Heterocyclic-Ring Opening

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Beyond C–H Activation with Uranium: A Cascade of Reactions Mediated by a Uranium Dialkyl Complex**

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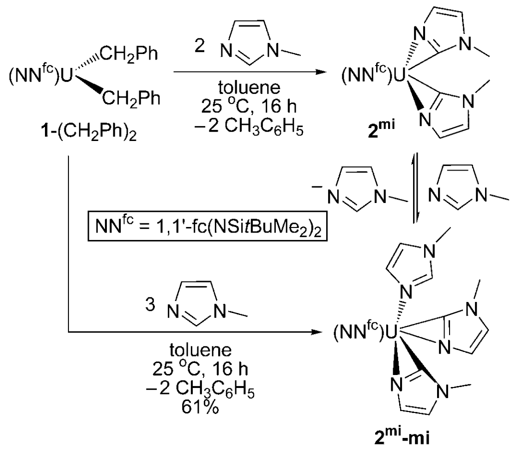
The ring opening of aromatic N heterocycles has been restricted to a few examples involving transition metals, such as niobium, tantalum, titanium, scandium, yttrium, and rhenium;[1–9] strong actinide–oxygen bonds could also drive the ring opening of pyridine *N*-oxides.[10] Our interest in the reactions of electrophilic alkyl complexes[11,12] supported by a ferrocene (fc) diamide ligand with aromatic N heterocycles[13–15] prompted us to investigate the reactivity of the uranium dibenzyl complex **1**-$(CH_2Ph)_2$ ($(NN^{fc})U(CH_2Ph)_2$; $NN^{fc} = 1,1'\text{-fc}(NSi\mathit{t}BuMe_2)_2$)[11,16] with imidazoles.

It has been reported that actinide complexes are more reactive than analogous Group IV complexes towards aromatic N heterocycles, and that C–H activation occurs from neutral dialkyl complexes as opposed to the cationic alkyl complexes of group IV metals.[17,18] We reasoned that diamide ligands may enhance the reactivity of the actinide complexes, since such ligands are known to support metal centers that are more electrophilic than those in metallocenes.[19] This characteristic becomes important when aromatic N heterocycles are involved, because these substrates tend to be strong Lewis bases and shut down further reactivity at the metal center.

The uranium dibenzyl complex **1**-$(CH_2Ph)_2$ features two alkyl ligands; therefore, we became interested in finding reactions that would involve two C–H activation events. We anticipated that this complex would show different reactivity from that reported by Guram and Jordan for a related zirconium complex ($[Cp_2ZrMe(THF)]^+$ did not engage in C–H activation with the imidazole ring; only coordination was observed).[20] The ability to undergo two C–H activation reactions is unique to uranium. It has been reported that both alkyl ligands of a uranium dialkyl complex react with the C–H bonds of terminal acetylenes;[21] however, reactions that involve two sp^2-hybridized C–H bonds are not known. One reason for this lack of reactivity may be the fact that the acidity of C(sp^2)–H bonds is lower than that of C(sp)–H bonds: the pK_a value of phenyl acetylene is 23.2,[22] whereas the pK_a value of 1-methylimidazole is 33.1 (experimental;[23] calculated: pK_a 35.1; the pK_a value of 1-methylbenzimidazole is 32.5).[24] Herein, we report a novel double C–H activation followed by the C–C coupling, ring opening, and migratory insertion of imidazoles; these reactions are uniquely promoted by **1**-$(CH_2Ph)_2$ and represent the first examples of the cleavage of aromatic N heterocycles by actinide complexes without the involvement of oxygen atoms or redox processes.[25]

The reaction between **1**-$(CH_2Ph)_2$ and 2 equivalents of 1-methylimidazole occurred at room temperature (Scheme 1). The ^{1}H NMR spectrum was indicative of a symmetrical complex, which was assigned to be $\mathbf{2^{mi}}$ on the basis of the observation that 2 equivalents of toluene were removed when the reaction was conducted in C_6D_6. However, crystals grown from a solution of $\mathbf{2^{mi}}$ had a different structure $\mathbf{2^{mi}}$-**mi** (Figure 1). The isolated complex $\mathbf{2^{mi}}$-**mi** has two η^2-N,C-imidazolyl ligands as a result of two C–H activation events; one additional 1-methylimidazole molecule is coordinated to uranium, *trans* to one of the η^2-N,C-imidazolyl fragments.



Scheme 1. C–H activation of two molecules of 1-methylimidazole mediated by the uranium dibenzyl complex **1**-$(CH_2Ph)_2$.

