J|A|C|S COMMUNICATIONS

Published on Web 06/04/2010

N−H Activation of Amines and Ammonia by Ru via Metal−Ligand Cooperation

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Activation of the N−H bond of amines and ammonia by a transition-metal center may play a role in developing new catalytic processes based on these abundant compounds.[1,2] However, this process is not simple because amines tend to bind to vacant coordination sites of metal complexes via their lone electron pair, thereby making subsequent N−H bond cleavage difficult. Here we report a novel way to activate N−H bonds that involves metal−ligand cooperation by a pincer complex with no change in the formal oxidation state of the metal.

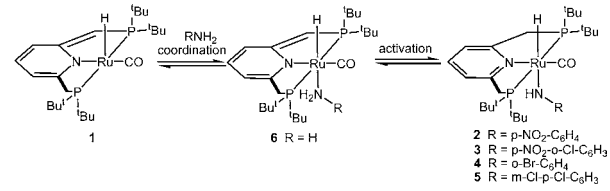
We recently discovered a new mode of metal−ligand cooperation involving aromatization/dearomatization of pyridine-based PNP and PNN pincer ligands. It has led to the activation of C−H and O−H bonds, including novel reactions involving alcohols and water.[3] We have now found that the dearomatized complex **1**[3e] is effective in the activation of N−H bonds.

Upon reaction of complex **1** with electron-poor anilines, N−H activation takes place with hydrogen transfer to the unsaturated ligand arm, leading to aromatization of the central pyridine ring (Scheme 1). Thus, adding 4-nitroaniline or 2-chloro-4-nitroaniline to a benzene solution of complex **1** led to the formation of complex **2** or **3**, respectively. Each of these new products exhibited only one peak in the $^{31}P\{^{1}H\}$ NMR spectrum, indicating equivalent phosphines, as opposed to the AB splitting pattern of the starting material. The ^{1}H NMR spectra also reflect a symmetrical environment around the metal center. Crystallographic characterization of **2** (Figure 1) revealed an octahedral geometry with an aromatic pyridine core and the amide ligand positioned trans to the hydride.

Reactions of the halide-substituted anilines 2-bromoaniline and 3,4-dichloroaniline resulted in equilibria involving the corresponding activated aromatic complexes **4** and **5**, which were observed by NMR spectroscopy, and the dearomatized starting material **1**, which was still present in solution in significant amounts even in the presence of a large excess (10 equiv) of the halogenated anilines. Thus, breaking of the N−H bond in our system is *reversible*, suggesting that the barrier for NH bond activation is low enough for the reaction to occur rapidly at room temperature and that product amines could be eliminated in potential catalytic cycles based on such systems.

We observed that the free reactants or the coordinated complex **6** are the preferred thermodynamic forms for more electron-rich amines, including aniline, isopropylamine, and ammonia. While a coordination complex was not directly observed by NMR spectroscopy for the first two substrates, in the case of excess NH_3 (∼1 atm in an NMR tube), the coordination complex **6** was clearly formed. The conversion to **6** was accompanied by a large (∼10 ppm) downfield shift of the metal hydride peak in the ^{1}H NMR spectrum and by a dramatic color change of the reaction mixture

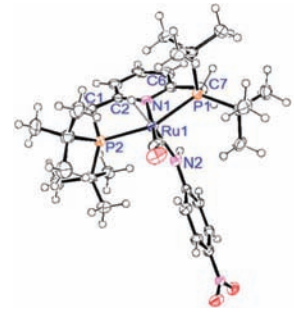
Scheme 1. General Scheme for Amine Coordination/Activation



from dark-green to light-yellow. The shift of the hydride for the cases of aniline and isopropylamine was only 2−3 ppm, depending on the concentration of the amine, and the color remained light-green. For all of these substrates, the $^{31}P\{^{1}H\}$ NMR spectra exhibited an unsymmetrical AB splitting pattern, indicating a dearomatized structure. Although the activated complex was unobserved for electron-rich amines, our evidence indicates that it is kinetically accessible (see below).

To probe the possibility of ammonia activation, we reacted complex **1** with an excess of ND_3 in C_6D_6 and selectively obtained the deuterated analogue **6-ND$_3$-a** 5 min after addition (Scheme 2). The reaction was highly stereospecific in that only one of the two CH_2 arm hydrogen signals in the ^{1}H NMR spectrum disappeared. No exchange of the vinylic hydrogen took place. Although we could not determine exactly which one of the two CH_2 hydrogens was exchanged,[4] such dramatic selectivity suggests that the activation process occurs on only one face of the ligand and in an intramolecular manner with one coordinated molecule of ND_3. The reverse reaction would affect only the (endo) hydrogen on the same face as the coordinated ND_3 moiety (Scheme 2). This result also suggests that activation of the NH bond in general, and perhaps the OH and CH bonds[3] of other substrates, would also occur in a *stereoselective* fashion.

After 16 h at room temperature, all of the arm hydrogens were replaced by deuterium and the metal hydride signal showed 70% deuterium incorporation [**6-ND$_3$-b**; see the Supporting Information (SI)]. Deuteration of the other sites may result from direct deprotonation by ammonia and/or the intermediacy of an aromatized Ru(0) isomer of **1**.[5]



Selected bond distances (Å):
Ru1-N2(2.187(4)) Ru1-N1(2.151(1));
Ru1-P1(2.348(1)); Ru1-P2(2.351(1));
C1-C2 (1.504(7)); C6-C7 (1.503(6))
Selected angles (deg)
P1-Ru1-P2 (158.7(1))
N1-Ru1-N2 (84.0(1))
N1-Ru1-P1 (80.3(1))

Figure 1. X-ray structure of complex **2**. Ellipsoids are shown at the 50% probability level.

