoxysilane **20** and para-substituted aryl siloxanes **21** (R = OMe, Me, Cl, CO_2Et) were performed and the results are summarized in Figure 2. The relative rate of transmetalation was enhanced by electron-withdrawing groups (EWG). Electron-withdrawing groups are better at stabilizing the developing negative charge on the ipso-carbon in transition state **17** through inductive effects. These results are in sharp contrast, however, with the studies of Hiyama[28] and Farina[30] with silicon and stannane derivatives, respectively, who found that EWG retarded the rates of coupling reaction.

More importantly, the excellent correlation observed in the Hammett analysis is consistent with the proposal that the rate-determining step is either the transmetalation or reductive elimination reaction. As was noted above, if π-allyl formation were the slow step, then no difference in the relative rates would have been observed since the substituents on the aryl ring would not be able to manifest their influence in the rate determining step of the coupling reaction.

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(34) Allylic acetates and carbonates undergo reversible π-allyl formation in the presence of Pd(0) catalysts. The reversibility of the reaction is diminished with carbonates since the carbonate anion decomposes to carbon dioxide and alkoxide under the typical coupling conditions. See ref [32b].

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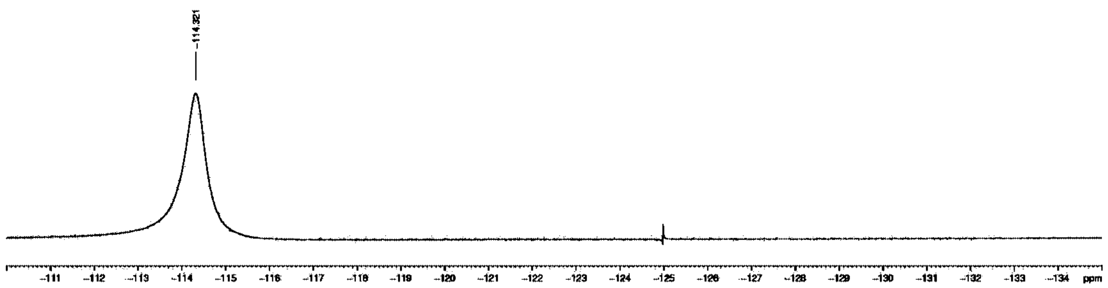
a) TBAF at 29 °C



b) TBAF and Triethoxyphenylsilane (1:1) at 29 °C

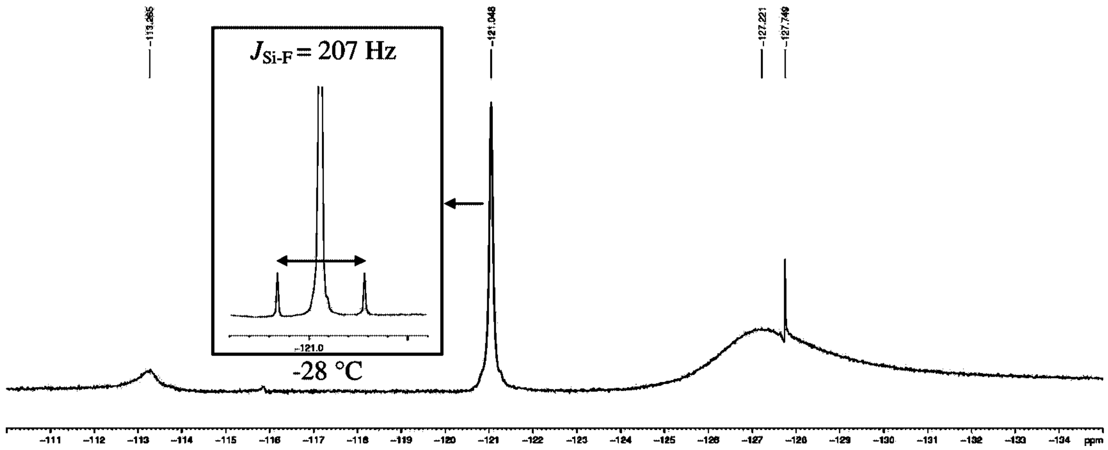


FIGURE 1. ^{19}F NMR spectra of silicate formation. (a) TBAF (Tetrabutylammonium fluoride) in THF at 29 °C (b) ^{19}F NMR spectrum of silicate complexes resulting from 1:1 TBAF-Triethoxyphenylsilane addition at 29 °C. Insert is ^{19}F signal at δ −121 after cooling to −28 °C.

