Carbon−Nitrogen Bond-Forming Reactions of Palladacycles with Hypervalent Iodine Reagents

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Palladium(II) complexes containing bidentate cyclometalated C∼N chelating ligands are shown to react with PhI═NTs at room temperature to insert "NTs" into the Pd−C bond. This "NTs" insertion reaction has been applied to palladacyclic complexes of azobenzene, benzo[*h*]quinoline, and 8-ethylquinoline. The newly aminated organic ligands can be liberated from the metal center by protonolysis with trifluoroacetic acid or HCl.

Introduction

Compounds containing carbon−nitrogen bonds are of great importance in many areas of chemistry, and as a result, transition metal catalyzed approaches to C−N bond formation have been the subject of intense recent research. In particular, Pd- and Cu-catalyzed aminations of aryl halides have proven to be powerful and widely used synthetic methods for the construction of arylamines.[1] However, despite their great utility, these transformations remain fundamentally limited by the fact that the aryl coupling partner must be prefunctionalized with a halide at the desired position, which increases the number of steps required in a synthetic sequence.

An alternative approach to the synthesis of amines would be the direct conversion of C−H bonds into C−N bonds—an attractive transformation from the standpoints of atom economy and synthetic simplicity.[2] Several effective methods for the intra- and intermolecular amination of sp^3 C−H bonds have been developed, and these typically utilize rhodium carboxylate, copper homoscorpionate, or metalloporphyrin based catalysts in conjunction with either PhI═NR or $PhI(OAc)_2/MgO/RNH_2$ as the aminating reagent.[3] The mechanism of these transformations generally involves direct insertion of a metallonitrene into the C−H bond. As a result, the observed selectivities typically parallel those of radical reactions, with preferential amination of activated and/or weak C−H bonds (e.g., tertiary, secondary, benzylic, or C−H bonds α to heteroatoms).[2]

Our group and others have developed a number of Pd-catalyzed processes for converting C−H bonds into C−O,[4] C−halogen,[4a,5] and C−C bonds[6] using iodine(III) reagents as terminal oxidants. In contrast to the aminations described above, these transformations proceed via C−H activation to form discrete organometallic palladacyclic intermediates.[7] As such, selectivity is dictated by proximity to a directing group and by steric effects, rather than by the strength/degree of activation of the C−H bonds. We have had a longstanding interest in extending these reactions to C−N bond formation, because such a transformation could serve as a valuable complement to both the amination of aryl halides and the metallonitrene insertion reactions described above. This report describes the development of a method for Pd^{II}-mediated oxidative C−H bond amination.[8,9] We demonstrate that diverse palladacyclic complexes (which were all initially formed by directed C−H activation) undergo stoichiometric amination reactions with PhI═NTs and related

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(1) For a review on Pd-catalyzed amination of aryl halides, see: Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131−209. For recent examples of Cu-catalyzed amination reactions, see: (a) Zhu, D.; Wang, R.; Mao, J.; Xu, L.; Wu, F.; Wan, B. *J. Mol. Catal. A* **2006**, *256*, 256−260. (b) Yeh, V. S. C.; Wiedeman, P. E. *Tetrahedron Lett.* **2006**, *47*, 6011−6016. (c) Shafir, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 8742−8743.

(2) For a relevant review, see: Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439−2463 and references therein.

(3) For a recent review, see: Espino, C. G.; Du Bois, J. *Modern Rhodium-Catalyzed Organic Reactions*; Wiley: New York, 2005; pp 379−416. For selected examples, see: (a) Fructos, M. R.; Trofimenko, S.; Diaz-Requejo, M. M.; Perez, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 11784−11791. (b) Liang, C.; Robert-Peillard, F.; Fruit, C.; Muller, P.; Dodd, R. H.; Dauban, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 4641−4644. (c) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378−15379. (d) He, L.; Chan, P. W. H.; Tsui, W.-M.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2004**, *6*, 2405−2408. (e) Espino, C. G.; Wehn, P. W.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935−6936. (f) Espino, C. G.; Du Bois, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 598−600. (g) Yu, X.-Q.; Huang, J.-S.; Zhou, X.-G.; Che, C.-M. *Org. Lett.* **2000**, *2*, 2233−2236. (h) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728−6729.

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(5) (a) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 11483−11498. (b) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523−2526. (c) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134−7135. (d) Giri, R.; Chen, X.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 2112−2115.

(6) (a) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972−4973. (b) Kalyani, D.; Deprez, N. R.; Desai, L.V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330−7331. (c) Daugulis, O.; Zaitsev, V. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4046−4048.

(7) For mechanistic investigations into these transformations, see: (a) Dick, A. R.; Kampf, J. W.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 12790−12791. (b) Dick, A. R.; Kampf, J. W.; Sanford, M. S. *Organometallics* **2005**, *24*, 482−485.

(8) For recent examples of the catalytic conversion of C−H bonds to C−N bonds, see the following. (a) Cu catalysis: Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790−6791. (b) Cu catalysis: Uemura, T.; Imoto, S.; Chatani, N. *Chem. Lett.* **2006**, *35*, 842−843. (c) $Pd^{II/0}$ catalysis: Tsang, W. C. P.; Zheng, N.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 14560−14561.

(9) While our work was in progress, a related Pd-catalyzed, directed C−H bond amination reaction using $K_2S_2O_8/NRH_2$ was reported: Thu, H.-Y.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048−9049.

