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Platinum-Catalyzed Phenyl and Methyl Group Transfer from Tin to Iridium: Evidence for an Autocatalytic Reaction Pathway with an Unusual Preference for Methyl Transfer

Stuart E. Smith,[†] Jennifer M. Sasaki,[†] Robert G. Bergman,*,[†] Joseph E. Mondloch,[‡] and Richard G. Finke[‡]

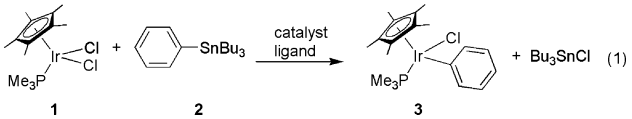
Department of Chemistry, University of California, Berkeley, California 94720-1460, and Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

Received November 15, 2007; E-mail: rbergman@berkeley.edu

Transition-metal-catalyzed cross-coupling reactions (cycle A in Scheme 1) have enjoyed wide application in organic synthesis and are now extensively used for the efficient formation of carbon−carbon and carbon−heteroatom bonds.[1] The synthesis of these complexes is believed to occur via intermediates containing metal−heteroatom and metal−carbon bonds.[1] In principle, analogous coupling reactions could be devised in which a metal complex could be used to catalyze the formation of a bond between a different metal center and a carbon or heteroatom (cycle B in Scheme 1), generating products potentially analogous to the above proposed intermediates. The ability to catalytically synthesize these types of complexes could have a wide impact on research areas in which such complexes are employed or are postulated as intermediates, especially if mechanistic insight can be gained to guide new synthetic developments.

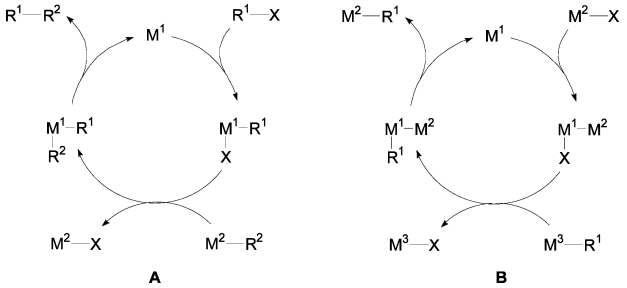
However, the application of transition-metal-catalyzed coupling reactions to the synthesis of organometallic complexes remains relatively rare. A few recent examples have come from the laboratories of Lo Sterzo[2] and Komiya.[3] In both cases, it has been proposed that insertion of a transition metal catalyst, M^1, into a transition metal complex M^2−X bond (X = halide, H) plays a key role in the overall transformation. The M^2−M^1−X intermediate is analogous to the R^1−M^1−X intermediate implicated in typical organic cross-coupling reactions (Scheme 1).[4] This M^2−M^1−X intermediate is then assumed to react via a transmetalation/insertion followed by reductive elimination, yielding the organometallic product.

It seems likely that many organometallic reactions that are catalyzed by a second metal complex remain to be discovered. To investigate this, we have explored the possibility that Stille-type reactions can be developed to promote the metal-catalyzed transfer of an alkyl or aryl group from a tin reagent to the iridium center in $Cp^*(PMe_3)IrCl_2$ (**1**) ($Cp^* = \eta^5$-C_5Me_5; eq 1). The resulting aryl/alkyl chloride complexes are important precursors to catalysts for H/D exchange[5] and for the hydration of alkenes[6] and C−H bond activation.[7] We have found that such reactions can be catalyzed by coordinatively unsaturated platinum complexes. However, the mechanism is much more complicated than the type of routes proposed previously.[2,3]



[†] University of California, Berkeley.
[‡] Colorado State University.

Scheme 1. Representative Mechanism for Metal-Catalyzed Cross-Coupling Reactions



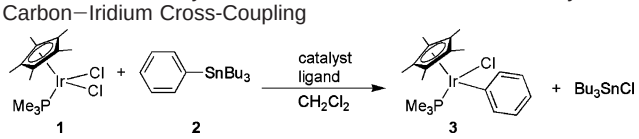
Our initial experiments targeted the transmetalation of a phenyl group from Bu_3SnPh (**2**) to **1** to generate [Ir]PhCl (**3**) ([Ir] = Cp^*-$(PMe_3)Ir$; eq 1), resulting in the formation of a new iridium−carbon bond. A variety of potential transition metal catalysts were examined to effect the desired cross-coupling reaction (Table 1). The most promising complexes were platinum-based. While catalysts derived from $Pt(dba)_2$ gave the best yields,[8] we chose to use $Pt(P^tBu_3)_2$ (**4**) for our subsequent studies due to its solubility and the ability to monitor **4** by both ^1H and ^{31}P NMR.

