

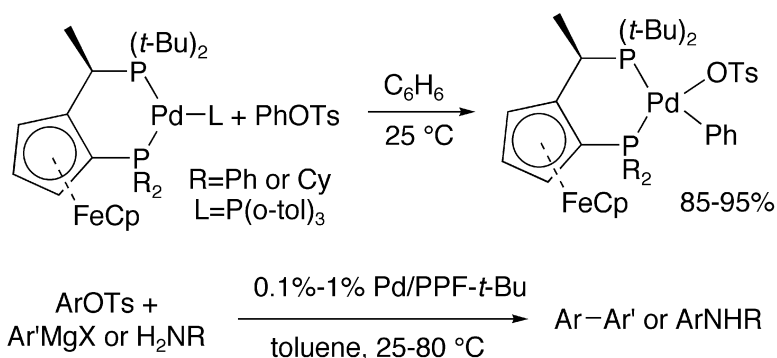
Communication

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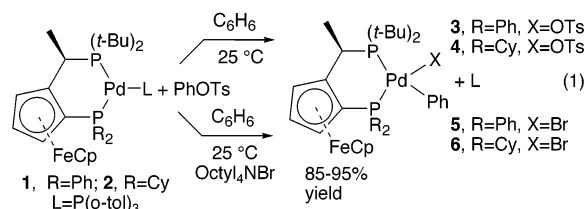
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The oxidative addition of aryl halides and sulfonates to palladium(0) is a fundamental organometallic transformation.¹ Many studies have been conducted on the oxidative addition of aryl halides to palladium(0),^{2–11} but fewer studies have been conducted on the oxidative addition of aryl sulfonates.^{9,11,12} The oxidative addition of aryl tosylates is particularly rare because of the low reactivity of this substrate. Yet, palladium-catalyzed couplings of aryl tosylates would be more attractive than the more common reactions of triflates because they are more crystalline than aryl triflates and are generated from less expensive reagents.

Cross couplings of aryl tosylates with nickel,^{13–15} iron,^{16,17} copper,¹⁸ or palladium catalysts have required high temperatures, activated aryl tosylates, or high catalyst loadings.^{14,19–22} Although complexes of hindered alkylphosphines have recently reacted with aryl chlorides,²³ most of them do not add aryl tosylates that lack activating groups. We report a Pd(0) complex that oxidatively adds aryl tosylates at room temperature to form isolable arylpalladium(II) tosylate complexes. This mild activation created palladium-catalyzed couplings of aryl tosylates with aryl Grignard reagents and amines at room temperature or at elevated temperatures with low loadings.



Pd(0) complexes generated from sterically hindered versions of the commercially available Josiphos ligands^{24,25} underwent addition of aryl tosylate under mild conditions. Reaction between Pd[P(*o*-tolyl)₃]₂ and PPF-*t*-Bu or CyPF-*t*-Bu at room temperature formed Pd(PPF-*t*-Bu)[P(*o*-tolyl)₃] (**1**) or Pd(CyPF-*t*-Bu)[P(*o*-tolyl)₃] (**2**, eq 1). Subsequent treatment of **1** with PhOTs produced the phenylpalladium tosylate complex **3** in 85% yield (eq 1) after 16 h at room temperature by the first oxidative addition of an aryl tosylate to generate an isolable addition product. Reaction in the presence of N(octyl)₄Br formed the phenylpalladium bromide complex **5** in 95% yield after only 9 h. Reactions of phenyl tosylate with CyPF-*t*-Bu complex **2** were even faster. Phenylpalladium tosylate **4** formed from **2** in 92% yield in less than 5 min. The same reaction in the presence of bromide formed the bromide complex **6** in 94% yield in less than 5 min. Two isomeric versions of **3–6** could form, but only one product that contained the palladium-bound phenyl *cis* to the smaller phosphine was observed by NMR and X-ray diffraction (see Supporting Information). Reactions of the analogues of **1** containing Josiphos ligands that lack a *tert*-butyl group formed the addition product in lower yields and with slower rates.

Added anions have been shown to influence the mechanisms of oxidative addition of aryl halides and sulfonates to Pd(0). This effect

has been typically attributed to coordination of the anion to Pd(0) prior to oxidative addition.^{3,5,12,26} Thus, we measured the order of reaction in different reagents by ³¹P NMR spectroscopy at 55 °C in THF solvent in the presence and absence of added bromide. The concentration of PhOTs was varied from 0.062 to 0.45 M; [N(octyl)₄Br] was varied from 0 to 0.34 M, and [P(*o*-tolyl)₃] was varied from 0.088 to 0.26 M. Compound **1** was formed *in situ* from Pd[P(*o*-tolyl)₃]₂ and PPF-*t*-Bu. Excellent fits to a first-order decay of **1** were obtained.²⁷ A first-order dependence of *k*_{obs} on [PhOTs] in both the presence and absence of added bromide was observed. Plots of 1/*k*_{obs} vs [P(*o*-tolyl)₃] from reactions in the presence and absence of added N(octyl)₄Br were linear, indicating that the reaction is inverse first order in P(*o*-tolyl)₃.

