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Notes

Heterolytic CH Activation and Catalysis by an O-Donor Iridium−Hydroxo Complex

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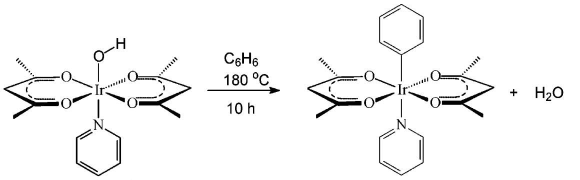
Summary: A well-defined, O-donor ligated iridium hydroxide complex is reported that is competent for benzene CH activation and long-lived catalytic H/D exchange between benzene and water. An inverse dependence of the H/D exchange rate on added pyridine, a kinetic isotope effect (KIE) of 2.65 ± 0.56 for CH activation with 1,3,5-trideuteriobenzene, a KIE of 1.07 ± 0.24 with C_6H_6/C_6D_6*, and DFT calculations are consistent with the CH activation proceeding via rate-determining benzene coordination followed by fast CH cleavage via a* σ*-bond-metathesis transition state.*

The CH activation reaction has been the focus of significant effort, given the potential for designing catalysts that can selectively functionalize hydrocarbons at low temperatures.[1] Heterolytic CH activation with M−X complexes (eq 1), where X is a heteroatom, is well suited for incorporation into catalytic cycles for the oxy functionalization of hydrocarbons and is relatively common with the electrophilic cations Pt(II), Pd(II), Hg(II), and Au(III)/Au(I).[2]

$$\mathrm{C{-}H + M{-}X \rightarrow M{-}C + H{-}X} \qquad (1)$$

However, heterolytic CH activation is not common with more electron-rich cations such as Ir(III) and, to our knowledge, catalytic oxy functionalization has not been reported with electron-rich complexes based on the middle transition metals.[3] Recently, we reported the first well-defined Ir(III) alkoxo complex that exhibited both stoichiometric and catalytic heterolytic CH activation.[4] To establish the generality and mechanism of this type of heterolytic CH activation reaction with more electron-rich metal complexes, we have examined the extension of the chemistry to the corresponding metal hydroxo complex. Several key considerations led us to explore this extension. (A) The chemistries of the hydroxo and methoxo groups, while expected to be similar, are not identical. (B) There is a possibility of β-hydride eliminations from the methoxo complex to generate metal hydrides[5] that could be very active for CH activation.[6] (C) We observe that in water, a desirable "green" solvent, the alkoxo complex is hydrolyzed to the corresponding metal hydroxo complex. (D) While catalytic CH activation with metal hydroxo complexes has recently been observed,[7] the complexes utilized in that study did not allow the corresponding stoichiometric CH activation products to be isolated and characterized. We report in this communication the first example of stoichiometric and catalytic heterolytic CH activation (eq 1; M = Ir(III), X = OH) with an air-, protic-, and heat-stable Ir(III) hydroxo complex that cleanly generates the CH activation product Ir−R and H_2O.

Specifically, we report the preparation of the O-donor iridium(III) hydroxide complex (acac-O,O)$_2$Ir^{III}(OH)(Py) (**1**; acac-O,O = κ^2*O,O*-acetylacetonate, Py = pyridine) and show that this complex undergoes stoichiometric, heterolytic CH activation with benzene to quantitatively generate the CH activation product (acac-O,O)$_2$Ir^{III}(Ph)(Py) (**2**) and water (eq 2). Combined theoretical and experimental evidence is presented in support of a mechanism involving preequilibrium dissociative loss of



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† University of Southern California.

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(1) We define the CH activation reaction as a reaction between a reactive species "M" that proceeds without the involvement of free radicals, carbocations, or carbanions to generate discrete M−C intermediates. (a) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (b) Shilov, A. E.; Shul'pin, G. B. *Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes*; Kluwer Academic; Dordrecht, The Netherlands, 2000. (c) Jia, C. G.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *38*, 633. (d) Crabtree, R. H. *Dalton Trans.* **2001**, *19*, 2437. (e) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (f) Periana, R. A.; Bhalla, G.; Tenn, W. J., III; Young, K. J. H.; Liu, X. Y.; Mironov, O.; Jones, C. J.; Ziatdinov, V. R. *J. Mol. Catal. A: Chem.* **2004**, *220*, 7.

