Palladium Alkoxides: Potential Intermediacy in Catalytic Amination, Reductive Elimination of Ethers, and Catalytic Etheration. Comments on Alcohol Elimination from Ir(III)

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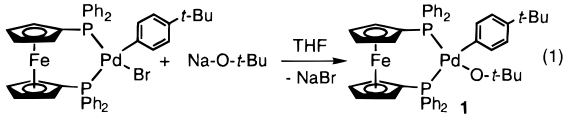
Our group and those of Boncella and Hillhouse recently observed carbon−nitrogen and −sulfur bond-forming reductive eliminations of amines[1−3] and sulfides[4] from palladium and nickel amides and thiolates. These observations led to improvements in the palladium-catalyzed amination of aryl halides.[5−9] In contrast, analogous chemistry to form ethers and alcohols from palladium alkoxides has been elusive.[3b,10−14] Further, the potential intermediacy of palladium alkoxides in aryl halide amination chemistry has not been evaluated. In this paper we report (1) the isolation of a palladium aryl alkoxo complex, (2) the formation of arylamines by reaction of this complex with HNRR′, (3) the reductive elimination of aryl ethers from an analog of this complex with an electron deficient aryl group, (4) the catalytic formation of alkyl aryl ethers with DPPF-ligated palladium, most likely by C−O bond-forming reductive elimination, and (5) the stability of an Ir(III) alkyl hydroxo complex previously reported to eliminate alcohol thermally.

Motivated by our recent rapid reductive eliminations of amines from DPPF−Pd(II) complexes and the potential for the intermediacy of alkoxides in tin-free amination chemistry,[6,9] we prepared (DPPF)Pd(*p*-*t*-BuC_6H_4)(O-*t*-Bu) (**1**) (DPPF = (1,1′-diphenylphosphino)ferrocene) by addition of Na-O-*t*-Bu to (DPPF)Pd(*p*-*t*-BuC_6H_4)(Br) (eq 1). Complex **1** was obtained in pure form as yellow crystals by crystallization from pentane at −30 °C.



(1)

Complex **1** decomposes in solution or as a solid over the course of hours at room temperature. The dominant metal products from this thermal chemistry are DPPF-ligated Pd(0) complexes. The primary organic products are biphenyl, *tert*-butylbenzene and 4,4′-di-*tert*-butylbiphenyl (Scheme 1).[15] No ether was observed. Even the heating of **1** in the presence of PPh_3, conditions known to dramatically increase yields of amine reductive eliminations, produced no ether. Thus, electronically neutral aromatic groups resist reductive elimination of ether in this system.

However, this stability toward ether formation may be crucial for effective catalytic amination of aryl halides by amines and alkoxide base. The amination of aryl halides by amines in the presence of NaO-*t*-Bu involves catalytic amounts of palladium aryl halide intermediates in the presence of stoichiometric quantities of NaO-*t*-Bu. Thus, it seems likely that aryl alkoxo complexes such as **1** exist in the reaction solutions. Considering recent N−H activation chemistry by dimeric hydroxo complexes,[16] the amination chemistry may occur by reaction of **1** with amine to form palladium amido aryl complexes.

To test this hypothesis, we studied the chemistry of **1** with amines (Scheme 1). Reaction between ditolylamine and **1** at room temperature gave the ditolylamido complex (DPPF)Pd(*p*-*t*-BuC_6H_4)((N(tol)$_2$) (**2**) in 75% yield. Complex **2** was independently prepared from (DPPF)Pd(*p*-*t*-BuC_6H_4)(Br) and KN(tol)$_2$; (DPPF)Pd(Ph)((N(tol)$_2$) was prepared and fully characterized previously.[2] Ditolylamide **2** quantitatively formed the triarylamine (4-*tert*-butylphenyl)bis(4-methylphenyl)amine after less than 4.5 h at 75 °C in the presence of PPh_3-d_{15}. Similarly, reaction between aniline and **1** formed HO-*t*-Bu and (DPPF)Pd(C_6H_4-*t*-Bu)(NHPh) (**3**) (92% yield) that displayed two new doublets in the $^{31}P\{^1H\}$ NMR spectrum, along with a new *t*-Bu group in the ^1H NMR spectrum, suggesting formation of monomeric anilide complex **3**. This assignment was confirmed by observing $^{31}P-^{15}N$ coupling to both phosphorus atoms of the DPPF (δ 26.1, dd, J_{NP} = 42 Hz, J_{PP} = 38 Hz; δ 5.3, dd, J_{NP} = 5 Hz, J_{PP} = 38 Hz) in reactions conducted with [^{15}N]-aniline. Complex **3** formed (4-*tert*-butylphenyl)phenylamine in 75−85% yield after 1 h at room temperature. Though precluding isolation, these data further support its identity as the anilido aryl complex. Addition of piperidine to **1** led to the formation of *N*-(4-*tert*-butylphenyl)piperidine after 1.5 h at room temperature in 57% yield. In this case, the presumed intermediate **4** was not observed, suggesting that the C−N bond-forming reductive elimination is faster than N−H activation of the alkylamine. These results demonstrate that the reaction chemistry of the alkoxo aryl complex with amines is faster than the decomposition in the absence of amine. Further, they show directly a pathway for formation of amido aryl species from aryl halide complexes, amine, and alkoxide base.