Accordingly, when **1**-$(CH_2Ph)_2$ was treated with 3 equivalents of 1-methylimidazole, the yield of isolated $\mathbf{2^{mi}}$-**mi** increased. Our observations indicate that, although complex $\mathbf{2^{mi}}$ is formed and persists in solution for a few hours at room temperature, an additional ligand is required for its stability over long periods of time. The ^{1}H NMR spectrum of the mother liquor derived from the crystallization of $\mathbf{2^{mi}}$-**mi** indicated a complex mixture, which proved intractable, as is consistent with the required decomposition of $\mathbf{2^{mi}}$ to provide an additional equivalent of 1-methylimidazole.

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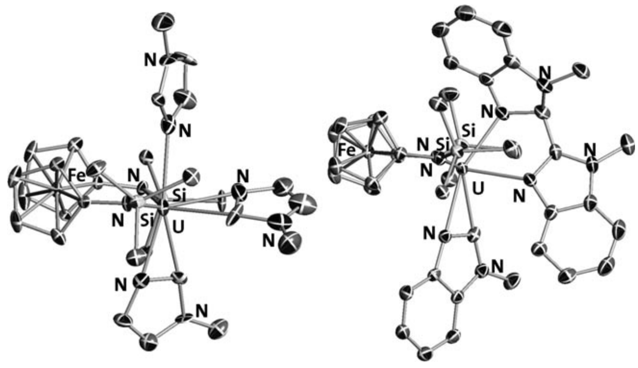
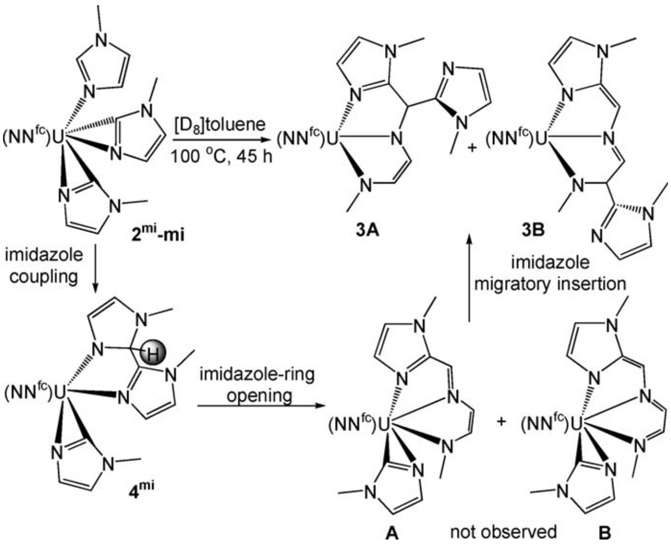


Figure 1. Thermal-ellipsoid representation (50% probability) of **2^{mi}-mi** (left) and **4^{mbi}** (right); H atoms, solvent atoms, and *t*Bu methyl groups were removed for clarity.

When a solution of **2^{mi}-mi** in [D$_8$]toluene was heated at 100 °C for 45 h, two new compounds, **3A** and **3B**, were observed (Scheme 2). Complexes **3A** and **3B** (Figure 2) feature a new ligand formed from the imidazole and two imidazolyl fragments initially present in **2^{mi}-mi**: one C–N bond in one of the rings was broken, whereas the other two rings resemble the original imidazole entities.



Scheme 2. Proposed mechanism for the **1**-(CH$_2$Ph)$_2$-mediated ring opening of 1-methylimidazole.

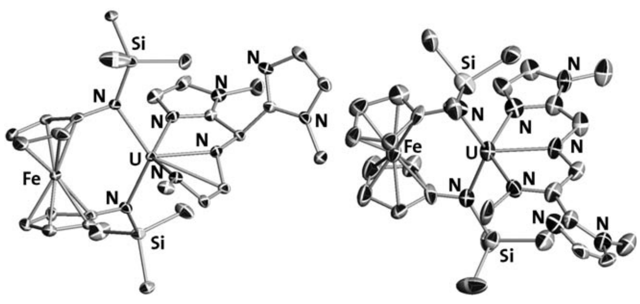
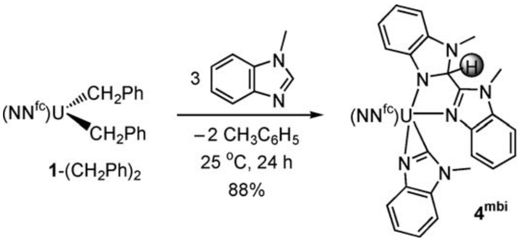


Figure 2. Thermal-ellipsoid representation of **3A** (left, 50% probability) and **3B** (right, 35% probability); H atoms, solvent atoms, *t*Bu methyl groups, and disordered counterparts were removed for clarity.

