Communication

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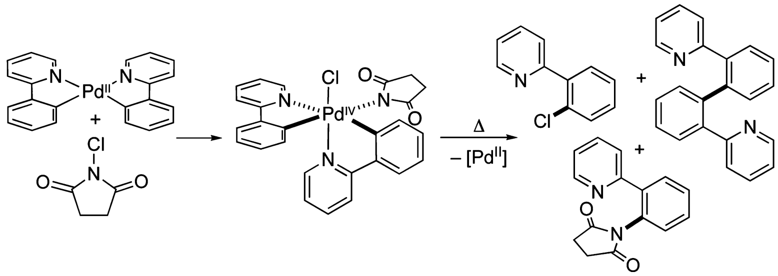

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Reactivity of Pd(II) Complexes with Electrophilic Chlorinating Reagents: Isolation of Pd(IV) Products and Observation of C−Cl Bond-Forming Reductive Elimination

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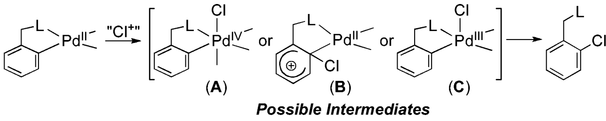
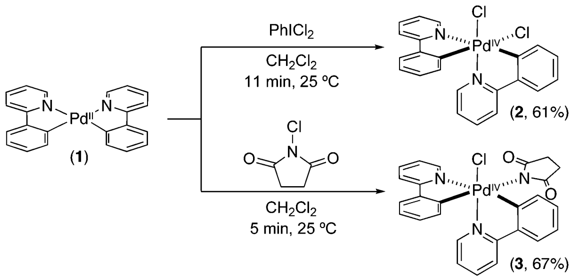
The selective halogenation of aromatic molecules is an important organic transformation, as aryl halides serve as key components of or precursors to a wide variety of natural products, pharmaceuticals, agrochemicals, and materials.[1,2] We recently reported that Pd^{II} catalysts in conjunction with electrophilic halogenating reagents [particularly iodobenzene dichloride (PhICl$_2$) and *N*-halosuccinimides (NXS, X = Cl, Br, I)] promote the ligand-directed conversion of arene C−H bonds into carbon−halogen bonds.[1] These transformations were proposed to proceed by a Pd$^{II/IV}$ catalytic cycle, with a Pd^{IV} complex of general structure **A** (eq 1) serving as a key intermediate.[1] This proposal was largely based on mechanistic studies of related Pd-catalyzed C−H bond acetoxylation reactions with PhI(OAc)$_2$, in which Pd^{IV} carboxylate analogues of **A** were isolated and characterized.[3a] However, at least two other mechanisms are also possible for these halogenation reactions. The first would involve direct electrophilic cleavage of the Pd^{II}−C bond without a change in oxidation state at the Pd center (i.e., via intermediate **B** in eq 1).[4] This type of pathway, which is similar to an organic S$_E$2 process, has significant precedent at late metal centers.[4] Alternatively, a single electron mechanism involving Pd^{III} intermediates (i.e., **C** in eq 1) could also be operating; for example, *N*-bromosuccinimide has been shown to react with related group 10 metal complexes to afford stable analogues of **C**.[5]



(1)

In order to gain further insight into the mechanism of C−H bond halogenation, we undertook studies of stoichiometric reactions between PhICl$_2$ or *N*-chlorosuccinimide and the model complex Pd^{II}(phpy)$_2$ (**1**, phpy = 2-phenylpyridine). Complex **1** was selected for investigation because the cyclometalated phenylpyridines are rigid, electron-donating, and contain nitrogen donor ligands, all features that are expected to stabilize high oxidation states and/or highly electrophilic intermediates, such as **A**, **B**, and **C**.[3a,5−7] Importantly, previous reports have described reactions of other Pd^{II} σ-alkyl or aryl complexes with electrophilic halogenating reagents to afford organic halide products,[7,8] but organometallic intermediates such as **A**, **B**, or **C** have rarely been observed. In limited instances, transient Pd^{IV} analogues of **A** were identified by ^{1}H NMR spectroscopy.[7] However, they typically exhibited low stability at ambient temperatures, which precluded further characterization and limited detailed reactivity studies.[7] *In contrast, we report herein that Pd^{II}(phpy)$_2$ reacts with both PhICl$_2$ and N-chlorosuccinimide (NCS) to form stable Pd^{IV} products.* Furthermore, we describe preliminary investigations of the reactivity of these complexes toward C−Cl, C−C, and C−N bond-forming reductive elimination.