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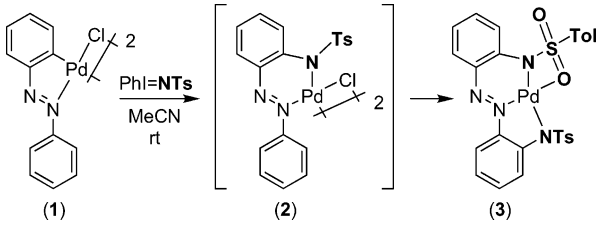
Publication on Web 02/16/2007

Scheme 1. Double Amination of Palladacycle 1



oxidants.[10] Investigations of the scope of these reactions as well as mechanistic insights into the key "NTs" insertion step are described below.

Results and Discussion

Our initial studies focused on demonstrating the feasibility of the stoichiometric oxidative amination of palladacycles (complexes that are typically formed via directed C−H activation reactions). We selected PhI=NTs[11] as the amination reagent on the basis of (i) our previous success using hypervalent iodine compounds in Pd-catalyzed C−H functionalization reactions and (ii) literature precedent for the insertion of "O" into Pd−C bonds using the analogous iodine(III) oxidant ArI=O.[12] The chloride-bridged azobenzene dimer **1** was chosen as the initial substrate, because its reactivity with ArI=O had been explored previously.[12]

When **1** was treated with 2 equiv of PhI=NTs (1 equiv per Pd) in MeCN at room temperature, the initially bright orange heterogeneous mixture gradually became deep purple over the course of 12 h. ^{1}H NMR analysis of the crude reaction showed significant quantities of unreacted starting material along with a complex mixture of products, and the major product (**3**) was isolated from this mixture via preparative TLC. Interestingly, this dark purple solid was not the expected monoaminated palladacycle **2**. Instead, ^{1}H NMR spectroscopy revealed the presence of resonances associated with two inequivalent NTs groups. As shown in Scheme 1, these data suggested that 2 equiv of the iodine(III) reagent was required to form the observed product (**3**). Indeed, when the stoichiometry of the reaction was adjusted (such that 2 equiv of PhI=NTs were added per 1 equiv of Pd), the ^{1}H NMR yield of **3** nearly doubled (from 19% to 32%). When the amount of PhI=NTs was further increased to 4−5 equiv per [Pd], the starting material was almost completely consumed, and product **3** was obtained in 50% yield by ^{1}H NMR spectroscopy (4 equiv) and 18% isolated yield (5 equiv).[13]

Crystals of **3** suitable for X-ray crystallographic analysis were obtained by slow diffusion of pentane into a chlorobenzene solution of **3** at room temperature, and a labeled view of the structure is shown in Figure 1. As anticipated on the basis of the ^{1}H NMR spectral data, **3** contains a Pd^{II} center ligated by two different NTs ligands and one nitrogen of the azobenzene. In the solid state, the fourth coordination site of this square-planar complex is occupied by a sulfonyl oxygen atom.[14] As summarized in Scheme 2, we believe that **3** is formed by (i) initial "NTs" insertion into the Pd−C bond, (ii) decoordination, σ-bond rotation, and recoordination to the other nitrogen atom of the azo linkage to form a more favorable five-membered palladacycle, (iii) ortho C−H activation of the adjacent ring, and (iv) a second "NTs" insertion event to afford the final product.

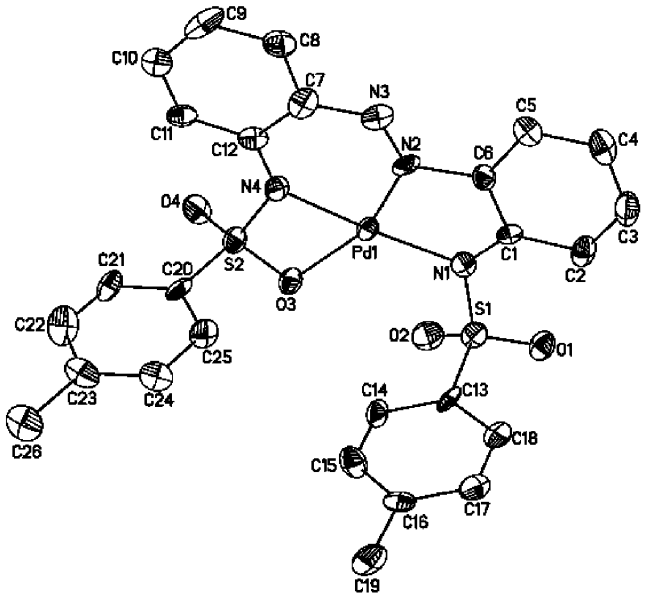
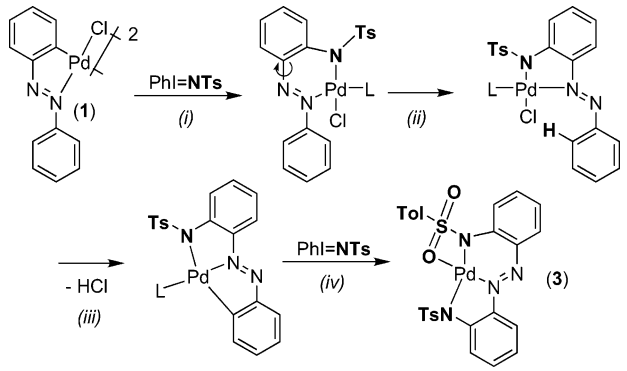


Figure 1. ORTEP diagram for complex **3**. H atoms are not shown. Selected bond distances (Å): Pd−N1 = 2.020, Pd−N2 = 1.931, Pd−N4 = 1.968, Pd−O3 = 2.279. Selected bond angles (deg): N2−Pd−N1 = 82.7, N2−Pd−N4 = 93.1, N4−Pd−N1 = 175.3, N1−Pd−O3 = 118.5, N4−Pd−O3 = 65.8, N2−Pd−O3 = 158.5.

