VIP C–H Activation

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Ligand-Accelerated Activation of Strong C–H Bonds of Alkanes by a (Salen)ruthenium(VI)–Nitrido Complex**

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Selective functionalization of C–H bonds continues to be of great interest to chemists. Inspired by enzymes, such as cytochrome P450 and methane monooxygenase (MMO), the use of metal–oxo complexes (M = O) for C–H bond activation has been extensively studied.[1] Analogous reactions with metal–imido (M = NR) species are also known.[2] However, there are only few reports of C–H bond activation by metal–nitrido (M≡N) complexes.[3] For instance, thermolysis of diruthenium–azido[4] and iridium–azido[5] complexes are reported to give the corresponding nitrides, which then undergo insertion into an aryl C–H bond to give amido complexes. Photolysis of azido complexes of cobalt[6] and uranium[7] also generate transient nitrido species that undergo insertion into the ligand C–H bond. Collisional activation of an iron–azido complex by means of electrospray ionization affords an intermediate iron(V)–nitrido species, which activates the C–H bond of the chelating ligand.[8] In the above examples, the nitrido species are putative or transient species which undergo intramolecular C–H bond activation. We report herein an example of intermolecular C–H bond activation of a number of alkanes by a well-characterized (salen)ruthenium(VI)–nitrido complex, $[Ru^{VI}(N)(L)(MeOH)]PF_6$ (**1**) (L = *N*,*N*′-bis(salicylidene)-*o*-cyclohexyldiamine dianion).[9]

Complex **1** reacts readily with xanthene in CH_3CN at room temperature, as monitored by UV/vis spectrophotometry (see Figure S1 in the Supporting Information). The reaction follows clean pseudo-first-order kinetics and the pseudo-first-order rate constant (k_{obs}), is independent of $[Ru^{VI}N]$, but depends linearly on [xanthene], with a second-order rate constant (k_2) of $(1.95 \pm 0.06) \times 10^{-1}\,M^{-1}s^{-1}$ at 298.0 K. Complex **1** reacts similarly with 9,10-dihydroanthracene (DHA), but with a smaller k_2 value of $(4.15 \pm 0.26) \times 10^{-3}\,M^{-1}s^{-1}$, in accordance with the stronger C–H bond of DHA compared with xanthene (Figure S2). A kinetic isotopic effect (KIE) of (3.3 ± 0.3) was obtained for DHA/[D_4]-DHA. Complex **1** does not react with alkanes with larger C–H bond dissociation energies (BDEs) than DHA (78.0 kcal mol^{-1}).[10] However, in the presence of 0.1 M pyridine (py), the oxidation of DHA by **1** is accelerated by over two orders of magnitude ($k_2' = 1.59\,M^{-1}s^{-1}$). More significantly, the system **1**/py can now activate C–H bonds as strong as those in cyclohexane (95.4 kcal mol^{-1}).[10] We have previously reported that **1** can be activated by py to undergo aziridination of alkenes.[11] However, py also activates **1** toward bimolecular coupling of the nitrido ligands.[12] Hence, we studied the reaction of **1**/py with alkanes under conditions of high dilution using a 50 mm cuvette in order to minimize this coupling reaction. Figure 1

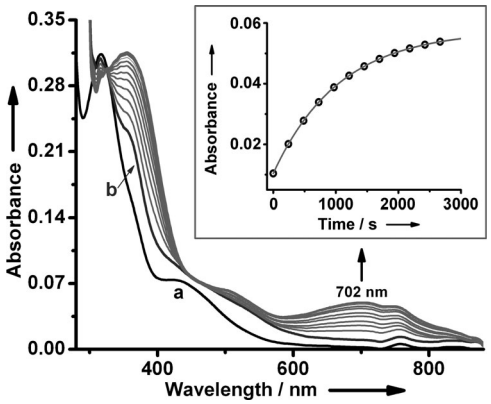

Figure 1. Spectral changes at 200 s intervals for the reaction of **1** (5.00×10^{-6} M) with cyclohexane (1.00 M) and py (0.1 M) in $(CH_2Cl)_2$ at 296.0 K (a: before mixing, b: 5 s after mixing). Inset shows the time trace at 702 nm and fit of the data to a first-order equation.