Initial studies focused on the reaction between Pd^{II}(phpy)$_2$ and PhICl$_2$ in CH$_2$Cl$_2$. Careful monitoring showed that a single major inorganic species was formed after 11 min of stirring at 25 °C, and this product (**2** in eq 2) was isolated as a yellow solid in 61% yield. Both the ^{1}H and ^{13}C NMR spectra of **2** are consistent with an octahedral Pd^{IV} complex possessing a *cis* geometry and two inequivalent phpy ligands. In addition, the ^{1}H NMR spectrum shows diagnostic upfield and downfield signals at 6.49 and 9.90 ppm, respectively, which are characteristic of unsymmetrical Pd^{IV} and Pt^{IV} complexes of general structure *cis*-M^{IV}(phpy)$_2$X$_2$.[3a,9] Notably, **2** is stable at room temperature in the solid state for at least 2 weeks and shows <5% decomposition after 10 h in CDCl$_3$ solution.



(2)

Remarkably, *N*-chlorosuccinimide (NCS) also reacted with Pd^{II}(phpy)$_2$ to produce a stable Pd^{IV} oxidative addition product. This reaction was complete within 5 min at 25 °C and afforded the novel complex **3** in 67% yield as a yellow solid. *To our knowledge, this is the first reported example of direct oxidative addition into the N−X bond of an N-halosuccinimide.* Complex **3** was initially characterized by ^{1}H and ^{13}C NMR spectroscopy, which exhibits signals consistent with *cis* oxidative addition and incorporation of a succinimide ligand. X-ray quality crystals were obtained by slow diffusion of pentane into a CHCl$_3$ solution of **3**. As depicted in Figure 1, the X-ray structure confirms the proposed *cis* orientation between the chloride and succinimide ligands. Furthermore, it shows that the succinimide is *trans* to a σ-phenyl ligand, while the chloride is *trans* to a pyridine nitrogen. As mentioned above, the clean formation of **3** stands in contrast to reactions of other group 10 metal complexes with *N*-halosuccinimides. For example, L$_2$X$_2$Ni^{II} species have been shown to react with NBS to afford the corresponding Ni^{III} bromides,[5] while reactions between L$_2$X$_2$Pt^{II} and NCS typically generate either L$_2$X$_2$PtCl(solvent)[10a] or L$_2$X$_2$PtCl$_2$ adducts.[10a,b]

The formation of complexes **2** and **3** clearly demonstrates that Pd^{IV} can be accessed with both PhICl$_2$ and NCS and thereby provides support for the viability of proposed intermediate **A** in the catalytic reactions.[11] In addition, **2** and **3** provide a unique opportunity to directly study carbon−halogen bond-forming reductive elimination from Pd^{IV}. Importantly, well-characterized examples of C−X coupling at Pd^{IV} are extremely rare.[7c,12] Attempts to observe such reactions have been hampered by the low stability of the Pd^{IV} starting materials and/or by the fact that most isolable Pd^{IV} halide complexes contain multiple σ-alkyl/aryl ligands, which undergo fast competing C−C coupling processes.[13] However, prior work from our group suggested that C−C reductive elimination from **2** and **3** might be minimized by the presence of rigid chelating phpy ligands,

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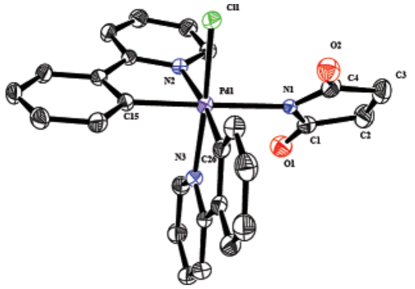
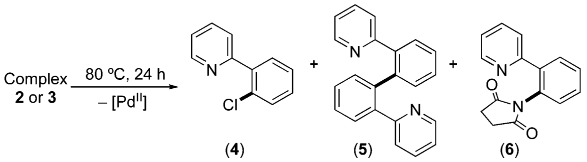


Figure 1. X-ray crystal structure of complex **3**.

