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General N−H Activation of Primary Alkylamines by a Late Transition-Metal Complex

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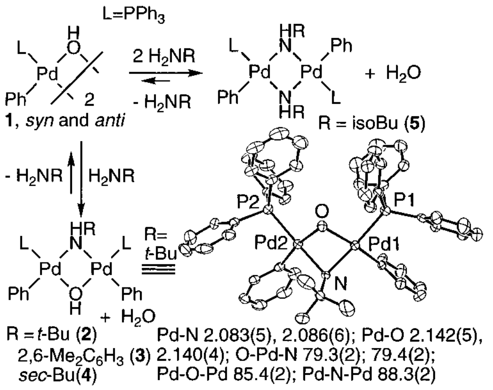
Catalytic chemistry of soluble transition-metal complexes with alkylamine substrates is not well developed.[1] A limited number of platinum-group alkylamido complexes have been isolated,[2−11] even fewer possess β-hydrogens,[6,8−15] and few examples have been formed directly from an amine.[6,16−20] We communicate the general and reversible activation of primary alkylamine N−H bonds by palladium complexes. These reactions allow for (1) isolation of palladium alkylamides that possess β-hydrogens, (2) the first X-ray structure of a low-valent late-metal alkylamide (3) information on the thermodynamic relationship between a bridging transition-metal hydroxide and its bridging amido analog, (4) strong evidence for an N−H activation mechanism that involves two amines along the pathway toward cleavage of a single amine N−H bond, and (5) an autocatalytic pathway requiring product amine in the reverse extrusion of amine by water.

Addition of excess primary amines to the triphenylphosphine-ligated palladium aryl hydroxide dimer **1**[21] led to complete consumption of **1**, elimination of water, and formation of palladium amides at either room temperature or slightly above room temperature, as outlined in Scheme 1. The direction of these reactions stands in marked contrast to reactions of main group systems and can be rationalized by hard/soft concepts. Alkali-metal amides, of course, react violently with water to form the corresponding hydroxides. The palladium mixed *tert*-butylamido hydroxo compound **2** was generated in 68% yield by ^{31}P NMR spectroscopy (P(*o*-tolyl)$_3$ internal standard) by heating **1** in neat *tert*-butylamine at 70 °C for 1 h and was isolated in 62% yield after recrystallization from THF/Et$_2$O. As one would then expect, anilines also reacted with **1**.[22] The mixed palladium 2,6-dimethylanilido hydroxo compound **3** was generated in 97% yield (^{31}P NMR spectroscopy) by mixing a THF solution of **1** with 10 equiv of 2,6-dimethylaniline at 70 °C for 1 h and was isolated in 58% yield.

Scheme 1



Pd-N 2.083(5), 2.086(6); Pd-O 2.142(5), 2.140(4); O-Pd-N 79.3(2); 79.4(2); Pd-O-Pd 85.4(2); Pd-N-Pd 88.3(2)

Remarkably, primary amines that would give palladium amides with β-hydrogens reacted cleanly with **1** to give product amido complexes as air stable, crystalline solids. In one case, a THF solution of **1** was reacted with 10 equiv of *sec*-butylamine at room temperature for 5 h to give a 96% yield of *sec*-butylamido complex **4** by ^{31}P NMR spectroscopy and 72% isolated yield. Similarly, the bis(isobutylamido)palladium complex **5** was generated as a single isomer in 87% yield and was isolated in 69% yield by stirring **1** in neat isobutylamine at room temperature for 15 min. Reaction of 1 equiv of isobutylamine gave 1/2 half equiv of product and 1/2 equiv of remaining starting material. It was not necessary to use neat amine to observe complete reaction of **1**, but high amine concentrations did reduce the formation of side products. The *syn* geometry of **2**, **3**, and **4** and the *anti* geometry of **5** shown in Scheme 1 were deduced from $^{31}P\{^1H\}$, ^1H, and $^{13}C\{^1H\}$ NMR spectral data, and were confirmed by X-ray diffraction in the case of compound **2**. Attempts to prepare analogous dialkylamido complexes by similar exchange reactions resulted in the decomposition of **1** and formation of PPh$_3$O.