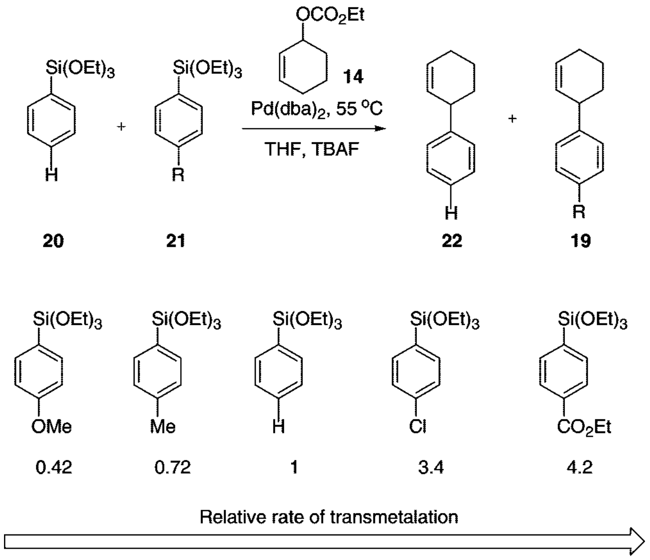


FIGURE 2. Summary of relative rates of coupling reactions with siloxane derivatives.

Having established the nature of the substituent effect for the siloxane coupling protocol, the magnitude of the stabilization that occurred in the transition state for the coupling was determined from the Hammett correlation. Hammett plots were obtained by plotting log (k/k_0) against substituent parameters σ_p, σ^-, and σ^+.[38] The plot of log (k/k_0) against σ_p gave the best linear correlation to the experimental data (Figure 3) with slope $\rho = 1.4$. The linear regression with σ_p value indicated that an inductive effect was chiefly responsible for stabilization of the transition state. The positive slope ($\rho = 1.4$) of the line indicated that coupling was sensitive to the electronic effects of substituents and that modest negative charge was to be found on the aromatic ring in the transition state **17** (Scheme 4).

It is noteworthy to reiterate the significance of the Hammett correlation: the observed substituent effects are consistent with formation of the π-allyl complex being a fast and reversible reaction as was noted above. If formation of π-allyl complex were rate-determining, then the Hammett plot should have had a slope of zero because the aryl siloxane was not involved in that step of the mechanistic cycle.

A nonzero slope for the Hammett plot was conclusive evidence that either the transmetalation or the reductive elimination is rate-determining (Scheme 4), and from the data provided it is not possible to unambiguously determine which of these two steps is rate-determining. For this coupling reaction, however, we propose that the rate-determining step is transmetalation, rather than reductive elimination, based on several

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(37) The addition of fluoride ion to siloxane is a complex process that provided at least two silicate complexes (described in the text). The equilibrium between the various silicates is dependent on stoichiometry of fluoride:siloxane and other electronic factors. The ^{19}F NMR spectra are also temperature dependent, indicating a dynamic process. A full discussion of the dynamics of silicate(s) formation including low temperature ^{19}F and ^{29}Si NMR spectroscopy will be reported in due course. Preliminary studies of silicate formation indicate that the electronic effects of the groups attached to the aryl ring have an effect on the relative quantities of each component, but additional studies have to be undertaken to determine the relative importance of each silicate to the overall coupling reaction.

(38) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *97*, 165–195.