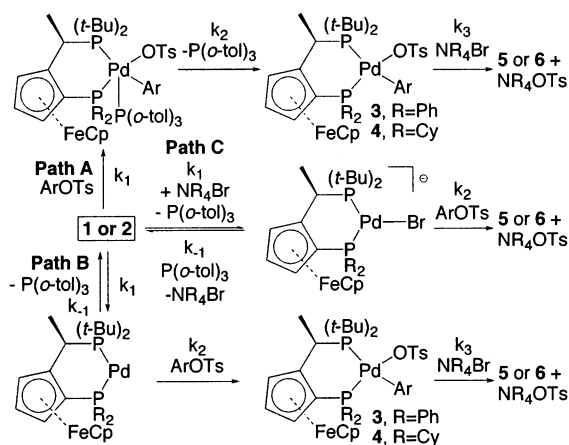
Plots of *k*_{obs} vs [NR₄X] from reactions conducted with added bromide and PF₆ were linear with a positive slope and a clear, nonzero *y*-intercept. The value of *k*_{obs} for reaction in the absence of bromide [(4.1 ± 0.6) × 10⁻⁴ s⁻¹] matched the *y*-intercept of the plot of *k*_{obs} vs [N(octyl)₄Br] [(3.9 ± 0.6) × 10⁻⁴ s⁻¹] and the plot of *k*_{obs} vs [NBu₄PF₆] [(3.3 ± 0.7) × 10⁻⁴ s⁻¹]. The slope of the plot of *k*_{obs} vs [NBu₄PF₆] was roughly 4 times greater than that of the plot of *k*_{obs} vs [N(octyl)₄Br]. Thus, reactions in the presence of [NBu₄PF₆] were *faster* than those conducted with added bromide. Low solubility of **1** limited quantitative data, but reactions in DMF and NMP were faster than reactions in less polar solvents. With 5 equiv of P(*o*-tol)₃ at 55 °C, reactions in DMF and NMP appeared complete in 0.5 h instead of 3.5 h in C₆H₆ or THF. Oxidative addition of PhOTs to **2** was complete within 5 min at 25 °C in THF, C₆H₆, or DMF.

Potential mechanisms for the reaction in eq 1 are shown in Scheme 1. Path A begins with direct oxidative addition of aryl tosylate to the 16-electron complex **1**, followed by dissociation of P(*o*-tolyl)₃. In the presence of bromide, the halogen would replace the coordinated tosylate after addition. This pathway predicts first-order behavior in aryl tosylate and zero-order behavior in both bromide and P(*o*-tolyl)₃. This pathway is inconsistent with the observed inverse-order behavior in P(*o*-tolyl)₃ and the positive-order behavior in bromide.

Path B is initiated by dissociation of P(*o*-tolyl)₃ from **1**, irreversible oxidative addition of aryl tosylate and subsequent more rapid exchange of bromide for tosylate to form **5** if bromide is present. This pathway predicts first-order behavior in aryl tosylate, inverse-order behavior in P(*o*-tolyl)₃, and zero-order behavior in added bromide. The kinetic orders in PhOTs and added P(*o*-tol)₃ are consistent with reaction by path B in the absence of added bromide.

Taken alone, the acceleration of rate by added bromide suggests that path C, which involves initial associative or dissociative exchange of bromide for P(*o*-tolyl)₃ and subsequent irreversible oxidative addition of aryl tosylate to the anionic Pd(0), occurs concurrently with path B in the presence of added bromide. This pathway predicts a reaction that is first order in aryl tosylate, inverse order in P(*o*-tolyl)₃, and first order in bromide. However, faster