shows the spectrophotometric changes for the reaction of **1** with cyclohexane in the presence of excess py in $(CH_2Cl)_2$. The reaction follows clean pseudo-first-order kinetics for over three half-lives. The pseudo-first-order rate constant k_{obs} depends linearly on [cyclohexane], and the reaction exhibits saturation behavior with respect to [py] (Figure 2). The rate law of the reaction is shown in Equation (1). The equilibrium constant K for the reversible binding of py to **1** is $(16.6 \pm 1.4)\,M^{-1}$, which agrees well with the value obtained from kinetic studies of alkene aziridination ($15.6 \pm 1.1\,M^{-1}$).[11]

$$\frac{-d[Ru^{VI}(N)]}{dt} = k_{py}[Ru^{VI}(N)][\text{alkane}]\left(\frac{K[py]}{1+K[py]}\right) \quad (1)$$

The second-order rate constant (k_{py}) was found to be $(1.68 \pm 0.05) \times 10^{-3}\,M^{-1}s^{-1}$ at 296.0 K. The oxidation of [D_{12}]cyclohexane occurs much more slowly with a KIE of (8.4 ± 0.2). The rate constants for C–H activation of other alkanes by **1** in the presence of 0.1 M py were also determined

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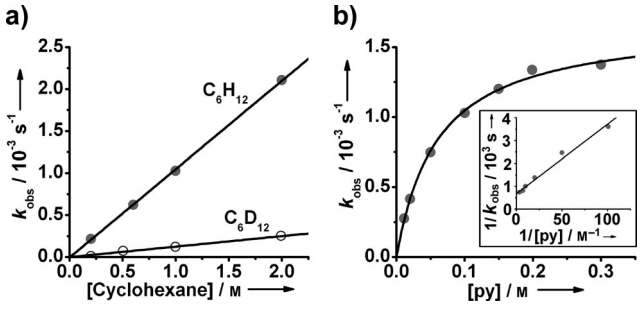


Figure 2. a) Plots of k_{obs} against $[C_6H_{12}]$ (solid circle) and $[C_6D_{12}]$ (open circle) in $(CH_2Cl)_2$ at 296.0 K. b) Plot of k_{obs} against [py]. Inset shows the corresponding double reciprocal plot.

(see Table S1 and Figures S3–S9 in the Supporting Information). Large KIE values were also obtained in the oxidation of toluene ($k(C_6H_5CH_3)/k(C_6H_5CD_3) = (10.1 \pm 0.2)$; Figure S9) and fluorene ($k(C_9H_{10})/k(C_9D_{10}) = (4.4 \pm 0.5)$; Figure S5). A linear correlation between the rate constant and the C–H BDE of the alkanes is found (Figure 3).[13–15] On the basis of this linear correlation and large KIE values, we conclude that the reaction between **1**/py and alkanes occurs by an initial

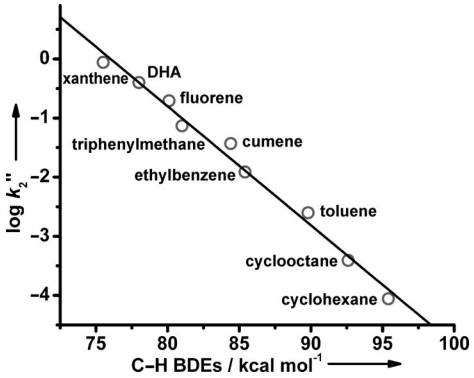


Figure 3. Plot of log k_2'' (second-order rate constants per active hydrogen atom in 0.1 M py) against C–H BDE of alkanes in $(CH_2Cl)_2$ at 296.0 K.

rate-limiting hydrogen atom transfer (HAT) step. In the oxidation of *para*-substituted toluenes, both electron-donating and electron-withdrawing substituents have an accelerating effect (Table S2), and a linear correlation was also observed between the reaction rate and the α-H hyperfine coupling constant (σ°) of *para*-substituted toluenes (Figure S10), which is consistent with a benzyl radical intermediate produced by HAT.[16]

We then investigated the fate of the alkyl radical produced in the initial HAT step. The ESI mass spectrum (ESI/MS, Figure 4) of the green solution from reaction of **1** with xanthene in CH_3CN shows the presence of two predominant species, the peak at $m/z = 504$ is assigned to $[Ru(L)(NCCH_3)_2]^+$, while the peak at $m/z = 658$ is assigned to $[Ru(HN{=}xanthene_{(-2H)})(L)(NCCH_3)]^+$ (**2**). In the presence of py in $(CH_2Cl)_2$, the observed species are $[Ru(L)(py)_2]^+$ ($m/z = 580$) and $[Ru(HN{=}xanthene_{(-2H)})(L)(py)]^+$ ($m/z = 696$).