Scheme 2. Proposed Mechanism of Formation of Product 3



We next turned our attention to palladacycles of benzo[*h*]-quinoline, which do not offer the possibility for a second ortho C−H activation event. A series of cyclometalated benzo[*h*]-quinoline complexes, including the acetate-bridged dimer **4**, the chloride-bridged dimer **5**, and the in situ generated monomeric pyridine complexes **6** and **7** (Figure 2), were treated with 1.3 equiv of PhI=NTs in MeCN. The crude reactions were then evaporated to dryness, treated with $CDCl_3$ containing 25% C_5D_5N (in order to convert any halide- and/or acetate-bridged Pd^{II} products to more readily detectable monomers), and assayed

(10) Mahy, J. P.; Battioni, P.; Bedi, G.; Mansuy, D.; Fisher, J.; Weiss, R.; Morgenstern-Badarau, I. *Inorg. Chem.* **1988**, *27*, 353−359.

(11) These iminoiodinane reagents are commonly used in the metal-catalyzed aziridination of olefins. In addition, analogous reagents are believed to form in situ in the amination reactions discussed in ref 3. For a relevant review, see: Halfen, J. A. *Curr. Org. Chem.* **2005**, *9*, 657−669.

(12) Bhawmick, R.; Biswas, H.; Bandyopadhyay, P. *J. Organomet. Chem.* **1995**, *498*, 81−83.

(13) Purification of this compound required both a basic extractive workup and multiple chromatographic separations. Complex **3** appears to be unstable under both of these conditions, resulting in low isolated yields.

(14) In solution, coordinated water is observed by ^{1}H NMR spectroscopy as a broad singlet, whose chemical shift varies significantly with concentration. Addition of ~2 equiv of pyridine to an NMR sample displaying one such singlet resulted in new peaks for both free and metal-bound pyridine. A new signal also appeared at ~1.6 ppm, consistent with free H_2O liberated from the metal center. See the Supporting Information for full details.

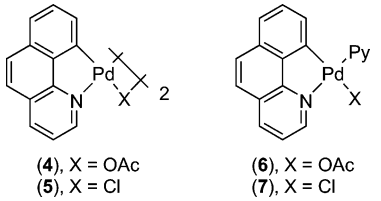
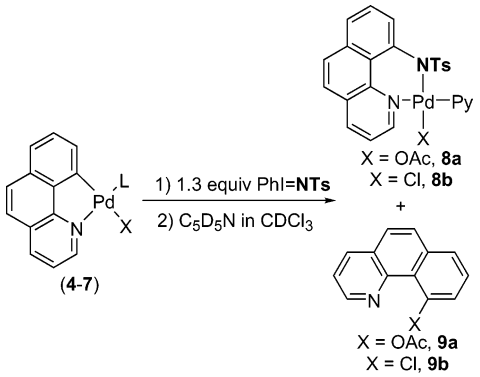


Figure 2. Benzo[*h*]quinoline complexes examined in amination reactions.

Table 1. Major Products Observed in Reactions of 4−7 with PhI═NTs



entry	complex	product (yield, %)	product (yield, %)
1	4[a]	**8a** (31)	**9a** (<2)
2	5[a]	**8b** (9)	**9b** (18)
3	6[a]	**8a** (16)	**9a** (5)
4	7	**8b** (51)	**9b** (<2)

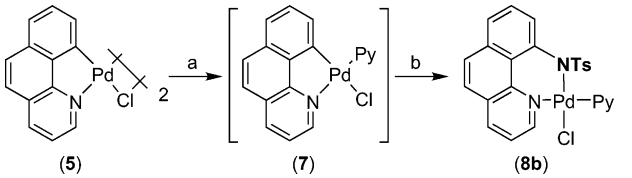
[a] Significant quantities of additional unidentified inorganic and organic side products were observed.

by ^{1}H NMR spectroscopy. With the Pd^{II} starting materials **4**−**6**, this sequence afforded a complex and largely inseparable mixture of inorganic and organic compounds. However, in all three cases, significant quantities (9−31%) of the desired "NTs" insertion product **8a** or **8b** were formed. These Pd^{II} complexes were identified in the crude ^{1}H NMR spectra, by comparison to independently synthesized samples of **8a**/**8b**. Interestingly, the organic products **9a**/**9b**, which result from C−X coupling (X = Cl, OAc, depending on the counterion associated with the starting Pd complex), could also be identified in some of these reactions.[4d] As summarized in Table 1, these chlorinated and/or acetoxylated organic products were formed in yields of up to 18%, and the formation of substantial quantities of these organic side products was inversely correlated to the yield of the desired "NTs" insertion product.

In contrast to the reactions of **4**−**6**, the monomeric chloride complex **7** reacted with PhI═NTs to produce a single major inorganic product (**8b**) in 51% yield (based on ^{1}H NMR spectroscopy of the crude reaction mixture), and complex **8b** was isolated as a yellow solid in 42% yield. The isolated yield could be improved to 78% when the reaction was conducted in THF (Scheme 3). Notably, the C−Cl bond-forming reductive elimination product **9b** was not observed in this transformation.

The structure of **8b** was confirmed by ^{1}H NMR spectroscopy, which clearly showed the incorporation of a single NTs moiety into the starting complex. In addition, crystals suitable for X-ray analysis were obtained by slow diffusion of ether into a chlorobenzene solution of **8b**, and the solid-state structure of **8b** is shown in Figure 3. In this square-planar palladium(II) complex, the chloride ligand resides trans to the new NTs moiety and the pyridine trans to the nitrogen atom of the benzoquinoline ligand. The Pd−N and Pd−Cl bond lengths are comparable to

Scheme 3. Amination of the Benzo[*h*]quinoline Palladacycle 7[a]



[a] Legend: (a) 8.0 equiv of pyridine (Py), THF, room temperature; (b) 1.3 equiv of PhI═NTs, THF, room temperature, 78% yield.