An ORTEP diagram of **2** is provided in Scheme 1 with the distances (Å) and angles of one of the two halves of the molecule. The four-membered ring core is markedly puckered. The dihedral angle between the O−Pd1−N and O−Pd2−N planes is 123.09° or 57° away from planar. As discussed recently,[22] some bridging hydroxo and amido complexes are bent and others are planar. The two halves of the core appear chemically, though not crystallographically, equivalent, and the two Pd−O and Pd−N distances are indistinguishable. Despite the larger size of nitrogen and the presence of an N-bound alkyl group, the Pd−N distances are shorter than the Pd−O distances. As demonstrated below, the shorter distance is not a result of a stronger Pd−N bond.[23]

The formation of palladium amides **2**−**5** from **1** was reversible. Addition of an excess of water to a THF solution of **2**−**5** resulted in the formation of **1** and the corresponding primary amine. Upon standing for up to 2 days, $^{31}P\{^1H\}$ NMR

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[12] A few *N*-alkylarylamido complexes possess β-hydrogens; see refs 13−15.

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[17] A few other examples have involved ammonia; see refs 18−20.

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spectroscopy showed the presence of only the amido complexes **2**−**5** and **1**. However, when solutions were allowed to stand for more than 4 days, the solutions turned from clear to brown, and the formation of triphenylphosphine oxide began to be observed.

The equilibrium in eq 1 was established in the presence of an amount of water that led to partial conversion of **1** to **4**.

$$\mathbf{1} + H_2N\text{-}sec\text{-}Bu \overset{K = 24}{\rightleftharpoons} \mathbf{4} + H_2O \qquad (1)$$

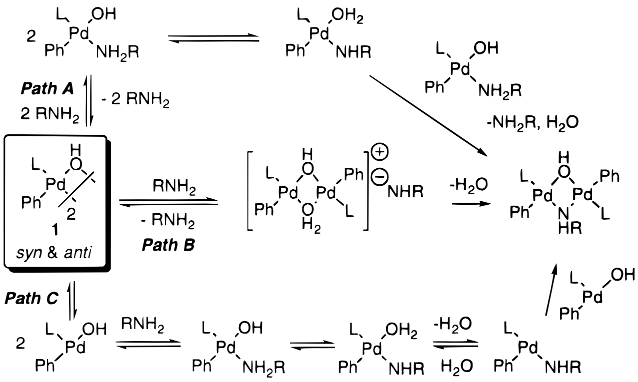
$$\Delta G = -1.9 \text{ kcal/mol}$$

After the reaction reached equilibrium, the concentrations of **1** and **4** were measured by ^{31}P NMR spectroscopy,[24] and an equilibrium constant of 24 ± 1 was obtained. Because equal numbers of molecules lie on either side of eq 1, $\Delta S°$ for this reaction is likely to be small and $\Delta G_{298}° \cong \Delta H°$.[25] From the resulting ΔH_{rxn} of 1.9 ± 0.1 kcal·mol^{-1}, the known 119 kcal·mol^{-1} O−H bond strength of water, and the N−H bond strength of *sec*-butylamine presumably similar to the known 100 kcal·mol^{-1} value for H_2NMe,[26] one can conclude that the bridging Pd−μ-OH−Pd interaction is stronger than the bridging Pd−μ-NHR−Pd interaction by roughly 17 kcal·mol^{-1}.[27] It is difficult to directly compare these results to those for terminal amido and hydroxo systems,[10] but the metal−hydroxo linkages are stronger than the metal−amido linkages in both cases.

The mechanism for N−H bond cleavage that follows from our kinetic data is, perhaps, counterintuitive but is consistent with fundamental information on ligand substitution and proton transfer. Kinetic data were obtained at 25 °C by monitoring the decay of the equilibrating isomers of the hydroxide dimer **1** by ^1H NMR spectroscopy in THF-d_8 solvent. Conditions of excess amine were employed, ensuring its constant concentration throughout the reaction and complete consumption of **1**. The reaction was first order in **1** and *second* order in [NH_2-*sec*-Bu], despite the single amide ligand in the product **4**.[28] Reaction rates were independent of [PPh_3] (k_{obs}= 1.1 × 10^{-4} s^{-1} for 0.130−0.390 M) and were qualitatively unaffected by added water.