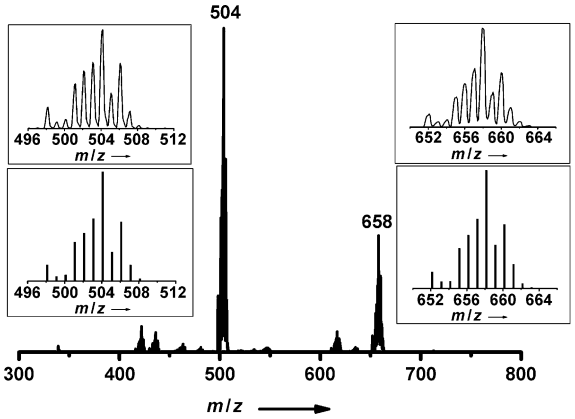


Figure 4. ESI/MS of **1** (3.62×10^{-5} M) with xanthene (4.82×10^{-2} M) in CH_3CN. Insets show the expanded (top) and calculated (bottom) isotopic patterns.

Similar results were obtained for DHA (Figure S11–S12). Complex **2** has been isolated as the green crystalline PF_6^- salt. The ESI/MS analysis of **2** in CH_3CN shows the parent ion at $m/z = 658$. Compound **2**-PF_6 has a magnetic moment of $\mu_{eff} = 1.92\ \mu_B$ (Guoy method) at room temperature, consistent with its formulation as a d^5 Ru^{III} complex. The IR spectrum shows a ν(N–H) stretch at 3292 cm^{-1}. The structure of **2**-PF_6 has been determined by X-ray crystallography (Figure 5). The cation consists of a six-coordinate ruthenium center bound by a salen ligand, an acetonitrile, and an imine ligand (N(H) = $xanthene_{(-2H)}$) that is derived formally from insertion of the nitrido ligand of **1** into an alkyl C–H bond of xanthene, together with the loss of a hydrogen atom from the α-carbon center. The newly formed imine ligand is disordered. The N3–C23 distance of 1.313(10) Å (N3A–C23A = 1.292(11) Å) is typical of C=N bonds. The Ru1–N3 distance of 2.083(10) Å (Ru1–N3A = 2.068(11) Å) is comparable to the Ru–NH_3 distance (2.083(4) Å) in $[Ru^{III}(NH_3)(L)(NCCH_3)]PF_6$.[17]

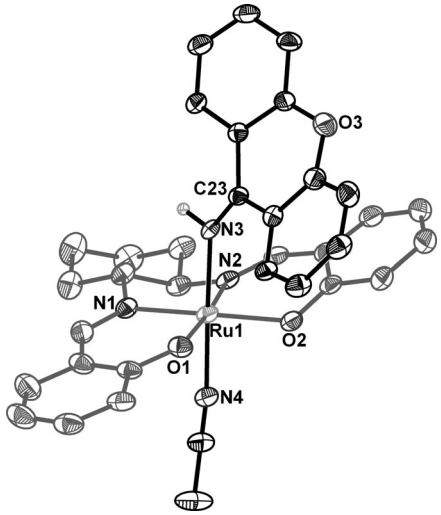
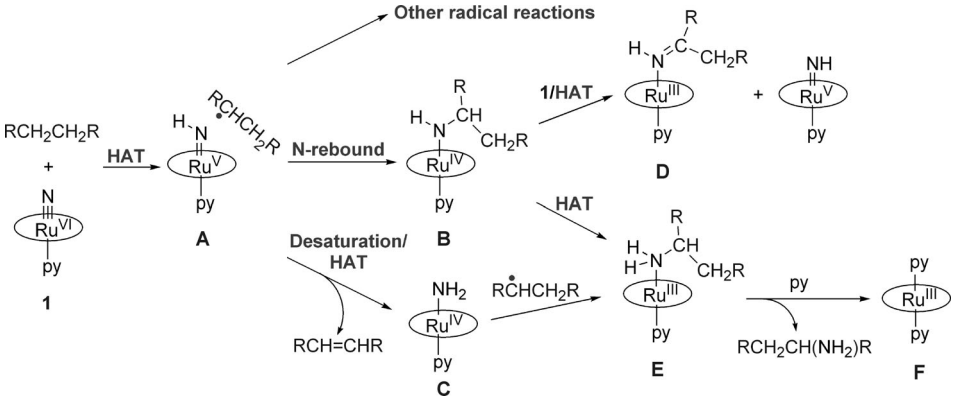


Figure 5. Molecular structure of **2**. Thermal ellipsoids are drawn at 30% probability. Hydrogen atoms (except N3–H) are omitted for clarity.