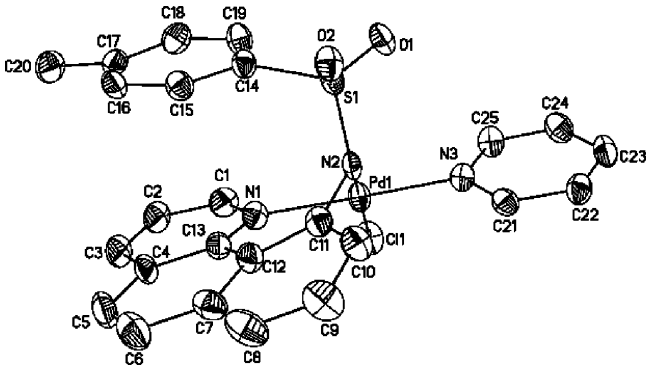
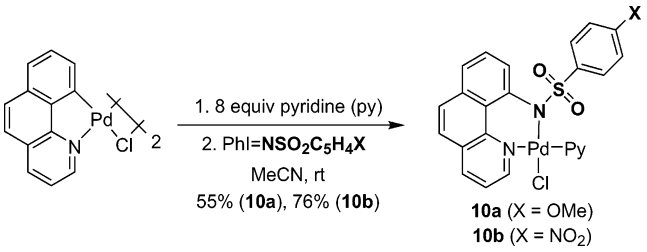


Figure 3. ORTEP diagram for complex **8b**. H atoms are not shown. Selected bond distances (Å): Pd−N1 = 2.050, Pd−N2 = 1.997, Pd−N3 = 2.026, Pd−Cl = 2.3277. Selected bond angles (deg): N2−Pd−N1 = 86.84, N2−Pd−N3 = 89.14, N3−Pd−N1 = 175.97, N1−Pd−Cl = 93.67, N3−Pd−Cl = 90.30, N2−Pd−Cl = 175.04.

Scheme 4. Amination of Palladacycle 7 with Electronically Diverse Oxidants



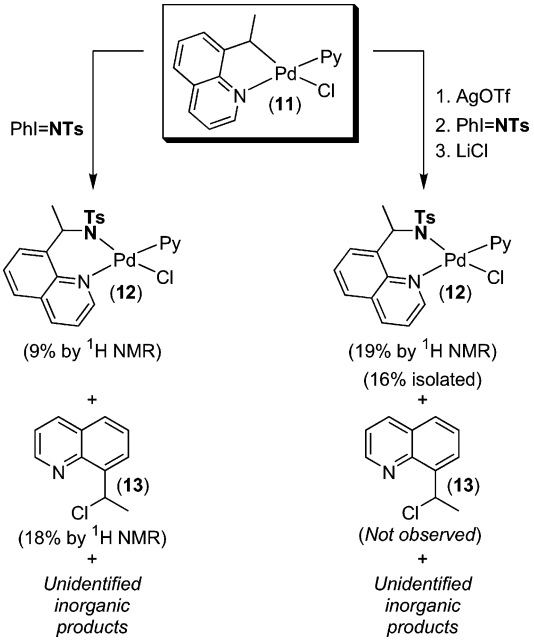
those found in related complexes,[15] and, as expected, the bond to the anionic nitrogen is the shorter of the two Pd−N bonds (1.997 versus 2.050 Å). The most remarkable feature of this structure is a face-to-face interaction between the aryl ring of the Ts group and the benzoquinoline ligand. Interestingly, this interaction twists the rigid benzoquinoline significantly out of planarity ($\tau_{N1-C13-C12-C11}$ = 14.9(7)°).

The reactions of the in situ generated palladacycle **7** with hypervalent iodide oxidants derived from electronically diverse benzenesulfonamides were also explored. As summarized in Scheme 4, these transformations proceeded in modest to good yields with oxidants containing both electron-donating and electron-withdrawing substituents on the aryl group of the sulfonamide. When the rates of sulfonamide insertion into isolated monomer **7**[16] were measured under identical reaction conditions, the formation of **8b** was found to proceed to completion within 30 min, while the reactions to form **10a** and **10b** required 2 and 2.5 h, respectively, to reach complete

(15) (a) Bugarčić, Z., D.; Liehr, G.; van Eldik, R. *Dalton Trans.* **2002**, 951−956. (b) Peters, J. C.; Harkins, S. B.; Brown, S. D.; Day, M. W. *Inorg. Chem.* **2001**, *40*, 5083−5091.

(16) Cockburn, B. N.; Howe, D. V.; Keating, B. F.; Johnson, B. F. G.; Lewis, J. *J. Chem. Soc., Dalton Trans.* **1973**, 404−410.

Scheme 5. Amination of 8-Ethylquinoline Palladacycle 11



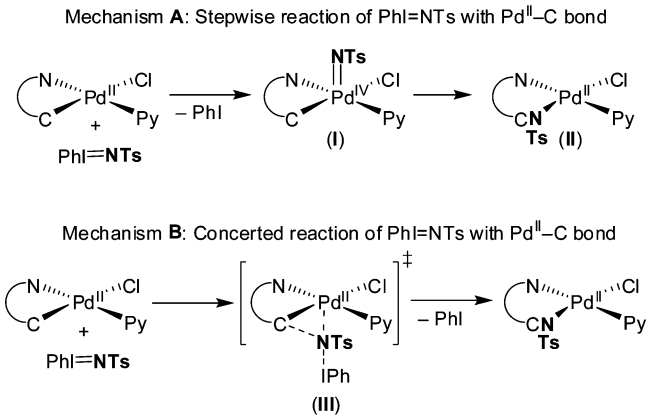
conversion. However, it is difficult to draw definitive mechanistic conclusions from these kinetic data, due to the dramatically varied solubilities of these iodine(III) aminating reagents as well as their susceptibility toward hydrolysis under the reaction conditions.