In an effort to lower the reaction temperature, the use of Me_3-SnPh (**5a**) was explored with the hope that decreased steric repulsion would increase the reaction rate. Surprisingly, use of this compound did not furnish **3**. Instead, exclusive methyl transfer was observed at 75 °C, yielding [Ir]MeCl (**6**). The selectivity for methyl transfer contrasts with the preferential aryl transfer from tin reagents observed in organic cross-coupling reactions,[9] as well as with the organometallic reactions studied by Lo Sterzo where selective alkynyl transfer from R_3Sn−R′ (R = Bu, Me, R′ = alkyne) is observed.[10] Tin reagents bearing both Ph and alkyl groups commonly transfer the Ph rather than the Me group in electrophilic reactions.[11] In our system, only methyl transfer is observed with the tin reagents Me_2SnPh_2 (**5b**) and $MeSnPh_3$ (**5c**), in addition to $SnMe_4$ (**5d**), where only methyl transfer is possible (Table 2).

In the *absence* of the Pt catalyst **4**, a slow background reaction is observed. However, in this thermal process, selective *phenyl* transfer occurs at 105 °C from **5c**, while both phenyl and methyl transfers occur from **5a** (Table 2).[12] At 75 °C, these reactions are extremely sluggish. Thus, **4** is crucial to controlling the rate and chemoselectivity of the reaction.

Our first evidence for mechanistic complexity appeared when reaction monitoring revealed that all of the cross-coupling reactions studied showed the gradual formation of a new Pt−H complex, identified as $(P^tBu_3)_2Pt(H)(Cl)$ (**7**). Since the source of the HCl in this complex was unclear, we sought to determine whether the presence of adventitious acid could be responsible for the catalytic

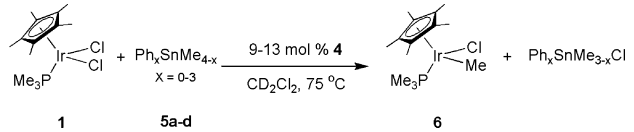
Table 1. Preliminary Examination of Transition-Metal-Catalyzed Carbon−Iridium Cross-Coupling



catalyst (mol %)	ligand (mol %)	temp (°C)	time (h)	% **3**[a]
$Pt(PPh_3)_4$ (9)	NA[d]	135	26	0
$(COD)PtCl_2$ (30)	$P(^tBu)_3$ (45)	135	26	0
$[(COD)IrCl]_2$ (20)	$P(^tBu)_3$ (57)	135	26	0
$(CH_3CN)_2PdCl_2$[c] (15)	NA	105	23	<2
$(COD)_2Ni$ (55)	$P(^tBu)_3$ (80)	135	26	6
$(COD)_2Ni$ (36)	NA	135	26	9
$Pt(P^tBu_3)_2$ (9)	NA	130	22	20
$Pt(dba)_2$[b] (15)	NA	135	21	40
$Pt(dba)_2$ (9)	$P(Mes)_3$ (9)	130	22	48

[a] Yield of product measured by ^{31}P NMR. [b] Pt black formed. [c] Reaction performed in DMF, and Pd black formed almost immediately. [d] NA = not applicable.

Table 2. Platinum-Catalyzed Sn−Me Transfer to **1**



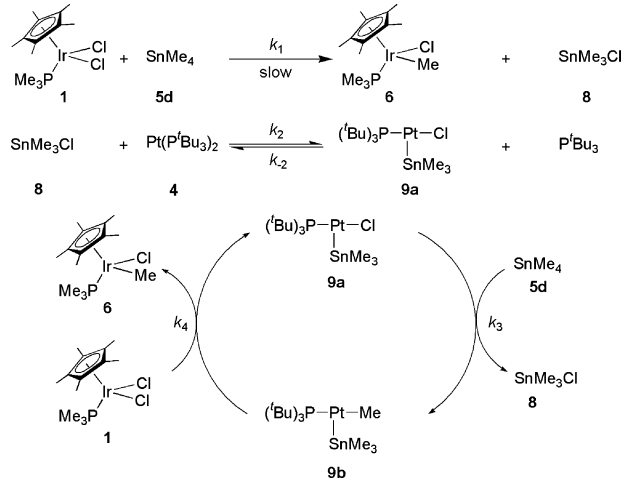
tin complex	time (h)	% **1**[a]	% **6**[a]
Me_3SnPh (**5a**)[b]	25	18	74
Me_2SnPh_2 (**5b**)	46	36	59
$MeSnPh_3$ (**5c**)[c]	140	57	24
Me_4Sn (**5d**)	29	15	85

[a] Yield of product measured by ^{31}P NMR. [b] Reaction performed in THF-d_8. [c] Catalyst was generated in situ from $Pt(dba)_2$ and $P(^tBu)_3$.

