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An Unusual Hydrogen Migration/C−H Activation Reaction with Group 3 Metals

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Supporting Information

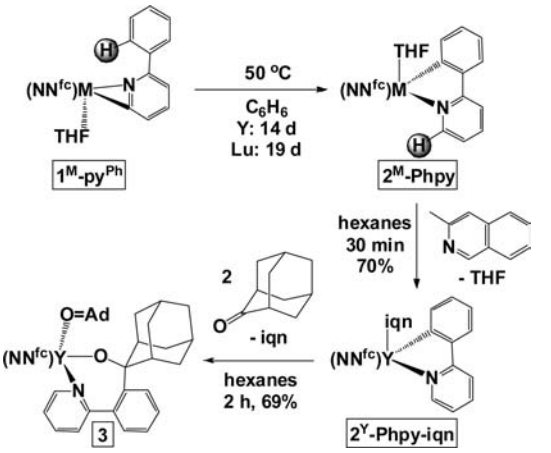
ABSTRACT: A novel hydrogen migration from the phenyl ring to the pyridine ring of an yttrium pyridyl complex supported by a 1,1′-ferrocene diamide ligand is reported. Density functional theory calculations were instrumental in probing the mechanism for this transformation.

The importance of hydrogen-transfer reactions in catalytic cycles involving transition metals is well recognized.[1−4] Recent experimental and theoretical studies have shown that the activation of X−H (X = H, C, Si, O, etc.) bonds by transition-metal complexes employs one of the following processes: α- or β-hydrogen transfer, hydrogen exchange, oxidative addition, reductive elimination, metathesis, or nucleophilic addition.[1−10] The discovery of a new elementary reaction for hydrogen migrations would enhance our understanding of established processes and lead to novel transformations.

While studying the reactivity behavior of group 3 metal alkyl[11−15] and uranium dialkyl[16,17] complexes supported by a 1,1′-ferrocenylene diamide ligand[18] toward aromatic N-heterocycles,[19−24] we noticed three different hydrogen-transfer reactions: within the same heterocycle,[12] between two heterocycles,[13] and to the reaction medium.[25] Although new for the type of metal complexes scrutinized, these transformations occurred within dearomatized systems and some had precedent.[26] Herein we report a novel hydrogen migration from the phenyl ring to the pyridine ring of $(NN^{fc})M(\eta^2\text{-}N,C\text{-}6\text{-phenylpyridyl})(THF)$ ($\mathbf{1^M\text{-}py^{Ph}}$; NN^{fc} = fc(NSi^{t}BuMe$_2$)$_2$, fc =1,1′-ferrocenylene, M = Y or Lu). This transformation occurs between two aromatic rings; the involvement of the metal center classifies this reaction as a C−H activation process. Furthermore, the formation of a five-membered-ring metallocycle, previously unknown as a product of C−H activation in the chemistry of d^0f^n metals,[27] was observed.

In the course of surveying the reactivity behavior of the ortho-metalated complex $\mathbf{1^Y\text{-}py^{Ph}}$, an unusual observation was made: its synthesis from $(NN^{fc})Y(CH_2Ph)(THF)$ and 2-phenylpyridine was straightforward in toluene but could not be achieved in benzene. That behavior prompted us to investigate the stability of $\mathbf{1^Y\text{-}py^{Ph}}$ in benzene. When a C_6D_6 solution of $\mathbf{1^Y\text{-}py^{Ph}}$ was heated, the formation of a new product, $\mathbf{2^Y\text{-}Phpy}$, was observed after 14 days of stirring at 50 °C (Scheme 1). It is interesting to point out that products resembling $\mathbf{2^Y\text{-}Phpy}$ (five-membered-ring metallocycles)[27] are routinely observed for palladium complexes[28] but that only three-membered-ring metallocycles are obtained from σ-bond metathesis reactions involving d^0f^n metal−carbon bonds.[29−32]

Scheme 1. Formation of 2^M-Phpy from 1^M-py^{Ph} and Reaction with Adamantanone



The analogous lutetium complex $\mathbf{1^{Lu}\text{-}py^{Ph}}$ underwent a similar reaction, affording $\mathbf{2^{Lu}\text{-}Phpy}$ after 19 days at 50 °C (see the Supporting Information for details). The yttrium complex, in which THF was replaced by 3-methylisoquinoline (iqn), was characterized by single-crystal X-ray diffraction ($\mathbf{2^Y\text{-}Phpy\text{-}iqn}$, Figure 1). The transformation of $\mathbf{1^M\text{-}py^{Ph}}$ to $\mathbf{2^M\text{-}Phpy}$ is not reversible, and the reaction of $\mathbf{2^Y\text{-}Phpy\text{-}iqn}$ with adamantanone gives the expected Y−C migratory-insertion product, **3** (Scheme 1 and Figure 1).