Although the transformation of **2^{mi}-mi** into **3A** and **3B** took some time at 100 °C, no intermediates could be isolated or characterized. However, when the reaction was carried out with **1**-(CH$_2$Ph)$_2$ and 1-methylbenzimidazole, it was possible to isolate and characterize a new product, **4^{mbi}** [Eq. (1)]. We therefore concluded that the coupling of two imidazole rings (that is, to form **4^{mi}** in Scheme 2) probably occurs prior to the ring-opening event.[26]



(1)

The coupling of two imidazole rings dearomatizes one of them and poises it for ring opening, which presumably occurs because more stable structures with delocalized double bonds can be formed in this way.[14] We propose that the ring-opening reaction leads to two intermediate isomer structures, **A** and **B**, which differ only with respect to the positions of their conjugated double bonds (Scheme 2). These intermediates **A** and **B** are transformed into the final products, **3A** and **3B**, through the migratory insertion[27–31] of the imidazolyl ring not involved in coupling. We previously reported a structure similar to **A** for group III complexes.[15] The formation of both isomers for uranium was observed by ^{1}H NMR spectroscopy from the beginning of the reaction, whereby **3A** appeared first; the production of **3A** and **3B** ceased after 45 h at 100 °C. On the basis of ^{1}H NMR spectroscopy, compound **3A** was formed in 51% yield, whereas **3B** was formed in 11% yield (see the Supporting Information).

Given that the complex **4^{mbi}** could be isolated, it was expected that a transformation analogous to that observed for **2^{mi}-mi** would occur. However, when **4^{mbi}** was heated in solution, it was converted only very slowly into a complex mixture of products. Compounds analogous to **3A** and **3B** were identified by ^{1}H NMR spectroscopy, but the large extent of decomposition that occurred under the harsh reaction conditions ([D$_8$]toluene, 100 °C, one month) made it impossible to separate them from the reaction mixtures.

Since it was the C–N bond of the coordinated imidazole ligand in **2^{mi}-mi** that was cleaved to yield **3A** and **3B**, **1**-(CH$_2$Ph)$_2$ may be powerful enough to be used in the ring opening of other heterocycles. This observation highlights the difference in the reactivity of the uranium complexes from that reported earlier for scandium complexes:[14,15] the scandium imidazolyl complex analogous to **2^{mi}** cannot be generated in the absence of a base; therefore, a stronger Lewis base than 1-methylimidazole would be required to displace this ligand.

In conclusion, we have shown that a neutral uranium dibenzyl complex mediates the C–H activation of two aromatic N heterocycles, followed by an unprecedented cascade of reactions that lead to the ring opening and functionalization of imidazole rings. We are currently exploring the scope of this ring-opening reaction by extending it to other heterocycles. This approach is appealing, as complex **2^{mi}** can be generated in situ, and the subsequent coordination of a wide range of Lewis bases is likely to occur readily.

Experimental Section

2^{mi}-mi: A solution of 1-methylimidazole (0.0285 g, 3 equiv) in toluene (2 mL) was added to a solution of **1**-$(CH_2Ph)_2$ (100 mg, 0.116 mmol) in toluene (4 mL), and the resulting mixture was stirred vigorously for 16 h at room temperature. The solvent was then removed under reduced pressure, and the dried product was extracted into hexanes, filtered through Celite, concentrated, and placed in a freezer at −35 °C. Large crystals of **2^{mi}-mi** (0.0650 g, 61 %) formed after several hours. ^{1}H NMR (C_6D_6, 500 MHz, 25 °C): $\delta = 18.60$ (s, 2 H, imidazole-CH), 12.19 (s, 18 H, $SiC(CH_3)_3$), 9.14 (s, 12 H, $SiCH_3$), 6.32 (s, 2 H, imidazole-CH), −3.48 (s, 6 H, NCH_3), −13.60 (s, 4 H, Cp-C), −19.15 ppm (s, 4 H, Cp-CH); elemental analysis calcd (%) for $C_{34}H_{54}N_8FeSi_2U$ (**2^{mi}-mi**): C 44.15, H 5.88, N 12.12; found: C 44.25, H 5.79, N 11.88.