Analogous NTs insertion reactions were also examined with palladacycles containing sp^3 Pd−C bonds. For example, the 8-ethylquinoline complex **11** reacted with 1.3 equiv of PhI═NTs to afford **12** in 9% yield (as determined by ^{1}H NMR spectroscopy) along with a number of unidentified Pd-containing species (Scheme 5). Interestingly, the C−Cl bond-forming reductive elimination product **13** was identified as the major organic byproduct of this reaction. Removal of the chloride ligand from **11** with AgOTf prior to addition of the oxidant eliminated this competing transformation and increased the ^{1}H NMR yield of aminated palladacycle **12** to 19%.[17]

There are at least two possible mechanisms for the "NSO_2-Ar" insertion reactions: a stepwise process (Scheme 6, mechanism **A**) and a concerted pathway (Scheme 6, mechanism **B**). The stepwise mechanism would involve (i) initial nucleophilic attack of the Pd(II) center on PhI═NTs, (ii) loss of PhI to form a discrete Pd(IV) imido intermediate (**I**), and (iii) collapse of this intermediate to afford the insertion product. Alternatively, the concerted process would proceed by a transition state involving a three-centered interaction between the Pd(II) center, the bound carbon, and the "NTs" group (**III** in Scheme 6).

While these two mechanisms are difficult to definitively distinguish from one another, we currently favor mechanism **A** for several reasons. First, the closely related reaction of ArI═O with palladacycles has been proposed to proceed via a stepwise mechanism similar to **A**.[18] In addition, Pd^{IV}−oxo intermediates analogous to **I** have been proposed as intermediates in the reactions of Pd−C bonds with both inorganic and organic peroxides.[19] Finally, the observation of organic side products **9a**, **9b**, and **13** resulting from C−X coupling (X = OAc, Cl) is also consistent with a mechanism involving Pd^{IV} intermediates. Both C−OAc[7a] and C−Cl[5a,b,20] bond-forming reductive elimination have been shown to be facile from Pd^{IV} centers; in contrast, analogous reactions at Pd^{II} complexes are generally kinetically slow and/or thermodynamically unfavorable.[21,22] As such, we hypothesize that **9b** and **13** are generated by a C−Cl coupling reaction from intermediate **I** that is competitive with "NTs" insertion into the Pd−C bond.

Scheme 6. Possible Mechanisms for Insertion of "NTs" into the Pd−C Bond



With optimal conditions for the NTs insertion reaction in hand, we next sought to liberate the newly aminated organic ligands from the Pd center via protonoloysis of the Pd−N bond. A series of acidic reaction conditions were examined to achieve this goal, and the results are reported in Table 2. Interestingly, no C−N bond cleavage was observed in neat AcOH at room temperature or at 100 °C (Table 2, entries 1 and 2). In contrast, neat trifluoroacetic acid afforded appreciable (∼15%) conversion to product **8b′** at room temperature (entry 3). The addition of 5 equiv of HCl resulted in quantitative cleavage of the Pd−N bond to afford **8b′** (entry 5), and analogous conditions were also effective for the release of **3′** from complex **3** (entry 6) and of **12′** from complex **12** (entry 7). Notably, with the success of these protonolysis reactions, we have established the feasibility of the three elementary steps—(i) cyclopalladation, (ii) oxidative amination, and finally (iii) protonolysis—required for Pd-catalyzed directed oxidative C−H amination reactions.

In conclusion, this report has described a new mild reaction for the stoichiometric conversion of C−H bonds into amines via palladacyclic intermediates. This transformation is proposed to proceed via a stepwise mechanism involving a Pd^{IV}−imido intermediate. Efforts to achieve catalytic C−N bond formation via this pathway are ongoing in our laboratories. Notably, while this work was in progress, Che and co-workers reported a related

(17) Significant quantities of $(py)_2PdCl_2$ were also identified by ^{1}H NMR in both the crude reaction mixture and partially purified samples (Rajput, J.; Moss, J. R.; Hutton, A. T.; Hendricks, D. T.; Arendse, C. E.; Imrie, C. *J. Organomet. Chem.* **2004**, *689*, 1553−1568). The origin of its formation is unclear at this time, but we believe it contributes significantly to the low yield.

(18) (a) Kamaraj, K.; Bandyopadhyay, D. *Organometallics* **1999**, *18*, 438−446. (b) Kamaraj, K.; Bandyopadhyay, D. *J. Am. Chem. Soc.* **1997**, *119*, 8099−8100.

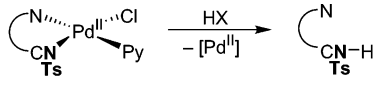
(19) (a) Valk, J.-M.; Boersma, J.; van Koten, G. *Organometallics* **1996**, *15*, 4366−4372. (b) Alsters, P. L.; Teunissen, H. T.; Boersma, J.; Spek, A. L.; van Koten, G. *Organometallics* **1993**, *12*, 4691−4696.