Given the unusual nature of the transformation from $\mathbf{1^M\text{-}py^{Ph}}$ to $\mathbf{2^M\text{-}Phpy}$, we became interested in understanding its mechanism. The peculiar solvent effect described earlier (benzene vs toluene) was corroborated by the fact that the reaction also takes place in diethyl ether but not in hexanes, indicating that the intermediate is more polar than the starting material and the product. The first indication that an intramolecular mechanism is likely was the fact that no deuterium incorporation was observed when the reaction was carried out in C_6D_6 instead of C_6H_6.

Furthermore, a crossover experiment involving the deuterated phenylpyridyl complex $\mathbf{1^Y\text{-}py^{Ph}\text{-}}d_5$ and the *p*-tolyl-substituted pyridyl complex $\mathbf{1^Y\text{-}py^{tol}}$ (eq 1) indicated that the ortho

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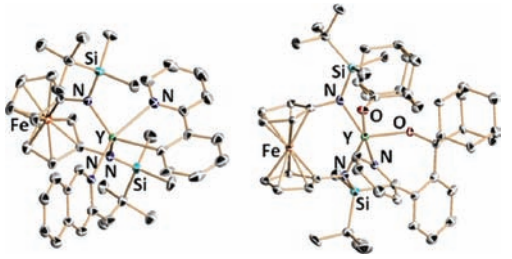
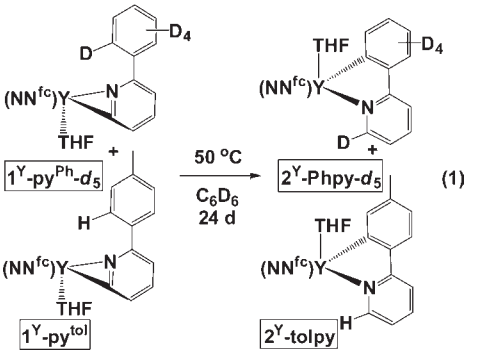


Figure 1. Thermal-ellipsoid (50% probability) representations of 2^{Y}-**Phpy-iqn** (left) and **3** (right). H atoms and solvent molecules have been omitted for clarity.

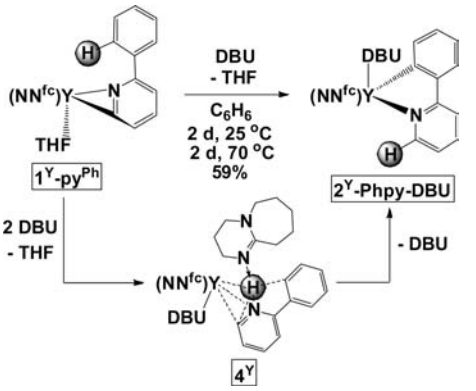
deuterium of 1^{Y}-py^{Ph}-d_5 migrated only within the same molecule to give 2^{Y}-**Phpy-**d_5. This result was corroborated by the fact that a mixture of deuterated phenyl and *p*-tolyl-substituted pyridyl complexes showed two distinct deuterium signals when monitored using ^{2}H NMR (C_6H_6, 25 °C) spectroscopy (see the Supporting Information for details). In addition, the formation of the deuterated complexes showed a kinetic isotope effect (KIE) of 1.3.