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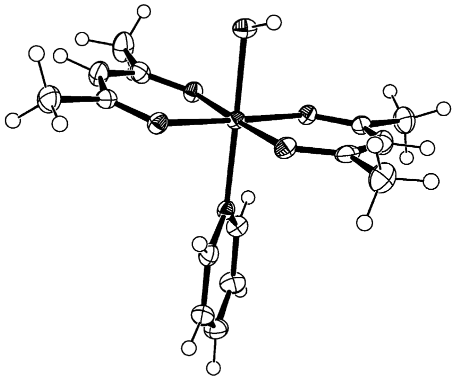

Figure 1. ORTEP diagram of complex **1**, showing ellipsoids at the 50% probability level. A molecule of cocrystallized $CHCl_3$ has been omitted for clarity. Selected bond distances (Å): Ir1−O5, 2.018(4); Ir1−N1, 2.044(5).

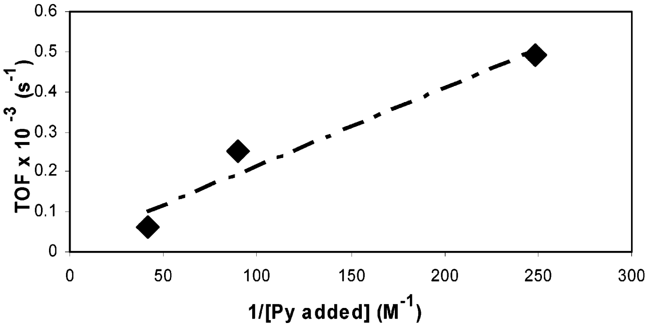

Figure 2. Plot of TOF versus 1/[Py] for C_6H_6/D_2O H/D exchange with **1** (10 mM).

Py, followed by rate-determining benzene coordination and fast CH cleavage via a σ-bond metathesis transition state. Complex **1** is stable and is competent for catalyzing H/D exchange reactions between benzene and water.

Complex **1** was synthesized from the methoxo complex (acac-O,O)$_2$Ir^{III}(OCH_3)(CH_3OH) (**3**) in quantitative yield by reaction with water at 70 °C, followed by treatment with pyridine. The compound is an air- and water-stable, hygroscopic yellow solid that has been fully characterized by ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, high-resolution mass spectrometry, and X-ray crystallography. The −O*H* resonance in the ^{1}H NMR is significantly broadened but sharpens at low temperature and is visible at −50 °C at −0.96 ppm. An ORTEP diagram of this complex is shown in Figure 1, and details of the structure determination are provided as Supporting Information.

The stoichiometric CH activation of benzene with **1** (eq 2) was carried out in neat C_6H_6 at 180 °C for 10 h in a glass bomb. Removal of all volatiles in vacuo and dissolution with $CDCl_3$ solvent containing 1,3,5-trimethoxybenzene as an internal standard showed that **2**, the corresponding phenyl complex, was produced in a yield of 74 ± 3% based on added **1**. Complex **2** was separated from the reaction mixture by preparative TLC and identified by comparison of the ^{1}H and ^{13}C NMR spectra and mass peaks to those of independently prepared and fully characterized **2**.[4] Reactions with toluene are typical of other well-defined CH activation reactions,[1] and only the meta and para aromatic CH bonds are activated in a ∼2:1 ratio. A free-radical mechanism is unlikely, as the both the CH activation rate and yield are insensitive to added oxygen.