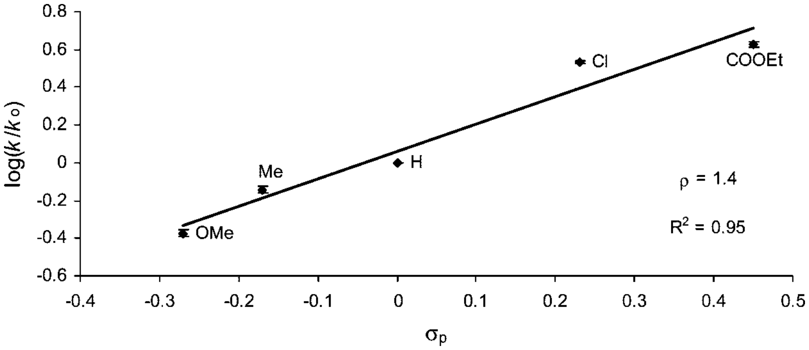

FIGURE 3. Hammett analysis of allyl−aryl coupling using σ_p values.

lines of circumstantial evidence. First, since no coupled product **6** was obtained in the pancratistatin synthesis (Scheme 1), it is reasonable to assume that the transmetalation had not occurred to give palladium complex **13** (Scheme 3). Although the rationale for this conclusion is complex, the analysis is important for the mechanistic study in question. Formation of π-allyl complex **8** (Scheme 3) was fast and reversible; thus the experimentally observed rearrangement of the cyclohexenyl carbonate was observed as a byproduct in this coupling. If the rate-determining step was transmetalation, then a slow transmetalation reaction would provide greater opportunity for rearrangement and decomposition of the cyclohexenyl starting material without leading to coupled product. If, on the other hand, reductive elimination were the rate-determining step, *coupled product, even if only trace amounts, would have been obtained since it is unlikely that transmetalation was reversible.* Reductive elimination must result in formation of coupled product or reduced arene (via beta-hydride elimination followed by reductive elimination). No trace of either coupled product or reduced arene was observed under these conditions.

A second piece of evidence supporting the conclusion that transmetalation is rate-determining is derived from the study of Kurosawa on the reductive elimination of diorganopalladium complexes.[39] Kurosawa was able to prepare allyl−aryl palladium complexes (utilizing other methodology) and measured the rate of reductive elimination at 0 °C. If extrapolated to 55 °C, as in our coupling protocol, the rates of reductive elimination would be much faster than the rate of coupling observed, thus suggesting that transmetalation, and not reductive elimination, is rate-determining step for the allyl−aryl coupling reaction reported in our study. Admittedly, the evidence is circumstantial, since the Kurosawa system included different ligands on the metal center than our coupling protocol.

Even more significant is that Kurosawa demonstrated that electron-deficient alkenes *promoted* the reductive elimination in his system. This observation is particularly germane to our coupling system in which dba (dibenzylideneacetone) is a ligand on the catalyst that functions for this coupling. Assuming that the silicate system behaves analogously to the Kurosawa analog, we would anticipate that the reductive elimination step would be facilitated by the presence of electron-deficient ligand as was observed by Kurosawa.[39,40]

As has been noted by Denmark in his mechanistic studies of analogous silanol-based aryl-aryl coupling reactions, there is no unambiguous evidence for the intermediacy of a diorganopalladium (II) complex that undergoes reductive elimination to produce the product (Scheme 4).[26] In the allyl−aryl system described herein, it is possible that π-allyl complex **15** reacted with the activated silicate **16** via a substitution reaction to yield the product directly. Nonetheless, one would observe that this step would be rate-determining.

Further support for our hypothesis that the rate-determining step in the coupling reaction is transmetalation, and not reductive elimination comes from Hartwig's laboratory. Hartwig has reported several mechanistic studies of palladium-catalyzed coupling reactions in which reductive elimination is the rate determining step.[41] In each of these studies, however, an isolable palladium (II) complex was prepared and then decomposed thermally via reductive elimination to provide product. Hammett analyses of these systems have shown significant substituent effects, but the results are not as straightforward as is observed in our system. For C−S bond formation, the substituent effect was *qualitatively* similar to those observed in our study, namely faster rates with electron-withdrawing substituents, but there was no correlation with Hammett sigma values. They were able to correlate the rates of reductive elimination only with a mixed Hammett value that included both inductive and resonance contributions.[42] Analogous situations were observed for C−N and C−C coupling reactions, respectively.[43,44]