Scheme 1

Table 1. Pd-Catalyzed Couplings of ArOTs and ArMgBr^a

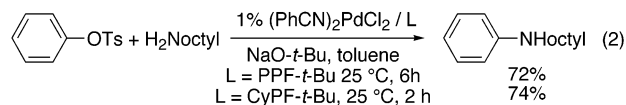
ArOTs	Ar'MgX	0.1%-1% Pd(DBA) ₂ 0.1%-1% PPF- <i>t</i> -Bu toluene, 25-80 °C	Ar-Ar'	Yield ^b
MeO-C ₆ H ₄ -OTs	<i>p</i> -tolylMgBr	1% Pd/L	25 °C, 5h	86%
		0.1% Pd/L	80 °C, 1h	84%
MeO-C ₆ H ₄ -OTs	<i>o</i> -tolylMgBr	1% Pd/L	25 °C, 12h	72%
		0.1% Pd/L	80 °C, 1h	65%
OMe-C ₆ H ₄ -OTs	<i>p</i> -tolylMgBr	1% Pd/L	80 °C, 3h	65%
		0.1% Pd/L	80 °C, 3h	48%
OMe-C ₆ H ₄ -OTs	<i>o</i> -tolylMgBr	1% Pd/L	80 °C, 15h	65%
		0.1% Pd/L	80 °C, 24h	52%
CF ₃ -C ₆ H ₄ -OTs	<i>p</i> -tolylMgBr	1% Pd/L	25 °C, 1h	65%
		0.1% Pd/L	80 °C, 1h	68%
Naphthalene-1-yl-OTs	<i>p</i> -tolylMgBr	1% Pd/L	80 °C, 10h	40%
		0.1% Pd/L	25 °C, 1h	77%
Naphthalene-1-yl-OTs	<i>p</i> -tolylMgBr	1% Pd/L	80 °C, 1h	79%
		0.1% Pd/L	25 °C, 5h	70%
Naphthalene-1-yl-OTs	4-F-C ₆ H ₄ MgBr	1% Pd/L	80 °C, 1h	67%
		0.1% Pd/L	25 °C, 3d	65%
Naphthalene-1-yl-OTs	4-OMe-C ₆ H ₄ MgBr	1% Pd/L	25 °C, 3d	65%
		0.1% Pd/L	80 °C, 4h	62%

^a 1 mmol ArOTs and 2.0 equiv ArMgBr. ^b Isolated yields are an average of two runs.

rates in the presence of more weakly coordinating anions imply that the more polar medium created by the added bromide and not direct coordination of this ion to palladium accounts for the faster rates. Consistent with this assertion, reactions in more polar solvents in the absence of added halogen occurred faster. This large acceleration of oxidative addition of an aryl electrophile to Pd(0) in more polar solvents²⁸ is unusual.^{2,10,11,29}

These room-temperature oxidative additions of aryl tosylates allowed us to develop palladium-catalyzed cross-couplings of aryl tosylates under mild conditions. Results of the reactions of aryl tosylates with aryl Grignard reagents are summarized in Table 1. Reactions with 0.1–1.0 mol % Pd(dba)₂ and PPF-*t*-Bu in toluene at either room temperature or 80 °C produced the corresponding biaryls in good yields in many cases. Most reactions were complete within 24 h. Reactions with 0.01 mol % catalyst were slow and gave lower yields of biaryl. Two equivalents of nucleophile were required for complete conversion of the aryl tosylate due to competing homocoupling of the Grignard reagent. Both electron-donating and -withdrawing aryl tosylates underwent reaction. Sterically hindered aryl tosylates and Grignard reagents also reacted, although in lower yields.

The palladium-catalyzed amination of aryl tosylates at 110 °C was reported previously,^{19,22} but the mild additions of aryl tosylates now allow for the amination of aryl tosylates under milder conditions. Octylamine and phenyl tosylate underwent coupling at room temperature in 76% yield after only 6 h in toluene in the presence of 1 mol % PdCl₂(PPF-*t*-Bu) and 2.5 equiv of NaO-*t*-Bu (eq 2). In addition, reaction in the presence of 1 mol % of PPF-*t*-Bu and commercially available PdCl₂(PhCN)₂ formed the arylamine in 72% yield after 6 h. The increased rate of addition by the Pd(0) complex of CyPF-*t*-Bu further increased the rate of amination. Octylamine coupled with phenyl tosylate in 74% yield after 2 h at 25 °C.



The mild activation of aryl tosylates reported here has several important consequences. First, the mild addition allows for palladium-catalyzed Kumada and amination reactions with unactivated aryl tosylates at room temperature. Second, the rapid oxidative addition step shows that the scope of couplings of aryl tosylates can be limited by transmetalation and reductive elimination¹⁵ instead of oxidative addition. As a result, aryl tosylates may ultimately replace the more expensive and less convenient aryl triflates in many coupling applications.

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Supporting Information Available: Experimental methods, kinetic data, procedures, and spectral data; X-ray crystallographic data for **5** and **6** (PDF); X-ray crystallographic files for **5** and **6** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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