Table 1. Reductive Elimination Reactions from **2** and **3**[a]



entry	complex	solvent	%4	%5	%6
1	**2**	C_5H_5N	<1	60	
2[b]	**2**	AcOH	49	7	
3	**3**	C_5H_5N	6	81	8
4[b]	**3**	AcOH	67	5	<1

[a] Yields determined by GC based on an average of four runs. [b] Free 2-phenylpyridine (6% in entry 2 and 7% in entry 4) accounted for the remainder of the volatile organic products in these reactions.

allowing competing carbon−heteroatom bond-forming processes to be observed.[3a]

Our studies began with complex **2**, which could undergo C−C or C−Cl bond-forming reductive elimination to afford **4** or **5**, respectively (Table 1). When **2** was heated at 80 °C for 24 h in pyridine, the C−C coupled product **5** was the sole organic species observed by GC and GCMS (Table 1, entry 1).[14] Moving to other common solvents (e.g., benzene, nitrobenzene, acetone, and MeCN) led to the formation of mixtures of **4** and **5** (Table S1).[15] However, interestingly, in AcOH (the most effective medium for Pd-catalyzed halogenation reactions),[1b,c] thermolysis of **2** afforded a >5:1 ratio of **4**/**5** (entry 2). *To our knowledge, this is the first report of carbon−halogen bond-forming reductive elimination occurring in preference to C−C coupling at a Pd^{IV} center.*

Complex **3** presents an even more interesting situation where reductive elimination could afford three possible organic products—**4**, **5**, and/or the C−N coupled product **6**. Similar to complex **2**, thermolysis of **3** in pyridine resulted in predominantly C−C reductive elimination to afford **5** as the major organic product (Table 1, entry 3). However, intriguingly, this reaction also afforded modest (8%) yield of the amide product **6**. This is particularly notable because C−N bond-forming reductive elimination from high oxidation state late metal complexes is very rare.[16] *Additionally, this result suggests that optimization of reaction medium and catalyst structure might allow catalytic C−N bond formation with NCS as the terminal oxidant*.[17] When the solvent was changed to benzene, nitrobenzene, acetone, or MeCN, only traces of **6** were observed along with mixtures of **4** and **5**. Furthermore, in the catalytic reaction solvent AcOH, none of amide **6** was observed, and C−Cl bond-forming reductive elimination predominated (entry 4). While the origin of these solvent effects remains under investigation, these results demonstrate that the distribution of observable organic reductive elimination products is highly sensitive to the reaction medium.

In conclusion, this communication describes the reactions of $PhICl_2$ and NCS with Pd^{II}(phpy)$_2$ to afford room temperature stable oxidative addition adducts **2** and **3**. Furthermore, these novel complexes are shown to undergo competing C−Cl, C−C, and C−N bond-forming reductive elimination reactions. Both the accessibility and the observed reactivity of **2** and **3** provide support for a Pd$^{II/IV}$ mechanism in Pd-catalyzed halogenation reactions. Future studies will explore the mechanism of reductive elimination in these systems as well as apply these findings to the development of new and more efficient Pd$^{II/IV}$-catalyzed reactions.

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Supporting Information Available: Experimental details and spectroscopic and analytical data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (b) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523. (c) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 11483.

(2) Other Pd-catalyzed directed halogenations: (a) Fahey, D. R. *J. Chem. Soc., Chem. Commun.* **1970**, 417. (b) Fahey, D. R. *J. Organomet. Chem.* **1971**, *27*, 283. (c) Kodama, H.; Katsuhira, T.; Nishida, T.; Hino, T.; Tsubata, K. *Chem. Abstr.* **2001**, *135*, 344284. (d) Giri, R.; Chen, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 2112. (e) Wan, X.; Ma, Z.; Li, B.; Zhang, K.; Cao, S.; Zhang, S.; Shi, Z. *J. Am. Chem. Soc.* **2006**, *128*, 7416.

(3) (a) Dick, A. R.; Kampf, J. W.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 12790. (b) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300. (c) Yoneyama, T.; Crabtree, R. H. *J. Mol. Catal. A* **1996**, *108*, 35.