The studies summarized above have established that Hammett analysis is an excellent method for gathering mechanistic information regarding the transition state (**17**) for the transmetalation step of the mechanism (Scheme 4). *Furthermore, this Hammett methodology can be employed for investigating the roles of catalyst-ligand combinations in the coupling reaction.* Typically, the development of an "optimized" catalyst system for a coupling reaction involves the empirical development of conditions and reagents using various ligand−metal ratios and is based on yield or turnover of product. The actual role that the ligand (L_n in **17**, Scheme 4) plays in transmetalation cannot be assessed except in a qualitative sense: the reaction yield was high or low. Adding ligand or substituting a new metal may change the yield of the reaction, but does not provide precise mechanistic information about the rate-determining step. However, once the relative rates for various substituents had been measured *under standardized conditions*, we were able to extend our Hammett study to include various catalyst-ligand

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(39) (a) Kurosawa, H.; Emoto, M.; Urabe, A.; Miki, K.; Kasai, N. *J. Am. Chem. Soc.* **1985**, *107*, 8253–8254. (b) Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333–6340.

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(41) (a) Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936–1947. (b) Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852–860. (c) Shekhar, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 13016–13027.

(42) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205–9219.

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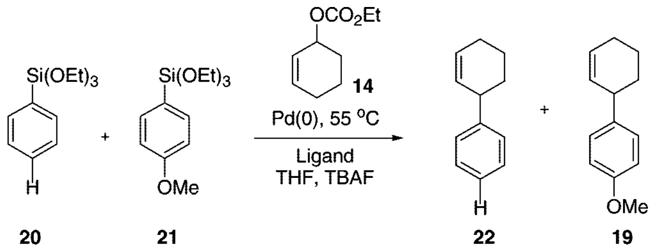
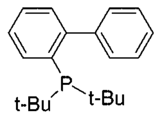
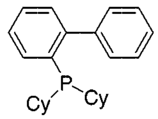
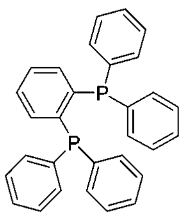
(44) Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398–3416.

TABLE 1. Role of Ligands in the Allyl−Aryl Coupling Reaction



Entry	Pd (0) Source (10 mol %)	Ligand (20 mol %)	Relative Rate	Yield (%)[a]	
1	$Pd(dba)_2$	-	0.42	80	 I  II  III
2	$Pd_2(dba)_3$	-	0.42	63	
3	$Pd_2(dba)_3{\cdot}CHCl_3$	-	0.40	61	
4	$Pd(dba)_2$	$AsPh_3$	0.39	53	
5	$Pd(dba)_2$	$PPh_2(C_6F_5)$	0.42	32	
6	$Pd(dba)_2$	PCy_3	0.42	55	
7	$Pd(dba)_2$	P(*o*-tolyl)$_3$	0.43	48	
8	$Pd(dba)_2$	PPh_3	0.25	<20[b]	
9	$Pd(dba)_2$	I	0.33	<20[b]	
10	$Pd(dba)_2$	II	-	NA	
11	$Pd(dba)_2$	III	-	NA	
12	$Pd(dba)_2$	P(2-Fu)$_3$	-	NA	
13	$Pd(dba)_2$	-	0.45	79[c]	
14	$Pd(dba)_2$	-	0.39	64[d]	
15	$Pd(OAc)_2$	PCy_3	0.39	<20[b]	
16	$Pd(OAc)_2$	$AsPh_3$	0.44	<20[b]	
17	$Pd(OAc)_2$	PPh_3	-	NA	
18	$Pd(OAc)_2$	P(2-Fu)$_3$	-	NA	
19	Pd_2(dba-4,4'-OMe)$_3$	-	0.39	55	
20	Pd(dba-4,4'-CF$_3$)$_2{\cdot}H_2O$	-	0.41	51	

[a] Yield determined by gas chromatography using a standard. [b] Yield determined by column chromatography. [c] DMF was used as a solvent. [d] Dioxane was used as a solvent. Note: relative rates and yields in entry 1 are averages of three runs, entries 2−9, 15−16, and 19−20 are averages of two runs. P(2-Fu)$_3$ is tri-2-furylphosphine (TFP).