3A and **3B**: The conversion of **2^{mi}-mi** into **3A** and **3B** was established by ^{1}H NMR spectroscopy. Complex **2^{mi}-mi** (0.0292 g, 0.032 mmol), 1-methylimidazole (1 equiv), and hexaethylbenzene (1 equiv, standard) were placed in a J. Young tube in [D_8]toluene, and the tube was heated at 100 °C. After 45 h, the peaks for **3A** and **3B** began to decrease in intensity. Conversion after 45 h: 62.4 % (**3A**: 51.1 %, **3B**: 11.3 %; see the Supporting Information for spectra and details on the isolation of each compound). **3A**: ^{1}H NMR (C_6D_6, 500 MHz, 25 °C; see the Supporting Information for full assignment): $\delta = 42.44$ (s, 3 H, NCH_3), 18.02 (s, 1 H), 16.10 (s, 2 H, Cp-CH), 7.48 (s, 1 H), 6.14 (1 H), 4.16 (s, 18 H, $SiC(CH_3)_3$), 1.00 (s, 3 H, NCH_3), −2.23 (s, 6 H, $SiCH_3$), −3.30 (s, 6 H, $SiCH_3$), −3.93 (s, 3 H, NCH_3), −4.75 (s, 4 H, Cp-CH), −12.51 (s, 2 H, Cp-CH), −20.39 ppm (s, 1 H); elemental analysis calcd (%) for $C_{34}H_{53}FeN_8Si_2U$: C 44.20, H 5.78, N 12.13; found: C 44.01, H 5.68, N 11.78. **3B**: ^{1}H NMR (C_6D_6, 500 MHz, 25 °C; see the Supporting Information for full assignment): $\delta = 18.71$ (s, 6 H, $SiCH_3$), 13.29 (s, 6 H, $SiCH_3$), 13.19 (s, 18 H, $SiC(CH_3)_3$), 5.06 (s, 1 H), 5.00 (s, 1 H), 3.78 (s, 1 H), 3.58 (s, 3 H, NCH_3), 3.34 (s, 3 H, NCH_3), 0.62 (s, 1 H), −5.82 (s, 1 H), −5.86 (s, 3 H, NCH_3), −5.85 (s, 1 H), −8.26 (s, 2 H, Cp-CH), −8.62 (s, 2 H, Cp-CH), −11.76 (s, 2 H, Cp-CH), −22.78 (s, 1 H), −23.41 ppm (s, 2 H, Cp-CH); elemental analysis calcd (%) for $C_{34}H_{53}FeN_8Si_2U$: C 44.20, H 5.78, N 12.13; found: C 44.55, H 5.75, N 11.83.

4^{mbi}: A solution of 1-methylbenzimidazole (0.0856 g, 3 equiv) in toluene (4 mL) was added to a solution of **1**-$(CH_2Ph)_2$ (0.1863 g, 0.216 mmol) in toluene (6 mL), and the resulting mixture was stirred vigorously at room temperature for 24 h. The reaction mixture was then filtered through Celite, and the solvent was removed under reduced pressure. The dried product was extracted into hexanes, filtered through Celite, concentrated, and placed in a freezer at −35 °C. Large crystals of **4^{mbi}** (0.2068 g, 88 %) formed after one night. ^{1}H NMR (C_6D_6, 500 MHz, 25 °C): $\delta = 16.00$ (s, 12 H, $SiCH_3$), 15.76 (s, 18 H, $SiC(CH_3)_3$), 7.89 (s, 2 H, imidazole-CH), 6.25 (s, 2 H, imidazole-CH), 4.80 (s, 2 H, imidazole-CH), −0.36 (s, 2 H, imidazole-CH), −6.83 (s, 6 H, NCH_3), −13.47 (s, 4 H, Cp-CH), −21.61 ppm (s, 4 H, Cp-CH); elemental analysis calcd (%) for $C_{49}H_{67}FeN_8Si_2U$, with one molecule of hexane, as found in the ^{1}H NMR spectrum of dried crystals: C 53.78, H 6.42, N 9.65; found: C 54.01, H 6.64, N 9.75.

X-ray crystal structures: Crystals suitable for X-ray crystallography were obtained from various concentrated solutions placed in a freezer at −35 °C in the glove box. Inside the glove box, the crystals were coated with oil (STP oil treatment) on a microscope slide, which was then taken out of the glove box. X-ray crystal data were collected on a Bruker AXS single-crystal X-ray diffractometer by using MoK_α radiation and a SMART APEX CCD detector. The data were reduced by SAINTPLUS, and an empirical absorption correction was applied by using the package SADABS. The structures were solved and refined by using SHELXTL (Brucker 1998, SMART, SAINT, XPREP AND SHELXTL, Brucker AXS Inc., Madison, Wisconsin, USA).[32] All atoms were refined anisotropically, and hydrogen atoms were placed in calculated positions unless specified otherwise.

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