(4) For discussions of S_E2 cleavage of late metal−carbon bonds, see: (a) Kalberer, E. W.; Houlis, J. F.; Roddick, D. M. *Organometallics* **2004**, *23*, 4112. (b) Hill, G. S.; Rendina, L. M.; Puddephatt, R. J. *Organometallics* **1995**, *14*, 4966. (c) Alibrandi, G.; Minniti, D.; Romeo, R.; Uguagliati, P.; Calligaro, L.; Belluco, U. *Inorg. Chim. Acta* **1986**, *112*, L15.

(5) Oguro, K.; Wada, M.; Sonoda, N. *J. Organomet. Chem.* **1979**, *165*, C10.

(6) For examples, see: (a) Grove, D. M.; van Koten, G.; Louwen, J. N.; Noltes, J. G.; Spek, A. L.; Ubbels, H. J. C. *J. Am. Chem. Soc.* **1982**, *104*, 6609. (b) Vigalok, A.; Rybtchinski, B.; Shimon, L. J. W.; Ben-David, Y.; Milstein, D. *Organometallics* **1999**, *18*, 895.

(7) (a) Alsters, P. L.; Engel, P. F.; Hogerheide, M. P.; Copijn, M.; Spek, A. L.; van Koten, G. *Organometallics* **1993**, *12*, 1831. (b) Lagunas, M.-C.; Gossage, R. A.; Spek, A. L.; van Koten, G. *Organometallics* **1998**, *17*, 731. (c) van Belzen, R.; Elsevier, C. J.; Dedieu, A.; Veldman, N.; Spek, A. L. *Organometallics* **2003**, *22*, 722. (d) Uson, R.; Fornies, J.; Navarro, R. *J. Organomet. Chem.* **1975**, *96*, 307.

(8) For examples, see: (a) Vicente, J.; Saura-Llamas, I.; Bautista, D. *Organometallics* **2005**, *24*, 6001. (b) Alsters, P. L.; Boersma, J.; van Koten, G. *Organometallics* **1993**, *12*, 1629. (c) Backvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335. (d) Wong, P. K.; Stille, J. K. *J. Organomet. Chem.* **1974**, *70*, 121.

(9) Chassot, L.; von Zelewsky, A. *Helv. Chim. Acta* **1986**, *69*, 1855.

(10) (a) Zhang, F.; Broczkowski, M. E.; Jennings, M. C.; Puddephatt, R. J. *Can. J. Chem.* **2005**, *83*, 595. (b) Scollard, J. D.; Day, M.; Labinger, J. A.; Bercaw, J. E. *Helv. Chim. Acta* **2001**, *84*, 3247.

(11) Importantly, the isolation of **2** and **3** does not definitively exclude the intermediacy of **B** or **C** in the catalytic transformations.

(12) For C−X bond-forming reductive elimination from Pt^{IV}, see: (a) Yahav-Levi, A.; Goldberg, I.; Vigalok, A. *J. Am. Chem. Soc.* **2006**, *128*, 8710−8711. (b) Goldberg, K. I.; Yan, J.; Breitung, E. M. *J. Am. Chem. Soc.* **1995**, *117*, 6889. (c) Ettorre, R. *Inorg. Nucl. Chem. Lett.* **1969**, *5*, 45.

(13) For example, see: (a) Canty, A. J.; Hoare, J. L.; Davies, N. W.; Traill, P. R. *Organometallics* **1998**, *17*, 2046. (b) Canty, A. J.; Traill, P. R.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **1992**, *433*, 213. (c) Canty, A. J.; Watson, A. A.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **1989**, *367*, C25.

(14) Reductive elimination is expected to generate two (from **2**) or three (from **3**) different coordinatively unsaturated Pd^{II} products, which appear to undergo rapid disproportionation/decomposition at 80 °C. As a result, the inorganic products of these reactions have not been definitively identified/characterized.

(15) In solvents other than AcOH and pyridine, the mass balance of organic products (as determined by GC and GCMS) was <50%. We believe that this is due to competing cyclometalation of products **4**−**6** by the Pd^{II} byproducts of reductive elimination.

(16) For C−N reductive elimination from Pt^{IV}, see: Pawlikowski, A. V.; Getty, A. D.; Goldberg, K. I. *J. Am. Chem. Soc.* **2007**, *129*, 10382.

(17) Initial efforts have shown that Pd(OAc)$_2$-catalyzed chlorination (or amination) of 2-phenylpyridine does not proceed in pyridine.

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