combinations. In particular, we were interested in determining whether the rate of transmetalation could be enhanced by changing ligands on the palladium. Ligands with different electronic and steric properties[45] might be able to stabilize the transition state **17** (Scheme 4) differently and hence affect the rate of transmetalation. An example is illustrative: as shown in Table 1, entry 1, the best catalyst for the coupling of siloxanes and cyclohexenyl carbonate (**14**) is $Pd(dba)_2$. Changing the catalyst to either $Pd_2(dba)_3$ or $Pd_2(dba)_3{\cdot}CHCl_3$ resulted in a considerable decrease in the yield of coupled product. Why the yield is diminished is less clear since all three of these Pd-complexes are thought to behave comparably as Pd(0) sources. By comparing the relative rates of *p*-anisoylsiloxane/phenylsiloxane (**21**:**20**) with all three catalyst systems, it was observed that the ratio of 0.42 ± 0.02 was maintained. The result clearly demonstrated that the rate-determining step in the coupling reaction was identical with all three catalysts systems and that another step in the mechanism must be responsible for the diminished yields of product. The effect of various added ligands on the coupling reaction was evaluated and the results are summarized in the Table 1.

Strongly electron-donating ligands (PCy_3 and P(*o*-tolyl)$_3$, entries 6 and 7) with cone angles significantly greater than triphenylphosphine, gave higher yields of coupled products than triphenylphosphine, respectively, but did not alter the relative rate of arylated products. The larger cone angle of these phosphines would be expected to provide a π-allyl complex with a low coordination number due to steric bulk, thus facilitating transfer of aryl group from the fluoride-activated siloxane. More electron-withdrawing ligands (entries 5 and 12) significantly reduced the yields of couple product also, but had no effect on the relative rates. $AsPh_3$ (entry 4) gave a better yield of coupled products when compared with PPh_3 (entry 8). Since, the As−Pd bond is longer than the P−Pd bond; the As−Pd complex might be experiencing less steric hindrance from phenyl groups. With stannane derivatives, Farina had also shown that poor donicity of $AsPh_3$ allowed the ligand to dissociate readily from palladium intermediates, thus enhancing the rate of transmetalation ($>10^3$) compared to PPh_3.[7] Large

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[45] Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313–348.

deviations from the relative rate ratios were observed for the addition of ligands such as PPh_3 and the Buchwald ligand I[46] (entries 8 and 9). Unfortunately, the yields of coupling products in these systems were so low that it is inappropriate to draw meaningful conclusions about the coupling reactions.

We have also studied effect of electronic nature of dba (dibenzylideneacetone) ligand on relative rate of the coupling reaction. [Pd_2(dba-4,4′-OMe)$_3$] and [Pd(dba-4,4′-CF_3)$_2$·H_2O] catalysts were prepared[47] and a competition experiment of allyl carbonate **14** was performed. The change of electronic character of the dba ligands, respectively, did not change the relative rate; however, the yield of coupled product was altered (entries 19 and 20, Table 1).

Conclusion

In summary, Hammett analysis of the allyl−aryl coupling reaction of para-substituted siloxane derivatives with cylcohexenyl carbonate has shown that the rate of coupling was enhanced by electron-withdrawing substituents. This observation was consistent with the rate-determining step of the coupling reaction being either transmetalation or reductive elimination. In addition, the Hammett analysis indicated that significant negative charge resides on the aromatic ring in the transition state of the rate-determining step. Competition studies as a function of ligand type revealed that electronic as well as the steric nature of ligands on the metal site dramatically affect yield of coupled product, but rarely affect the relative rates of the coupling reaction. Hammett analysis of coupling reactions involving siloxane derivatives provide rich detail into the intermediates involved in the catalytic reaction and additional mechanistic studies will be reported in due course. Although we do not describe the development of new catalysts based on the results of this study, we have employed the information gained from these experiments to develop a new family of catalysts for the siloxane coupling process that overcomes the limitations highlighted in the Introduction. These results will be reported in due course.