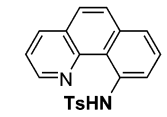
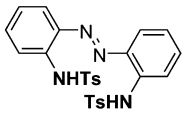
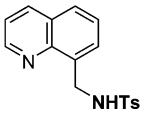
(20) (a) Alsters, P. L.; Engel, P. F.; Hogerheide, M. P.; Copijn, M.; Spek, A. L.; van Koten, G. *Organometallics* **1993**, *12*, 1831−1844. (b) Lagunas, M.; Gossage, R. A.; Spek, A. L.; van Koten, G. *Organometallics* **1998**, *17*, 731−741. (c) Fahey, D. R. *J. Organomet. Chem.* **1971**, *27*, 283−292.

(21) For C−Cl bond-forming reductive elimination from Pd^{II}, see: (a) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 1232−1233. (b) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 13944−13945.

(22) For studies of the electronic requirements of C−O bond-forming reductive elimination from Pd^{II}, see: (a) Widenhoefer, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 6504−6511. (b) Widenhoefer, R. A.; Zhong, H. A.

Table 2. Acid Cleavage To Release the Aminated Ligands



Entry	Product	Conditions	% Conversion[a]
1		Neat AcOH, 25 °C	n/r
2		Neat AcOH, 100 °C	n/r
3		Neat CF_3CO_2H, 25 °C	15%
4		1 equiv HCl, 25 °C	80%
5		5 equiv HCl, 25 °C	100%
6		10 equiv HCl, 25 °C	100%
7		5 equiv HCl, 25 °C	42%[b]

[a] Percent conversion determined by ^{1}H NMR spectroscopy. [b] Isolated yield.

Pd-catalyzed directed oxidative C−H amination reaction that uses $K_2S_2O_8$ as a stoichiometric oxidant.[9] The further development of this methodology will provide an attractive complement to existing transformations such as the catalytic amination of aryl halides and nitrene insertion into activated C−H bonds.

Experimental Section

Instrumentation. NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^{1}H; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^{1}H; 100.57 MHz for ^{13}C) spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet of doublets (td), triplet of triplets (tt), triplet (t), doublet of quartets (dq), quartet (q), multiplet (m), and broad resonance (br). High-resolution mass spectral data were obtained on a Micromass AutoSpec Ultima magnetic sector mass spectrometer.

Materials and Methods. Benzo[*h*]quinoline was purchased from TCI America or Aldrich and used as received. Azobenzene was purchased from Acros and recrystallized from ethanol prior to use. PhI=NTs[23] and the OMe- and NO_2-substituted variants[24] were prepared according to literature procedures from commercially available sulfonamides. Cyclopalladated complexes of azobenzene,[25] benzo[*h*]quinoline,[26,27] and 8-ethylquinoline[28] were prepared by directed C−H activation reactions using literature procedures. $PdCl_2$ and Na_2PdCl_4 were purchased from Pressure Chemical and used as received. Solvents were purchased from Fisher Scientific and used without further purification. All reactions were carried out under an ambient atmosphere. Flash chromatography was performed on Silicycle Silica P flash silica gel (40−63 μm particle size, 60 Å pore diameter, 50 m^2/g surface area), and thin layer chromatography was performed on EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F_{254}. Preparative TLC was performed on Whatman PK6F silica gel plates (60 Å, 500 μm layer thickness).

Product 3. Complex **1** (150.0 mg, 0.23 mmol, 1 equiv) was suspended in MeCN (15 mL), and PhI=NTs (700.0 mg, 1.9 mmol, 4 equiv relative to [Pd]) was added. The resulting mixture was stirred at 25 °C for 12 h, during which time the color changed from bright orange to dark purple. Additional oxidant (173.0 mg, 0.46 mmol, 1 equiv) was added, and the mixture was stirred for an additional 24 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 0.5 M aqueous NaOH (to remove free H_2NTs) until the aqueous layer remained colorless. The organic layer was dried with $MgSO_4$, and the solvent was removed under vacuum to afford a dark purple solid. The crude product was purified by chromatography on silica gel (gradient column from 100% toluene to 10% MeCN in toluene; $R_f = 0.13$ in 10% MeCN in toluene). The product was further purified by preparative TLC (with 10% MeCN in toluene as eluent), which provided complex **3** (51.2 mg, 18% yield) as a purple solid that was ∼90% pure by ^{1}H NMR spectroscopy. Pure material was obtained from a second purification by preparative TLC (with 10% MeCN in toluene as eluent), in which only the bottom of the purple band with $R_f = 0.13$ was isolated. The low isolated yields of complex **3** appear to be due to decomposition of this product during the basic extraction and during chromatographic purification on silica gel. ^{1}H NMR ($CDCl_3$): δ 7.94 (1H, dd, J = 8.5, 1.0 Hz), 7.88−7.85 (3H, multiple peaks), 7.75 (1H, dd, J = 8.0, 1.5 Hz), 7.68 (2H, d, J = 8.5 Hz), 7.64 (1H, dd, J = 8.5, 1.5 Hz), 7.48 (1H, ddd, J = 8.5, 7.5 Hz, 2.0 Hz), 7.27 (1H, td, J = 7.5, 1.5 Hz), 7.23 (2H, d, J = 8.0 Hz), 7.21 (1H, ddd, J = 8.0, 7.0, 1.0 Hz), 7.06 (2H, d, J = 8.0 Hz), 6.77 (1H, ddd, J = 8.0, 7.0, 1.5 Hz), 2.35 (3H, s), 2.27 (3H, s). ^{13}C NMR (DMSO-d_6): δ 150.05, 148.10, 147.78, 141.77, 140.05, 139.85, 134.59, 134.18, 132.96, 129.15, 128.84, 128.50, 128.21, 127.36, 126.18, 126.00, 124.87, 123.01, 122.39, 118.12, 20.84, 20.82. HRMS-electrospray (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{22}N_4O_4S_2PdNa$, 647.0015; found, 647.0026.