In an effort to increase the reaction rate and test whether an external base induces any change, it was found that 1,8-diazabicycloundec-7-ene (DBU) has a profound effect: conducting the transformation of 1^{Y}-py^{Ph} in the presence of 2 equiv of DBU led to a decrease in time from 14 to 4 days (Scheme 2). Notably, the reaction with 1 equiv of DBU was not straightforward. While monitoring the reaction mixture containing 2 equiv, it was noticed that an intermediate, 4^{Y}, could be observed by ^{1}H NMR spectroscopy. Unfortunately, 4^{Y} was unstable and very soluble even in *n*-pentane, and attempts to obtain crystals yielded only 2^{Y}-**Phpy-DBU**. By means of HMBC, HMQC, DEPT, and COSY NMR experiments, it was found that the structure of 4^{Y} contains two types of DBU fragments: one directly coordinated to the metal center and one involved in the hydrogen transfer (Scheme 2). This indicates that while the reaction is intramolecular, the H transfer across the phenylpyridine is greatly enhanced by the presence of an external base. In fact, the HMBC and HMQC 2D NMR spectroscopy experiments suggest that the transferred proton is strongly associated to the shuttling DBU molecule, to the extent that little to no interaction between the phenyl group and the proton was observed, greatly expediting the transfer of the proton from the phenyl ring to the pyridyl ring (see p S17 in the Supporting Information).

The analogous transformation of 1^{Lu}-py^{Ph} to 2^{Lu}-**Phpy** in the presence of 2 equiv of DBU was also attempted in an effort to increase the rate of this reaction. In this case, however, no formation of the product 2^{Lu}-**Phpy-DBU** was observed. Instead,

Scheme 2. Transformation of 1^{Y}-py^{Ph} to 2^{Y}-Phpy-DBU and Proposed Intermediate



the final product was 4^{Lu}, which shows greater stability than the yttrium-based analogue. Unfortunately, attempts to crystallize 4^{Lu} were unsuccessful. Although the coordination of DBU is unusual, the structure of an oxide-bridged dilutetium complex, **5**, which contains one DBU ligand coordinated to each metal, was obtained during our efforts to crystallize 4^{Lu} (see the Supporting Information for details).

The crossover experiment depicted in eq 1 was repeated using 1^{Y}-py^{Ph}-d_5 and 1^{Y}-py^{tol} in the presence of 4 equiv of DBU to determine whether the transformation was similar. The formation of solely 2^{Y}-**Phpy-**d_5**-DBU** and 2^{Y}-**tolpy-DBU** also supports an intramolecular pathway for the DBU-mediated reaction.

Density functional theory (DFT) calculations were instrumental in probing the nature of the mechanism for the transformation of 1^{M}-py^{Ph} to 2^{M}-**Phpy**. Geometry optimizations were carried out using full molecules, without removal of peripheral groups. It was found that the product 2^{Y}-**Phpy** is 6.5 kcal/mol more stable than the reactant 1^{Y}-py^{Ph}. The calculated relative stabilities of the phenylpyridyl fragments were compared to determine whether they are independent of the metal. It was found that the pyridyl carbanion is 2.8 kcal/mol more stable than the phenyl carbanion. This suggests that $(NN^{fc})Y$ is essential for the formation of the product because it stabilizes the phenyl carbanion relative to the pyridyl carbanion.

A few possible pathways consistent with the intramolecular nature of the process were investigated. A concerted, direct hydrogen transfer was considered first (Figure 2). With the B3LYP functional, it was found that the transition state for the concerted process was too high in energy, at 109 kcal/mol. The high energy is likely a consequence of the structural distortion required in order to allow the phenylpyridine fragment to facilitate a concerted proton transfer (**TS1** in Figure 2).

A stepwise pathway involving a proton transfer to the pyridyl N atom (**TS2** in Figure 2) followed by a 1,2-H shift with a

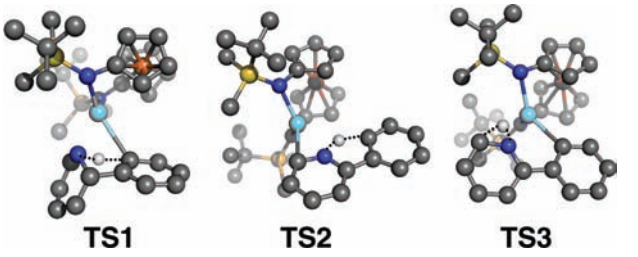


Figure 2. Possible transition-state structures for the transformation of 1^{M}-py^{Ph} to 2^{M}-**Phpy**.