Application of the principle of microscopic reversibility could suggest that **1** should catalyze H/D exchange between D_2O and benzene, a relatively rare reaction,[8] under conditions comparable to those for the stoichiometric CH activation reaction of benzene by **1**. However, it is important to note that this would only be possible *if* (A) the barrier for the microscopic reverse of eq 2 is *not* substantially larger than the forward reaction (this would be the case if eq 2 is thermodynamically very favorable) and (B) the complex is sufficiently stable under the conditions required for catalysis. Significantly, the observation that the stoichiometric CH activation of benzene with **1** proceeds in high yield *could* suggest that the reaction is thermodynamically favorable and that $\Delta G_{rxn} < 0$ for eq 2. Consequently, if this value is large, e.g., <-10 kcal/mol, it may not be possible to observe catalysis under conditions comparable to those for the stoichiometric CH activation reaction. To examine these possibilities, we investigated whether **1** could catalyze H/D exchange between D_2O and benzene.

The studies, carried out at 190 °C, show that **1** does catalyze the H/D exchange between mixtures of C_6H_6 and D_2O. The catalysis was examined over a time period of ∼86 h, during which time a total turnover number (TON) of 329 and an average turnover frequency (TOF) of 1.1×10^{-3} s^{-1} were observed based on added **1**. The system is thermally quite stable, as the dependence between TON and time was linear (see the supporting Information) throughout the 86 h experiment. As discussed above, the observation of catalysis also indicates that if eq 2 is thermodynamically favorable, the driving force is likely less than 10 kcal/mol. As in the case of the methoxo complex,[4] we expect that the CH activation proceeds via a mechanism involving substrate coordination and CH cleavage by hydrogen transfer to the hydroxo group. Since **1** is a 6-coordinate, 18-electron complex, it is likely that the benzene coordination proceeds via a five-coordinate intermediate generated by dissociative loss of pyridine in a preequilibrium step. To examine this, we investigated the dependence of the reaction rate on added pyridine. As shown in Figure 2, the observed linear dependence of the TOF for H/D exchange versus 1/[Py] is consistent with this proposal. This result would predict that the aquo complex (acac-O,O)$_2$Ir(OH)(H_2O) would be a more effective catalyst (since water is a more labile ligand), and preliminary results on the synthesis and tests with this complex show this to be the case (see the Supporting Information).

To further probe the mechanism of the CH activation reaction, we compared the deuterium kinetic isotope effect (KIE) for reaction of **1** with a mixture of C_6H_6 and C_6D_6 with that for 1,3,5-trideuteriobenzene. This comparison can allow the distinction between rate-determining benzene coordination and rate-determin-

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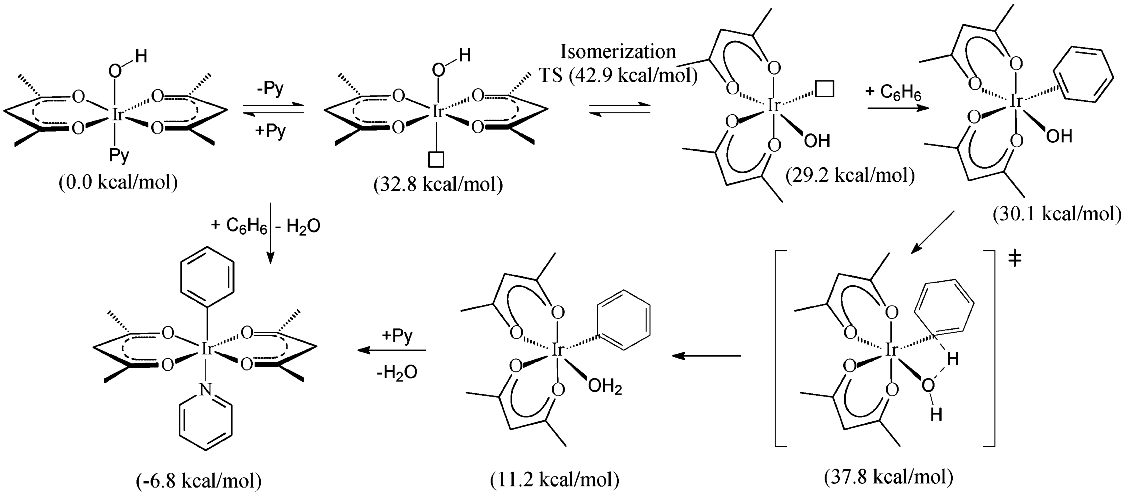
Scheme 1. Proposed Mechanism for the Reaction of 1[a]