Experimental Section

Formation of Hypercoordinate Silicates. Triethoxyphenylsilane (0.18 mmol, 43 mg) was mixed with 1 M TBAF (0.18 mmol, 0.18 mL) in 0.50 mL THF and ^{19}F NMR spectrum was recorded after 10 min at 29 °C. ^{19}F spectrum indicated two major resonances at δ −121 and −127 and two minor resonances at δ −113 and −128 (see Figure 1b). After 1 h, TBAF and siloxane mixture was cooled to −28 °C. Upon cooling, the ^{19}F signal at δ −121 sharpened, showing silicon satellites ($J_{Si-F} = 207$ Hz).

Diesters 10 and 11. Sodium hydride (37.9 mg of 60% dispersion in oil, 0.948 mmol, 3.00 equiv) was washed with 3 × 3 mL of hexane and 3 × 3 mL of anhydrous THF. To a suspension of the oil-free sodium hydride in 2 mL THF was added 0.152 mL (1.01 mmol, 3.20 equiv) of diethyl malonate and the resulting suspension stirred for 10 min. The diethyl malonate anion **9** was then added to a solution of 104 mg (0.316 mmol, 1.00 equiv) of allyl carbonate **5** dissolved in 2 mL anhydrous THF. This was followed by addition of 41.4 mg (0.158 mmol, 0.500 equiv) triphenyl phosphine and 7.09 mg (0.0316 mmol, 0.100 equiv) of palladium acetate. The reaction mixture was allowed to stir at 65 °C for 24 h. The solution was filtered through celite and the filtrate was extracted with 5 × 25 mL Et_2O and washed with 25 mL H_2O. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give the diesters as brown oil. Flash column chromatography on silica gel (20% EtOAc/80% hex, $R_f = 0.29$) gave 88 mg (70%) of a mixture of diesters **10** and **11** (**10**:**11** = 4.8:1) as a light-yellow oil; Diesters **10** and **11**: IR (CCl_4) 3439 (w), 2984 (m), 2936 (w), 2913 (w), 1737 (s) 1506 (s), 1373 (m), 1220 (s) cm^{-1}; Diester **10**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82−5.72 (m, 2H), 4.77 (br s, 1H), 4.52 (s, 1H), 4.28 (s, 1H), 4.24−4.13 (m, 5H), 4.06 (q, $J = 7$ Hz, 2H), 3.45 (s, 2H), 1.39 (s, 3H), 1.34 (s, 3H), 1.27−1.19 (m, 9H); Diesters **10** and **11**: FAB mass spectrum *m/z* (relative intensity) 532 ([M + Cs]$^+$, 75), 342 (32), 179 (22), 133 (100); HRMS (FAB) calcd for [M + Li]$^+$ 406.2053, found 406.2056.

Allyl Carbonate 14. To 2.09 g (21.3 mmol, 1.00 equiv) of commercially available 2-cyclohexen-1-ol in 20 mL anhydrous CH_2Cl_2 and 2.57 mL (31.9 mmol, 1.50 equiv) anhydrous pyridine was added 3.17 mL (31.9 mmol, 1.50 equiv) of ethyl chloroformate dropwise via syringe under argon. The reaction was allowed to stir at room temperature for 7 days. The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL), washed with H_2O (50 mL), dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography on silica gel (5% EtOAc/95% hex, $R_f = 0.51$) afforded 2.32 g (64%) of the allyl carbonate **14** as a colorless oil; IR (CCl_4) 3042 (w), 2981 (w), 2947 (m), 2875 (w), 2838 (w), 1737 (s), 1373 (s), 1265 (s), 1017 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97−5.93 (m, 1H), 5.77−5.73 (m, 1H), 5.10−5.09 (m, 1H), 4.16 (q, $J = 7$ Hz, 2H), 2.05 (m, 1H), 2.05−1.98 (m, 1H), 1.88−1.80 (m, 3H), 1.62 (m, 1H), 1.28 (t, $J = 7$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 133.2, 125.0, 71.5, 63.6, 28.2, 24.8, 18.5, 14.2. The ^{1}H NMR data was consistent with the data reported in the literature.[48]

Aryl Siloxanes 21. *p*-Anisoylsiloxane (R = OMe), *p*-tolylsiloxane (R = Me), and *p*-chlorophenylsiloxane (R = Cl) were prepared from commercially available *p*-bromoansiole, *p*-bromotoluene, and *p*-chloroiodobenzene respectively according to the procedure previously reported by the DeShong group.[49] *p*-Carboethoxyphenylsiloxane (R = CO_2Et) was prepared from ethyl-4-iodobenozate by Masuda's procedure.[50] The ^{1}H NMR spectral data of *p*-anisoylsiloxane (R = OMe),[49] *p*-tolylsiloxane (R = Me),[49] *p*-chlorophenylsiloxane (R = Cl),[51] and *p*-carboethoxyphenylsiloxane (R = CO_2Et)[50] were identical to that reported in the literature.