Note: the ^{1}H NMR signals associated with the Ts groups shifted significantly, depending on concentration. In addition, the ^{1}H NMR spectra of **3** often contained broad singlets, with chemical shifts that varied dramatically with concentration, which are due to coordinated/associated water molecules. See the Supporting Information for further discussion.

Product 8a. Complex **8b** (33.1 mg, 0.06 mmol, 1 equiv) was dissolved in 5 mL of CH_2Cl_2 in a 20 mL scintillation vial equipped with a Teflon stirbar. Silver acetate was added, and the mixture was stirred for 30 min. AgCl was removed by filtration through Celite, and the Celite pad was washed with CH_2Cl_2 (3 × 5 mL). The yellow solution was concentrated, and a solid was precipitated with Et_2O. The yellow solid was collected on a fritted filter (21.1 mg, 61% yield). ^{1}H NMR ($CDCl_3$): δ 8.96 (2H, dt, J = 5.1, 1.6 Hz), 8.68 (1H, dd, J = 5.5, 1.6 Hz), 8.04 (1H, dd, J = 8.0 , 1.5 Hz), 7.88−7.72 (5H, multiple peaks), 7.47−7.41 (3H, multiple peaks), 7.31 (1H, dd, J = 7.9, 5.5 Hz), 7.14 (2H, d, J = 8.1 Hz), 6.48 (2H, d, J = 7.9 Hz), 1.99 (3H, s), 1.79 (3H, s). ^{13}C NMR ($CDCl_3$): δ 177.54, 151.78, 151.30, 141.92, 140.44, 139.57, 139.13, 138.49, 137.96, 135.97, 130.28, 130.06, 129.11, 127.79, 127.39, 126.71, 126.36, 125.61, 124.91, 124.02, 121.69, 23.86, 21.06. HRMS-electrospray (*m/z*): calcd for $[C_{27}H_{23}N_3O_4PdS - C_5H_5N + Na^+]$, 534.9920; found, 534.9928.

Products 8b, 10a, and 10b (General Procedure). Complex **5** (51.2 mg, 0.08 mmol, 1 equiv) was suspended in MeCN or THF (8 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. Pyridine (50 μL, 0.66 mmol, 8 equiv) was added to convert **5** to the corresponding monomer **7**, and the reaction mixture was stirred until all of the solids dissolved. The iminoiodinane reagent (0.21 mmol, 2.6 equiv, 1.3 equiv per [Pd]) was added, and the reaction mixture was stirred at 25 °C for between 4 and 18 h. The solvent

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was removed under vacuum, and the product was purified by recrystallization. The reaction times and purification conditions varied between substrates and are reported in detail below.

Product 8b. Procedure 1 (in MeCN). Reaction time: 4 h. The product was recrystallized twice from CH_2Cl_2/Et_2O. Each crop of crystals was collected on a fritted filter and washed with ether (3 × 25 mL). Product **8b** was obtained as a pale yellow solid (48.2 mg, 42% yield).

Procedure 2 (in THF). Reaction time: overnight. The product was recrystallized from CH_2Cl_2/hexanes, collected on a fritted filter, and washed with a 60/40 mixture of hexanes and isopropyl alcohol (3 × 20 mL). Product **8b** was obtained as a pale yellow solid (70.9 mg, 78% yield). ^{1}H NMR ($CDCl_3$): δ 9.16 (1H, dd, J = 5.5, 1.6 Hz), 9.00 (2H, dt, J = 5.1, 1.6 Hz), 8.05 (1H, dd, J = 8.0, 1.6 Hz), 7.88−7.73 (5H, multiple peaks), 7.47−7.42 (3H, multiple peaks), 7.33 (1H, dd, J = 7.9, 5.5 Hz), 7.05 (2H, dt, J = 8.5, 2.0 Hz), 6.48 (2H, dd, J = 8.4, 0.4 Hz), 1.99 (3H, s). ^{13}C NMR ($CDCl_3$): δ 154.24, 152.59, 141.96, 140.61, 139.33, 138.93, 138.58, 138.16, 136.01, 130.39, 129.86, 128.39, 127.86, 127.64, 126.68, 126.22, 125.60, 125.04, 124.15, 121.96, 21.08. Anal. Calcd for $C_{25}H_{20}ClN_3O_2PdS$: C, 52.83; H, 3.55; N, 7.39. Found: C, 52.56; H, 3.26; N, 7.10.

Product 10a. Reaction time: overnight. Note: 4 equiv of oxidant per [Pd] was used. The product was recrystallized three times from CH_2Cl_2/Et_2O. Notably, the first addition of Et_2O to a CH_2Cl_2 solution of **10a** resulted in the precipitation of an unidentified black solid. The yellow solution was decanted away from this solid, and further addition of ether led to crystallization of the desired product **10a**. None of this black solid was observed in subsequent recrystallizations. Each crop of crystals was collected on a fritted filter and washed with ether (3 × 25 mL). Product **10a** was obtained as a light yellow solid (51.4 mg, 55% yield). ^{1}H NMR ($CDCl_3$): δ 9.21 (1H, dd, J = 5.5, 1.6 Hz), 9.00 (2H, dt, J = 5.2, 1.6 Hz), 8.08 (1H, dd, J = 7.9, 1.5 Hz), 7.88−7.72 (5H, multiple peaks), 7.47−7.43 (3H, multiple peaks), 7.35 (1H, dd, J = 7.9, 5.5 Hz), 7.09 (2H, dt, J = 8.9, 2.9 Hz), 6.17 (2H, dt, J = 8.9, 2.9 Hz), 3.56 (3H, s). ^{13}C NMR ($CDCl_3$): δ 160.89, 154.25, 152.57, 141.97, 138.97, 138.58, 138.41, 136.00, 134.30, 130.41, 129.88, 128.41, 128.07, 127.67, 126.77, 125.60, 125.03, 124.25, 122.09, 112.44, 55.37. Anal. Calcd for $C_{25}H_{20}ClN_3O_3PdS$: C, 51.38; H, 3.45; N, 7.19. Found: C, 51.54; H, 3.46; N, 7.08.