Our studies on directly-observed reductive elimination of amines and sulfides showed faster rates for electron deficient aryl groups.[4,17] Thus, we treated aryl halide complexes containing HC(O)−, PhC(O)−, F_3C−, and NC− in the *para*-position with NaO-*t*-Bu. The alkoxide products were too reactive to isolate, but GC/MS of the reaction mixtures after 0.5 h at room temperature showed formation of the alkyl aryl ethers, chemistry that contrasted that of **1**.

We focused our attention on Pd(DPPF)(*p*-C_6H_4CHO)(O-*t*-Bu) (**5**; Scheme 1), which showed the cleanest substitution chemistry and which contained an aldehyde resonance in the ^1H NMR spectrum to mark the aromatic group. Addition of

(1) Villanueva, L. A.; Abboud, K. A.; Boncella, J. M. *Organometallics* **1994**, *13*, 3921−3931.
(2) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 4708−4709.
(3) For an example of oxidatively induced reductive elimination from Ni(II) see: (a) Koo, K.; Hillhouse, G. L. *Organometallics* **1995**, *14*, 4421−4423. (b) Koo, K.; Hillhouse, G. L.; Rheingold, A. L. *Organometallics* **1995**, *14*, 456.
(4) Baranano, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 2937−2938.
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(6) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217−7218.
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(12) Matsunaga, P. T.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 2075−2077.
(13) Matsunaga, P. T.; Mavropoulous, J. C.; Hillhouse, G. L. *Polyhedron* **1995**, *14*, 175−185.
(14) A palladium-catalyzed cyclization to form oxygen heterocycles has now been reported: Palucki, M.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 10333.
(15) Organic products identified by ^1H NMR spectroscopy and GC/MS.
(16) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 4206−4207.
(17) Hartwig, J. F.; Richards, S.; Baranano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626−3633.

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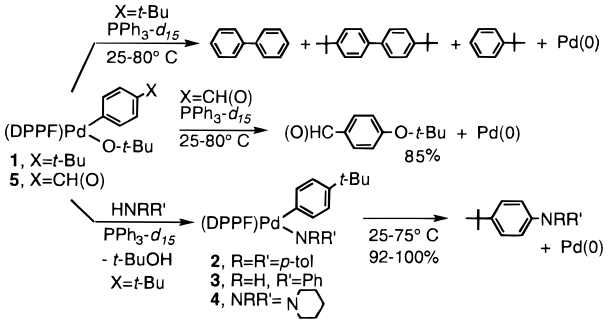
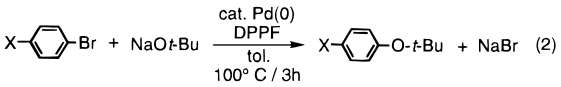
Scheme 1



NaO-*t*-Bu to Pd(DPPF)(*p*-C_6H_4CHO)(Br) produced two new $^{31}P\{^1H\}$ signals (δ 30.0 (d), 8.7 (d), $J = 37$ Hz), with similar shifts and coupling constants to those of isolated **1** (δ 29.5 (d), 6.8 (d), $J = 34$ Hz). In addition, the ^1H NMR spectrum of the reaction showed a new formyl resonance and a new *t*-Bu resonance well resolved from NaO-*t*-Bu, HO-*t*-Bu, or the product ether. These data strongly support the identity of **5** as Pd(DPPF)(*p*-C_6H_4CHO)(O-*t*-Bu).

Due to its room temperature reactivity, complex **5** could not be purified from the ether and Pd(0) reaction products. However, we separated **5** from unreacted NaO-*t*-Bu, in order to rule out formation of ether by direct reaction of free NaO-*t*-Bu with the metal-bound electron poor aromatic group. The reaction between NaO-*t*-Bu and a small excess of the palladium halide was stopped after ca. 60% of the halide was consumed. A 3-fold volume of pentane was added, the mixture was filtered, the solvent was removed, and the resulting solid was extracted into a 5:1 pentane/benzene mixture. After removal of solvent, a ^1H NMR spectrum in C_6D_6 showed no NaO-*t*-Bu and only alkoxide complex **5**, *p*-*t*-$BuOC_6H_4CHO$, and $(DPPF)_2Pd$. As shown in Scheme 1, **5** converted to *p*-*t*-$BuOC_6H_4CHO$ (85% yield, after correcting for the initial ether) and Pd(0) in roughly 1 h at room temperature or 10 min at 85 °C. Although a number of mechanisms are possible for this transformation, the formal definition is reductive elimination of ether.