[a] Calculated ΔG values are given in parentheses.

ing CH cleavage[9] (assuming negligible secondary isotope effects). The ratio of CH to CD activation by **1** was obtained from analysis of the H to D ratio, respectively, in the water produced as expected from eq 2. The H to D ratio in the water produced was obtained by postreaction with CH_3Li and quantification of the molar ratio of gaseous methane isotopomers by GC/MS (see the Supporting Information for details). The KIE for 1,3,5-trideuteriobenzene was found to be normal with $k_H/k_D = 2.65 \pm 0.56$. DFT calculations (B3LYP/LACVP** with ZPE and solvent corrections)[10] of the KIE ($k_H/k_D = 2.9$) compare well with this experimental value. In the case of the mixture of C_6H_6/C_6D_6 no KIE was observed ($k_H/k_D = 1.07 \pm 0.24$). Taken together, these results would suggest that the CH activation of benzene occurs via rate-determining benzene coordination followed by faster CH cleavage.

Consistent with the experimental results, DFT calculations of the CH activation mechanism, summarized in Scheme 1, show that the lowest energy pathway involves preequilibrium and dissociative loss of pyridine to generate a trans five-coordinate intermediate, followed by rate-determining trans–cis isomerization to generate the cis benzene complex and fast CH bond cleavage by a σ-bond metathesis transition state.

Significantly, the calculations, unlike those reported recently for a Ru(II) hydroxo species,[7] show that the stoichiometric CH activation reaction (eq 2) is energetically favorable, −6.8 kcal/mol, and is in accord with the generation of **2** from **1** in good yield. As discussed above, the relatively small driving force is consistent with the observation of H/D exchange between D_2O and benzene catalyzed by **1** (which is anticipated to occur by eq 2 and the microscopic reverse) under conditions comparable to those for for eq 2. The calculated overall barrier for reaction of **1** with benzene of 42.9 kcal/mol and lower barrier for Py loss are also consistent with the reaction proceeding at 180 °C with $t_{1/2} \approx 4.8$ h and the observed inverse rate dependence on Py, respectively. The calculations also support the interpretation of the KIE experiments that benzene coordination rather than CH cleavage is rate determining.

It is interesting that **1** exhibits stable catalysis (TON of >300 observed) and is not deactivated by the irreversible formation of bridging hydroxo species (assuming thermodynamic control)[11] that is common for coordinatively unsaturated metal hydroxo complexes. Our attempts at synthesis of these bridging hydroxo complexes have thus far been unsuccessful. Calculations show that the formation of a μ-hydroxo complex from two molecules of **1** is not very favorable ($\Delta G_{rxn} = -2$ kcal/mol) and may serve to explain the catalytic stability of **1**.

In summary, we have demonstrated that a discrete O-donor, air- and heat-stable hydroxo complex **1**, reacts with benzene to generate the corresponding phenyl complex **2** with cogeneration of water. **1** is an efficient catalyst for an H/D exchange reaction between benzene and water. Experimental and theoretical studies suggest that the reaction proceeds via rate-determining formation of an arene complex followed by faster CH cleavage by a σ-bond metathesis reaction.

Acknowledgment. We acknowledge Dr. M. Yousufuddin and Prof. Robert Bau for solving the crystal structure of **1** and Vadim R. Ziatdinov for helpful discussions. We thank the National Science Foundation (Grant No. CHE-0328121) and Chevron Energy Research & Technology Co. for financial support for this research.

Supporting Information Available: Text, figures, tables, and a CIF file giving synthetic procedures and spectroscopic details for complexes reported herein, details of experimental procedures (including kinetic studies and plots), crystallographic details for the complex **1**, and computational methods. This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] For further computational details, see the Supporting Information.

[11] We are examining higher TON and reaction times to ensure that the system is under thermodynamic control.