transformation of **1** to **6** by carrying out a control experiment with deliberately added acid. This revealed that HCl, in the absence of Pt, is capable of catalytically converting **1** to **6** with tin complexes **5a** and **5d**. However, with tin complex **5b**, both phenyl and methyl transfers occur, and only phenyl transfer occurs with **5c**.[13] This differentiates the acid-catalyzed from the metal-catalyzed pathway. In order to prevent complications resulting from the acid-catalyzed background, reactions catalyzed by **4** only were performed in the presence of base to scavenge adventitious acid. Amine bases were found to shut down the HCl-catalyzed transmetalation reaction. However, the resulting ammonium salts can apparently still protonate **4**, as hydride **7** was formed in the presence of the amine bases.[14] All other stronger bases examined (e.g., Verkade's base,[15] KO^tBu, sodium 2-methylbutan-2-oxide, (dimethylamino)trimethyltin(IV), sodium malononitrile) reacted with either **1**, the solvent, or **4**, rendering them incompatible. Chloride is not responsible for the conversion of **1** to **6** since it inhibits the transmetalation: reactions performed in the presence of 1 equiv of $(Ph_3P)_2N^+Cl^-$ did not produce any product.

Several experiments were carried out to establish the source of adventitious acid and remove it effectively. Basification of the glassware with 1 M NaOH, filtration of all reactants but **4** through basic alumina(I), and recrystallization of catalyst **4** from hexanes failed to stop the formation of **7**. It was ultimately discovered that silylation of the glassware prior to reaction prevented the production of **7**. Our tentative conclusion is that generation of HCl occurs via

Scheme 2. Proposed Mechanism



reaction of the product $SnMe_3Cl$ (**8**) with the surface hydroxyls of the glass, and only silylation is effective in inhibiting this process.

The effective removal of adventitious acid allowed us to initiate kinetic studies of the purely Pt-catalyzed reaction. Early experiments revealed a novel feature of the reaction: autocatalysis (vide infra). A plot of the loss of **1** versus time did not give simple kinetic behavior but, instead, demonstrated the presence of an induction period, which implies that **4** is not the active catalyst. Potential detailed mechanisms that might explain this induction period are (1) the generation[16] of colloidal Pt^0, (2) the presence of radical intermediates,[17] and (3) direct reaction of one of the products with the catalyst precursor, **4**.[18]

Evidence against the generation of a colloidal Pt^0 catalyst was obtained by performing control reactions in the presence of excess Hg^0.[19] No inhibition of the Me transfer reaction is seen, arguing against colloidal Pt^0 as the active catalyst. Similarly, evidence against a radical reaction was obtained by performing a reaction in the presence of the radical initiator AIBN (43 mol %) and a separate reaction in the presence of the radical inhibitor BHT (120 mol %). In both experiments, the induction period remained and there was no dramatic alteration in the reaction rate. Hence, it appears unlikely that the reaction proceeds through radical intermediates. The third potential mechanism was tested by addition of the stoichiometric products to the reaction mixture. Addition of **6** did not affect the induction period, but the addition of 10 mol % of $SnMe_3Cl$, **8**, substantially reduced it. Thus, it appears that reaction of **8** with **4** is required to form the active catalyst (Scheme 2).[20] Addition of 1 equiv of free $P(^tBu)_3$ to a reaction mixture containing 10 mol % of **8** and 12 mol % of **4** severely inhibits the reaction, indicating that dissociation of $P(^tBu)_3$ is also required for catalysis to ensue.[21]

A mechanism consistent with our currently available data is shown in Scheme 2. We propose that the induction period results from the slow direct reaction of **1** with **5d**, producing **6** and **8**. Once **8** forms, a second reaction occurs with the precatalyst **4** to produce a key species within the catalytic cycle, **9a**, eventually leading to autocatalysis and the signature sigmoidal curve of autocatalytic kinetics (Figure 1). Included in the Supporting Information is an explanation of how the proposed mechanism accounts for the observed autocatalysis and a fit to an idealistic autocatalytic model, which proved to be the key to discovering the proposed mechanism. All of these data provide compelling evidence for an autocatalytic mechanism. Additionally, we have been able to fit the more detailed mechanism proposed in Scheme 2 directly to the experimental data as shown in Figure 1.