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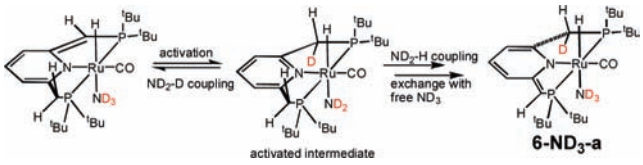
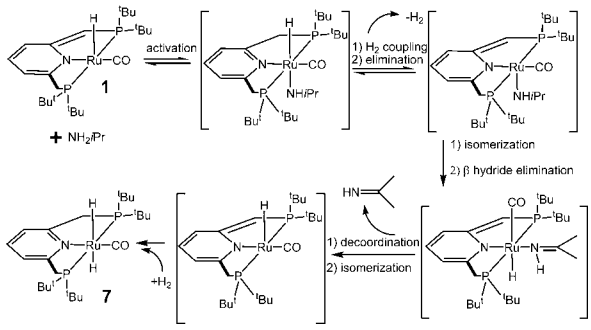
10.1021/ja103130u

Scheme 2. H/D Exchange in **6** with ND_3



Scheme 3. Possible Pathway for the Reaction of **1** and *i*PrNH$_2$



There are a number of reports on NH activation of NH_3[1] and amines[2] using transition metals. While most of these reports involve oxidative addition to mononuclear transtion-metal species, to date there has been no report on the reversible activation of NH_3 or amines via cooperation between a metal center and its ligand.

Additional indirect evidence for the activation of NH bonds was obtained by heating complex **1** with a 5-fold excess of isopropylamine at 80 °C for 1 week in a closed J. Young NMR tube. After 1 day of heating, the presence of the *trans*-dihydride complex **7** (Scheme 3) was evident, and after 1 week, the **7**:**1** ratio reached a value of 1:1. We believe that following N−H activation, H_2 elimination involving the hydride ligand and an arm proton takes place, as shown for an analogous hydrido−hydroxo (PNN)Ru complex on the basis of density functional theory (DFT) studies.[6] The reverse reaction has been demonstrated experimentally.[3h] Isomerization of the resulting unsaturated dearomatized complex followed by β-H elimination leads to the product **7** (Scheme 3). While we were unable to determine the fate of the organic products in the reaction, β-H elimination probably leads to isopropylimine, which can react with itself or excess amine.[7]

DFT studies[8] performed on the system reproduced the trend evident in the experimental data (Figure 2). The barriers for exchange between the coordinated (II) and activated (III) states were found to be low and accessible at room temperature.

The experimental trend toward a more stable NH-activated structure with electron-poor amines was also reproduced accurately.

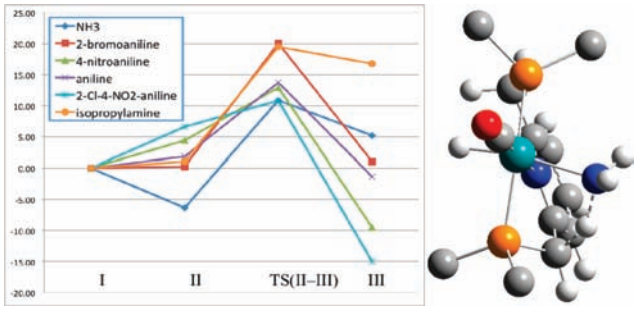


Figure 2. (left) Calculated free energies (ΔG_{298}, kcal/mol) for (I) the unbound starting materials and (II) coordinated and (III) NH-activated amine complexes. (right) Calculated structure of TS(II−III), the transition state for activation of NH_3 (Me groups on ^{t}Bu have been omitted for clarity).

The isopropylamine N−H-bond-activated complex is 16.8 kcal/mol above the unbound state (I), while 2-chloro-4-nitroaniline is almost 15 kcal/mol below the ground state I with a barrier of almost 26 kcal/mol for the reverse reaction. The observed equilibrium with 2-bromoaniline was also indicated here, as I and III have similar energies and the connecting barrier is not high. Ammonia did not follow the trend of the other amine compounds in that the coordinated NH_3 structure is 6.3 kcal/mol more stable than the free complex. In addition, the activated complex is ~5.2 kcal/mol higher in energy than the starting materials, precluding its direct spectroscopic observation; however, indirect evidence was gleaned from the isotopic exchange experiments. Even in the most unfavorable case, that of isopropylamine, the activated complex should still be accessible at room temperature. Indeed, the plausible pathway for formation of *trans*-dihydride **7** suggests its intermediacy (Scheme 3).

In conclusion, we have demonstrated N−H bond activation by a dearomatized (PNP)Ru complex that proceeds via metal−ligand cooperation involving aromatization/dearomatization of the ligand. These results represent a novel approach to N−H activation by transition-metal centers. Studies aimed at catalytic design based on this approach are in progress.

Acknowledgment. Support of this project by the Israel Science Foundation, the MINERVA Foundation, and the Bernice and Peter Cohn Catalysis Research Fund is gratefully acknowledged. E.K. is the recipient of The Marie Curie Postdoctoral Fellowship. D.M. is the Israel Matz Professor.

Supporting Information Available: Experimental procedures, full computational details, Cartesian coordinates (*XYZ*) of all DFT structures, and X-ray data for complex **2** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) Nuclear Overhauser effect (NOE) experiments were inconclusive in determining the absolute spatial configuration of the ND_3 and deuterated methylene arm.

(5) See the SI for details of the mechanism.

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(8) All of the calculations were performed at the PCN(C_6H_6)-M06+d/SDB-cc-pVDZ//M06-L+d/SDD(d)/DFBS level of theory. See the SI for full details.

JA103130U