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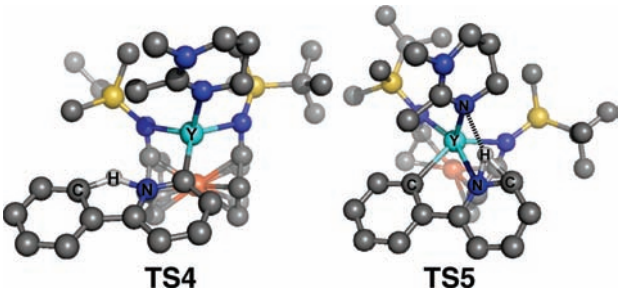

Figure 3. Possible transition structures for the transformation of $\mathbf{1^{M}\text{-}py^{Ph}}$ to $\mathbf{2^{M}\text{-}Phpy}$ in the presence of DBU.

concerted recoordination of N to Y (**TS3** in Figure 2) was investigated next. It was found that the hydrogen transfer to N involves a barrier of 55.8 kcal/mol (corrected using a dielectric continuum for benzene as the solvent), leading to an intermediate at 54.8 kcal/mol. The 1,2-H migration from the pyridyl N to the adjacent C has a relative barrier of 37.7 kcal/mol in the absence of an external base. Although these values are high, their order of magnitude is consistent with the very slow reaction observed experimentally (14 days at 50 °C). In addition, the analogous hydrogen-transfer reaction does not occur with 7,8-benzoquinoline, indicating that some flexibility is necessary for the first step to take place. The small value of the KIE (1.3) is also consistent with the proposed transition states **TS2** and **TS3** and supports the fact that the E−H (E = C, N) bonds are not completely cleaved during the hydrogen transfer.

The dramatic rate increase caused by the external base was also probed computationally. This study was conducted in two parts because of the large number of atoms required for the complex containing two DBU fragments. When one molecule of DBU was added to the yttrium complex, it was found that it binds exothermically by 5.9 kcal/mol to $\mathbf{1^{Y}\text{-}py^{Ph}}$; the binding of DBU to the product $\mathbf{2^{Y}}$**-Phpy** is exothermic by only 1.3 kcal/mol.

In the presence of one DBU molecule, the barrier to direct hydrogen transfer (the first proposed mechanism) was reduced to 89.4 kcal/mol, which is 19.6 kcal/mol lower than the value obtained in the absence of DBU. The barriers for the stepwise pathway (Figure 3) were also reduced, with **TS4** at 32.3 kcal/mol (vs 55.8 kcal/mol for **TS2**) and **TS5** at 21.3 kcal/mol (vs 37.7 kcal/mol for **TS3**). The transition states **TS4** and **TS5** show that the base only partially stabilizes the migrating proton since it remains strongly associated to the metal.

This finding is consistent with the fact that two molecules of base are required to effect the hydrogen transfer: one molecule of base interacts with the metal center, while the other assists the 1,2-H transfer directly. This hypothesis was tested by optimizing an additional molecule of base on the fixed C−H and N−H distances of **TS5**. This computational approach estimated a reduction of 2.6 kcal/mol in the barrier to hydrogen transfer relative to that using only one DBU (18.7 kcal/mol vs 21.3 kcal/mol). The finding supports the proposal that one molecule of base is bound to the metal center while an additional molecule of base assists the proton transfer, in agreement with the experimental findings described above.

In conclusion, we have described a new elementary reaction for a hydrogen migration process: this transformation occurs from the phenyl ring to the pyridine ring of $(NN^{fc})Y(\eta^2\text{-}N,C\text{-}6\text{-}phenylpyridyl)(THF)$ and can be assisted by the presence of a base such as DBU. DFT calculations were instrumental in probing the mechanism and support the experimental results: the pathway with the lowest energy barriers is a stepwise process involving initial proton transfer to the pyridyl nitrogen atom followed by a 1,2-H shift with a concerted recoordination of N to Y. Further studies will focus on the role of the ferrocene diamide ligand in mediating such a transformation and on applying the present findings to other substrates.

■ ASSOCIATED CONTENT

Supporting Information. Experimental details for compound syntheses and characterization, full crystallographic descriptions (CIF), and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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