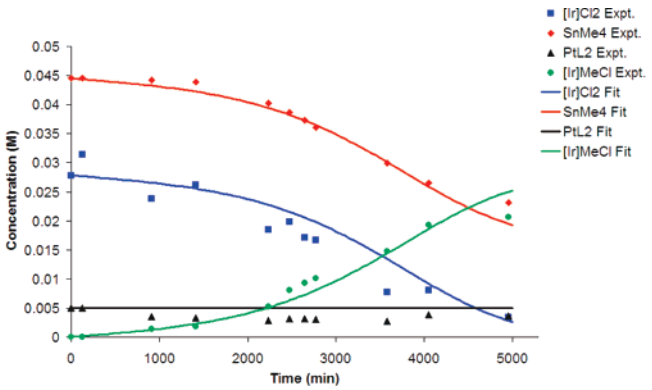


Figure 1. Concentration versus time data and curve-fit to the mechanism in Scheme 2. Conditions: **1** (0.0278 M) with **5d** (0.0445 M) and **4** (0.0050 M). The reaction was performed in dioxane-d_8 at 74 °C and monitored by ^{1}H NMR. There is some overlap of the ^{1}H NMR signals for **1**, **6**, and **4**, which is the reason for the relatively large amount of scatter about the curve-fit for **1** and **4**. Rate constants for the fit are $k_1 = 1.0 \times 10^{-3}$ M^{-1} min^{-1}, $k_2 = 2.0 \times 10^{-8}$ M^{-1} min^{-1}, $k_{-2} = 580$ M^{-1} min^{-1}, $k_3 = 1.0 \times 10^8$ M^{-1} min^{-1}, $k_4 = 3.8 \times 10^5$ M^{-1} min^{-1}. Additional fits and rate constants documenting the autocatalysis are provided in the Supporting Information.

The autocatalysis and sigmoidal kinetics in Figure 1 are of considerable fundamental interest. Specifically, they represent a process that is much more common in nature[22] but, at present, infrequently identified in relatively simple characterizable chemical systems,[22] in which a slower (sometimes even undesired or "wrong") reaction[22] evolves chemically to a faster, "smarter" process. This can be considered as a primitive type of chemical evolution,[22] in this case evolution of a superior, faster catalytic process.

In conclusion, an autocatalytic mechanism appears to be operational for this metal-catalyzed organometallic reaction, wherein a slow direct background reaction of **1** with **5d** is necessary to form **8**. Once **8** is formed, a reaction with the catalyst precursor **4** occurs to yield an active catalytic species **9a**. Additionally, even when the tin reagent bears Sn−Ph bonds, selective Sn−Me transfer occurs. Overall, this system is a rare example of a metal-catalyzed metal−carbon bond-forming reaction in which the catalyst is produced in an autocatalytic reaction. A key to the reaction is that the catalytic intermediate Pt(Me)(P^{t}Bu$_3$)SnMe$_3$ is superior to SnMe$_4$ in transferring a Me group to **1**. One presumes that this feature will extend to other M−Cl (M = transition metal) systems, although additional work will be required to elucidate the more general aspects of the mechanism proposed in Scheme 2. Current work is aimed at providing additional information on the reaction mechanism, synthesizing the putative catalytic intermediates, understanding the unusual selectivity for Me transfer, and applying this method to the synthesis of metal−heteroatom bonds.

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Supporting Information Available: Experimental details for the reaction of **1** with tin complexes and for the curve-fitting are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) We believe that the background reaction proceeds by slow ionization of **1**, yielding [Ir]Cl$^+$, followed by transmetalation of the Sn complexes to this cationic unsaturated intermediate. The ratio of Ph:Me transfer will then depend on the Sn complex employed.
(13) We believe that HCl protonates the Sn complex, generating the corresponding Sn−Cl complex, which then acts as a Lewis acid and assists in the ionization of **1**, thus facilitating the background reaction.
(14) Addition of anilinium chloride to **4** causes the quantitative formation of **7**. During further investigations into the HCl source, it was found that **4** slowly decomposes to **7** in CD$_2$Cl$_2$; thus, the ethereal solvents dioxane and THF were utilized instead. Varying the amount of added Hünig's base (1 and 11 equiv vs **1**) revealed that the rates remained qualitatively constant, confirming that the observed catalysis results from **4** and not from HCl. No colloidal Pt^0 is observed in these reactions, the only observable Pt species being **4** and **7** by NMR. The use of **7**, in the absence of **4**, produces **6** only after a substantial induction period, indicating that **7** is not the active catalyst.
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(20) A control experiment in which a co-catalytic amount of **8** was added to a reaction mixture devoid of **4** proceeds at a much slower rate than when **4** is present, demonstrating that the catalysis does not result solely from **8**.
(21) Addition of 55 mol % of N(hex)$_4$Cl to a reaction mixture containing 10 mol % of **8** and **4** also inhibits the reaction. It is currently unknown whether chloride dissociation from **8** is required prior to reaction with **4** or whether the chloride is simply binding an unsaturated intermediate. Current studies are focused on addressing these possibilities.
(22) Due to space limitations, the references documenting these points are available in the Supporting Information.

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