Product 10b. Reaction time: 8 h. The product was recrystallized twice from CH_2Cl_2/Et_2O. Each crop of crystals was collected on a fritted filter and washed with ether (3 × 25 mL). Product **10b** was obtained as a bright yellow solid (72.6 mg, 76% yield). ^{1}H NMR ($CDCl_3$): δ 9.20 (1H, dd, J = 5.4, 1.6 Hz), 8.96 (2H, dt, J = 4.9, 1.4 Hz), 8.07 (1H, dd, J = 8.0, 1.5 Hz), 7.93−7.79 (5H, multiple peaks), 7.53−7.44 (5H, multiple peaks), 7.39 (1H, dd, J = 8.0, 5.7 Hz), 7.32 (2H, dt, J = 8.7, 2.3 Hz). ^{13}C NMR ($CDCl_3$): δ 154.15, 152.52, 148.30, 147.29, 141.63, 138.89, 137.85, 136.15, 130.69, 130.09, 128.33, 127.14, 126.95, 126.86, 126.25, 125.27, 124.47, 122.50, 122.35. Note: only 19 (rather than the expected 20) carbon resonances were observed for **10b**, presumably due to overlapping peaks. Anal. Calcd for $C_{24}H_{17}ClN_4O_4PdS$: C, 48.09; H, 2.86; N, 9.35. Found: C, 48.27; H, 2.91; N, 9.38.

Product 12. Complex **11** (400 mg, 1.1 mmol, 1 equiv) was dissolved in MeCN (80 mL) in a 100 mL round-bottom flask equipped with a Teflon stirbar. AgOTf (545 mg, 2.1 mmol, 2 equiv) was added, and the reaction mixture was stirred for 30 min. The resulting suspension was filtered through Celite to remove AgCl, and the Celite pad was washed with MeCN (80 mL). PhI═NTs (515 mg, 1.4 mmol, 1.3 equiv) was added, and the resulting suspension was stirred for 8 h at 25 °C. The reaction mixture was filtered through Celite, and LiCl (90 mg, 2.1 mmol, 1.7 equiv) was added to the resulting orange solution. The reaction mixture was stirred for 30 min, and then the solvent was removed under vacuum. The crude oil was dissolved in CH_2Cl_2 (50 mL), and the organic layer was washed with H_2O (3 × 100 mL) and brine (1 × 100 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated under vacuum. The product was recrystallized twice from CH_2Cl_2/Et_2O, and each crop was collected on a fritted filter and washed with Et_2O (3 × 50 mL). The resulting mixture contained complex **12** and a second Pd^{II} species [$(py)_2PdCl_2$] in a 1:1.5 ratio by ^{1}H NMR spectroscopy (calculated yield: 93 mg (16%)). Removal of py_2PdCl_2 was accomplished by two additional recrystallizations from THF/Et_2O. The isolated yield of pure **12** was very low (∼4%) as a result of these multiple recrystallizations; however, the crude yield of this reaction was determined by ^{1}H NMR spectroscopy to be 19%. ^{1}H NMR ($CDCl_3$): δ 9.61 (1H, dd, J = 5.4, 1.6 Hz), 9.16 (2H, dt, J = 4.9, 1.5 Hz), 8.02 (1H, dd, J = 8.2, 1.6 Hz), 7.82 (1H, tt, J = 7.8, 1.6 Hz), 7.63 (1H, dd, J = 7.2, 1.4 Hz), 7.54 (1H, dd, J = 8.1, 1.5 Hz), 7.46 (1H, dd, J = 7.2, 0.8 Hz), 7.42 (2H, ddd, 7.7, 5.1, 1.4 Hz), 7.28 (2H, dt, J = 8.7, 2.2 Hz), 7.23 (1H, dd, J = 8.1, 5.4 Hz), 6.36 (2H, d, J = 8.1 Hz), 4.39 (1H, q, J = 7.2 Hz), 2.42 (3H, d, J = 7.1 Hz), 1.96 (3H, s). ^{13}C NMR ($CDCl_3$): δ 157.2, 153.2 140.6, 140.2, 140.0, 139.9, 139.3, 138.4, 132.1, 129.7, 128.2, 127.2, 127.0, 126.3, 125.0, 120.6, 56.0, 28.8, 21.0. HRMS-electrospray (*m/z*): calcd for [$C_{23}H_{22}ClN_3O_2PdS - C_5H_5N + Na^+$], 488.9632; found, 488.9636.

Determination of ^{1}H NMR Yields for the Reactions of "NTs" Insertion Products with Acid. A 20 mL scintillation vial equipped with a Teflon stirbar was charged with the Pd complex (0.04 mmol). A mixture of MeCN (8 mL) and an appropriate amount of HCl (added as 1 M HCl in ether) was added, and the reaction mixture was stirred for 24 h. The resulting mixture was diluted with H_2O (3 mL), and the organic products were extracted into EtOAc (3 × 5 mL). The organic layers were combined, dried with $MgSO_4$, filtered, and evaporated to dryness. The resulting oils were analyzed by ^{1}H NMR spectroscopy in order to determine the percent conversion. Notably, the reactions with AcOH and TFA were carried out using the acid as the solvent.

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Supporting Information Available: Text, tables, figures and CIF files giving additional experimental details regarding the synthesis and characterization of inorganic and organic products as well as X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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