Three possible mechanisms for the reaction of **1** with *sec*-butylamine are illustrated in Scheme 2. The second-order dependence of the reaction on [H_2N-*sec*-Bu] is consistent with only path A. Path A also predicts a first-order dependence on [**1**]. This first-order dependence results from reversible proton transfer and irreversible formation of **4** by reaction of two halves of the original **1**, one half existing as a mononuclear amido intermediate and the other half as a mononuclear hydroxo intermediate. Paths B and C would show a first-order dependence on [amine]. Other potential mechanisms involving phosphine dissociation are ruled out since they would be either inverse first order in [PPh_3] if dissociation were reversible, or zero order in [H_2N-*sec*-Bu] if dissociation were irreversible.

Scheme 2



In addition to the counterintuitive second-order dependence on [amine], proton transfer from the coordinated amine to form a coordinated water may also appear counterintuitive as a result of the 10 log unit difference between amine and water pK_a values in organic solvents.[29] However, this unfavorable equilibrium corresponds to only 14 kcal·mol^{-1} of the 22 kcal·mol^{-1} $\Delta G_{298}^{\ddagger}$ for the overall reaction. The reversible proton transfer also leads to an unusual prediction for k_H/k_D. The observed kinetic isotope effect for the formation of **4** from **1** will be dominated by an equilibrium isotope effect for the reversible proton transfer. The value of K_H/K_D for the proton transfer and therefore k_H/k_D for the overall reaction is likely to be less than 1 as a result of the higher υ_{OH} than υ_{NH}. We have, indeed, observed an inverse k_H/k_D of 0.7 ± 0.1 for the exchange of **1**−(μ-OD)$_2$ with D_2N-*sec*-Bu.

Finally, the reaction of amine with **1** by pathway A leads to an unusual prediction for the mechanism of the reaction of **4** with water to form **1**. Microscopic reversibility requires that the mechanism for the formation of **1** and amine from **4** and water be the reverse of path A and that the extra amine involved in the forward reaction also be involved in the reverse reaction. Thus, the reverse reaction should be first order in water and first order in product amine and should show autocatalytic behavior. Consistent with this prediction, addition of only water to **4** gave little reaction after several days, but addition of amine and water to **4** established the final equilibrium quantities of **1** and **4** after several hours.

In summary, we have revealed the first kinetic and thermodynamic data on a general N−H activation process of unactivated amines with late-transition-metal complexes, and these reactions produce palladium amides bearing β-hydrogens. We are continuing to study these processes as well as the reaction chemistry of the palladium amido products.

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Supporting Information Available: Spectroscopic and analytical data for **2**−**5**, crystallographic information for **2**, and representative kinetic data for reaction of **1** with *sec*-butylamine (25 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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[24] The concentrations of water and amine were calculated on the basis of their known starting concentrations and the stoichiometry of the reaction depicted in eq 1.

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[27] Although the geometries of **1** and **4** are different, the bond dissociation energy as defined by the homolysis of the metal−hydroxo or −amido bond incorporates the rearrangements that are necessary to give the most stable geometry of the radical formed by such bond homolysis. For a relevant discussion, see ref 34 of Hartwig, J. F.; Andersen, R. A; Bergman, R. G. *Organometallics* **1991**, *10*, 1875. The O−H bond energy is a weighted average of those in the two isomers of **1**.

[28] An amine concentration range of 89−950 mM was employed, and a plot of ln k_{obs} vs ln [H_2N-*sec*-Bu] gave a slope of 2.0 ± 0.1. Concentrations of 18 and 30 mM **1** were employed to ensure not only that first-order plots were linear but that k_{obs} values were independent of the initial concentration of **1.**

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