General Procedure for Competition Experiments for Allyl−aryl Coupling (Figure 2 and Table 1). To 121 mg (0.712 mmol, 1.00 equiv) of allyl carbonate **14**, 342 mg (1.42 mmol, 2.00 equiv) of aryl siloxane **20**, and 383 mg (1.42 mmol, 2.00 equiv) of *p*-anisoylsiloxane **21** (R = OMe) dissolved in 4 mL of anhydrous THF was added 40.9 mg (0.0712 mmol, 0.100 equiv) of Pd(dba)$_2$ under an atmosphere of argon. This was followed by addition of 2.84 mL (2.84 mmol, 4.00 equiv) of 1 M TBAF solution in THF, and the reaction mixture was stirred at 55 °C for 24 h. The product was extracted with 5 × 20 mL Et_2O and washed with 20 mL H_2O. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give coupling products **22** (R = H) and **19** (R = OMe). The crude product was filtered through a short silica plug. The relative quantity of 0.44 for *p*-anisoylsiloxane **21** (R = OMe) was determined from the amount of methoxyphenylcyclohexene **19** (R = OMe) obtained relative to phenylcyclohexene **22** using GC (gas chromatography). The same experimental procedure was

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[46] (a) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158–1174. (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550–9561.

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[49] For preparation of *p*-anisoylsiloxane and *p*-tolylsiloxane, refer to: (a) Manoso, A. S.; Ahn, C.; Soheili, A.; Handy, C. J.; Correia, R.; Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 8305–8314. For preparation of *p*-chlorophenylsiloxane, refer to: (b) Manoso, A. M.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449–7455.

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used to determine relative rates of different aryl siloxanes **21**.[52] Moreover, effects of different catalysts, ligands, and solvents on the relative rate of transmetalation were examined (Table 1), using analogous competition experiments, where yields were determined by GC using standard unless otherwise noted.

Alkene (22, 19). The ^{1}H NMR data of phenylcyclohexene **22**,[53] methoxyphenylcyclohexene (**19**, R = OMe),[54] methylphenylcyclohexene (**19**, R = Me),[55] chlorophenylcyclohexene (**19**, R = Cl)[55] matched to those previously reported. Carboethoxyphenylcyclohexene **19** (R = CO_2Et): IR (CCl_4) 2934 (m), 1719 (s), 1610 (m), 1271 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8 Hz, 2H), 7.26 (d, J = 8 Hz, 2H), 5.89−5.92 (m, 1H), 5.66−5.69 (m, 1H), 4.34 (q, J = 7 Hz, 2H), 3.42−3.46 (m, 1H), 1.99−2.08 (m, 3H), 1.50−1.71 (m, 3H), 1.36 (t, J = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 152.0, 129.6, 129.2, 128.9, 128.3, 127.7, 60.7, 41.9, 32.4, 24.9, 21.0, 14.3; LRMS (EI) 231 ([M + 1], 16), 230 ([M$^+$], 100), 185 (30), 157 (51), 129 (59); HRMS (EI) calcd for $C_{15}H_{18}O_2$ 230.1307 [M$^+$], found 230.1305.

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Supporting Information Available: Spectral data of diesters **10** and **11**, allyl carbonate **14**, aryl siloxanes **21** (R = OMe, Me, Cl, CO_2Et), and alkenes **22** (R = H) and **19** (R = OMe, Me, Cl, CO_2Et). This material is available free of charge via the Internet at http://pubs.acs.org.

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[52] The relative rates of aryl siloxanes in Figure 2 are average of three runs.

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