Complex **2** is most likely formed by an N-rebound mechanism after the initial HAT from xanthene to $Ru^{VI}{\equiv}N$. A similar mechanism should also occur with DHA. However, in the reaction of **1** with alkanes with stronger C–H bonds, such as ethylbenzene, toluene, cyclooctane, or cyclohexane, similar N-rebound ruthenium products were not observed by ESI/MS. For these substrates the predominant ruthenium species is $[Ru(L)(py)_2]^+$ ($m/z = 580$). We then tried to detect any organic products formed in these reactions by GC and GC–MS. When **1** was reacted with excess cyclohexane in $(CH_2Cl)_2$ in the presence of 0.1 M py, 8% (100% × mol of product/mol of **1**) of cyclohexylamine was found (Figure S13). Moreover, when Br_2 was added to the reaction mixture, 10% of 1,2-dibromocyclohexane could be detected, thus indicating that cyclohexene was originally present (Figure S14). No cyclohexylamine and 1,2-dibromocyclohexane were detected in the absence of **1**. These results suggest that in the reaction of **1** with cyclohexane, both N-rebound (formation of cyclohexylamine) and desaturation (formation of cyclohexene) reactions occur after the initial formation of the cyclohexyl radical. When cyclooctane was used as substrate, 35% of cyclooctene was found (Figure S15), but no cyclooctylamine could be detected, thus indicating that in this case desaturation predominates over N-rebound.[18] A general mechanism for the reaction of **1** with alkanes is shown in Scheme 1.



Scheme 1. Proposed mechanism for the reaction of **1** with alkanes.

The initial step involves rate-limiting HAT from the alkane (RCH_2CH_2R) to **1** to produce $Ru^{V}{=}NH$ (intermediate **A**) and the radical $RC^{\bullet}HCH_2R$, which then undergo parallel N-rebound and desaturation (through a second HAT) reactions.[19] $RC^{\bullet}HCH_2R$ probably also undergoes other radical reactions to give undetected products. The N-rebound ruthenium product (intermediate **B**) could undergo HAT (presumably to complex **1**) from an α-C–H bond to generate a ruthenium(III) imine product (compound **D**), as in the case of xanthene. Intermediate **B** could also be reduced to a ruthenium(III) complex (intermediate **E**), presumably by abstracting a hydrogen atom from a second substrate molecule. Intermediate **E** could then undergo substitution by py to generate $[Ru(L)(py)_2]^+$ (detected by ESI/MS) and free amine, as in the case of cyclohexane.

The accelerating effects of py on C–H bond activation by $[Ru^{VI}(N)(L)]^+$ may be due to a lowering of the reorganization energy and/or an increase in hydrogen atom affinity of the Ru^{VI}–nitrido species. Mayer has treated HAT reactions using a Marcus theory approach.[13a,d] According to the Marcus theory, the activation energy for HAT depends on the reorganization energy as well as the driving force. Kochi has reported that the epoxidation of alkenes by $[Cr^{V}(salen)(O)]^+$ is accelerated by pyridine *N*-oxide.[20] In the five-coordinate $[Cr^{V}(salen)(O)]^+$, the Cr atom is 0.53 Å above the salen plane, however it is pulled back to 0.26 Å upon axial ligation with pyridine *N*-oxide, and this is accompanied by a weakening of the Cr=O bond. It is likely that similar geometrical changes occur upon coordination of py to $Ru^{VI}{\equiv}N$, thus making the complex more product-like, and hence lowering the reorganization energy for HAT. *Trans* axial ligands have also been found to affect Fe=O bond strengths.[21] On the other hand, py coordination may also enhance the hydrogen atom affinity of $Ru^{VI}{\equiv}N$, which would increase the driving force for HAT. Goldberg and de Visser have reported that HAT reactions of a $Mn^{V}(O)$ species are accelerated by anionic axial ligands, which is due to an enhancement of its hydrogen atom affinity as a result of an increase in basicity of the $Mn^{IV}(O)$ species.[22] We are currently doing DFT calculations in order to gain more insight into the mechanisms of C–H activation by the **1**/py system.

In summary, we have provided definitive evidence for intermolecular C–H activation of alkanes with C–H bonds as strong as those in cyclohexane by a (salen)ruthenium(VI)–nitrido species. The initial rate-limiting step involves HAT to form an alkyl radical, which then undergoes N-rebound and desaturation pathways that are reminiscent of C–H activation by cytochrome P450 and metal–oxo species.[1,23] To the best of our knowledge, desaturation of alkanes by a metal–nitrido species is unprecedented. Our findings should provide insights into C–H functionalization using metal nitrides.

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