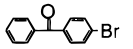
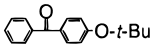
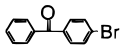
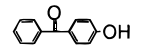
This result prompted us to test a variety of palladium complexes in the catalytic formation of aryl ethers. Intermolecular formation of ethers was observed in the presence of Pd(0), DPPF, NaO-*t*-Bu, and electron deficient aryl bromides (eq 2, Table 1). No significant formation of ether was observed



(2)

when electron neutral or electron rich aryl bromides were used or when the metal or DPPF was omitted. Sodium alkoxides containing β-hydrogens led to more arene than ether. Although this chemistry is thus far limited to production of *tert*-butyl ethers, the aryl alkyl ethers can be efficiently converted to phenols by treatment of the final reaction mixture with 2,2,2-trifluoroethanol and catalytic triflic acid, constituting an overall one-step conversion of aryl bromides to phenols. The ligands

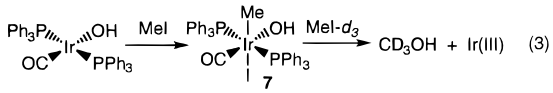
Table 1. Palladium-Catalyzed Etheration of Aryl Halides[a]

Arylhalide	Pd(0) Precursor	Product	Isolated Yield[b]
H(O)C-C$_6$H$_4$-Br	$Pd(dba)_2$	H(O)C-C$_6$H$_4$-O-*t*-Bu	66 %[c]
NC-C$_6$H$_4$-Br	$Pd(PPh_3)_4$	NC-C$_6$H$_4$-O-*t*-Bu	58 %
	$Pd(dba)_2$		69 %
	$Pd(dba)_2$		63 %[d]

[a] 10% Pd(0) catalyst, 12 mol % DPPF, and 1.2 equiv of NaO-*t*-Bu per ArBr in toluene at 100 °C for 8 h. [b] Isolated by chromatography on silica gel, 30:1 pentane/ether. [c] Isolated by chromatography on alumina, 30:1 pentane/ether. [d] 2,2,2-Trifluoroethanol and a catalytic amount of triflic acid were added to the crude mixture and stirred for 10 min; phenol isolation by chromatography on silica gel, 10:1 pentane/ether.

DPPE, BINAP, DPPP, and DPPBz were tested, but none proved more effective than DPPF.[18] The ratios of ether to arene determined by GC were 0.6:1 (DPPE), 3.2:1 (DPPP), 5.1:1 (BINAP, 16% unreacted ArBr), 14:1 (DPPBz), and 23:1 (DPPF). The good conversion and selectivity with DPPBz were surprising, considering its ineffectiveness in amination chemistry. Further catalytic chemistry, ether reductive eliminations, and general chemistry of palladium alkoxides will be reported in due course.

Considering the restrictions on ether elimination from Pd(II), we were puzzled by a previous report of methanol elimination from an Ir(III) methyl hydroxo complex.[11] At 0 °C, Ir(CO)(OH)(I)(Me)(P(*p*-tolyl)$_3$)$_2$ (**6**) was stated to first eliminate CH_3OH and then add MeI to form $Ir(CO)(I)_2(Me)L_2$. Complex **6** was not isolated due to its reactivity below room temperature. To investigate this chemistry for catalytic etheration, we added a 3-fold excess of MeI to the PPh_3 analog $Ir(CO)(OH)(PPh_3)_2$.[19] In contrast to the earlier findings with **6**, Ir(CO)(OH)(I)(Me)$(PPh_3)_2$ (**7**) was obtained in high yield and fully characterized including X-ray diffraction and was stable at room temperature.[20] Warming of this sample at 65 °C did not produce methanol, but warming of **7** at 65 °C in the presence of MeI-d_3 for several hours gave CD_3OH (eq 3). Thus, the formation of methanol in



(3)

the previous report probably resulted from well-established alkylation of the hydroxo group rather than from C−O bond-forming reductive elimination. Thus, thermally-induced reductive elimination of ethers in high yields is currently unique to the Pd(II) complexes in this report.

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Supporting Information Available: Spectroscopic, analytical, and X-ray data for **1**, **2**, and **7** (19 pages). See any current masthead page for ordering and Internet access instructions.

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(18) DPPE = 1,2-bis(diphenylphosphino)ethane, BINAP = 2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl, DPPP = 1,2-bis(diphenylphosphino)-propane, DPPBz = 1,2-bis(diphenylphosphino)benzene.

(19) Reed, C. A.; Roper, W. R. *J. Chem. Soc., Chem. Commun.* **1973**, 1370.

(20) No unusual structural features were observed. Data are provided as Supporting Information.