phosphonyl radical generation. Microbes might also exploit some variant of this chemistry. Formation and subsequent homolytic fragmentation of organophosphonate adduct would circumvent the high oxidation potentials associated with direct, oxidative generation of phosphonyl radicals.[1b] The relevance of such a mechanism will depend on ongoing characterization of the genes and intermediate metabolites associated with organophosphonate biodegradation.[11]

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The Selective Hydrogenation of Benzene to Cyclohexene on Pentaammineosmium(II)

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Heterogeneous catalytic hydrogenation of aromatic molecules has been reported with a number of Group VIII metals including Ni, Pt, Rh, and Ru.[1] Though cyclic olefins are undoubtedly intermediates in this process, their rapid hydrogenation usually precludes their isolation in high yield. Partial selectivity toward cyclohexene has been achieved with modified ruthenium surfaces,[2] but this is accompanied by a dramatic decline in catalytic activity. Homogeneous reduction to cyclohexene has also been accomplished on various metal centers to which the arene is η^6 coordinated.[3] In these cases, however, reducing agents more potent than hydrogen are required.

Recently we reported the synthesis of a novel class of pentaammineosmium(II) compounds in which an arene is coordinated η^2 to the metal center.[4] Relative to others reported,[5] these complexes offer unusual kinetic stability, allowing their convenient manipulation and study at room temperature. Both theoretical calculations[6] and crystallographic data[7] indicate that the η^2 mode of ligation disrupts the aromaticity of the arene. Thus, the benzene complex $[Os(NH_3)_5(\eta^2\text{-}C_6H_6)]^{2+}$ has been shown to be activated toward olefinic reactivity.[8] These considerations led us to investigate the hydrogenation of the complexes $[Os(NH_3)_5(\eta^2\text{-}C_6H_6)](OTf)_2$ (**1**) and $[\{Os(NH_3)_5\}_2(\eta^2\text{:}\eta^2\text{-}\mu\text{-}C_6H_6)](OTf)_4$ (**2**) under mild conditions.

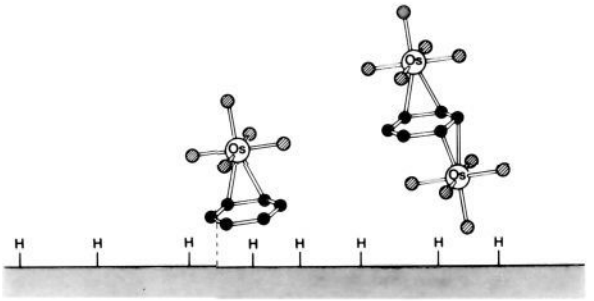

Figure 1. Steric interference in the catalytic hydrogenation of η^2-coordinated benzene complexes.

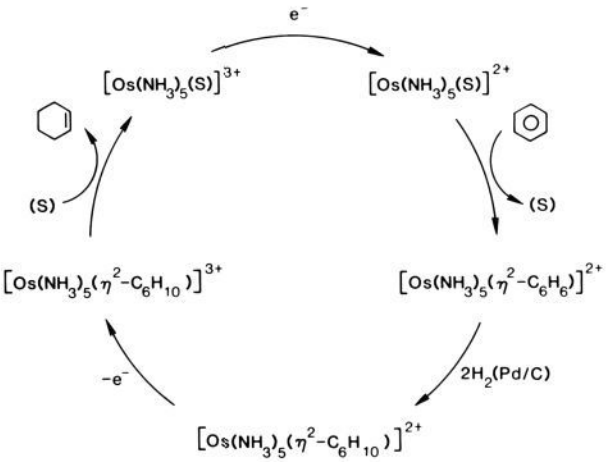

Figure 2. A cycle for the selective hydrogenation of benzene to cyclohexene.

Under 1 atm of hydrogen at 30 °C, Pd^0 on carbon (Pd/C) is ineffective as a catalyst for the hydrogenation of benzene.[9] However, when a MeOH solution of **1** is subjected to these conditions, the cyclohexene complex $[Os(NH_3)_5(\eta^2\text{-}C_6H_{10})](OTf)_2$ (**3**) is produced in quantitative yield.[10] ^1H NMR, cyclic voltammetric, and microanalytical data[11] confirm that complex **3** is obtained as a pure solid. Further support for the proposed identity of **3** is gained from the direct reaction of pentaammineosmium(II) with cyclohexene in which an identical product is obtained.[12] When the hydrogenation is repeated under similar conditions without the addition of the Pd^0 catalyst, the formation of **3** is not detected.

A proton NMR spectrum of **3** features five inequivalent resonances (3.40, 2.68, 1.52, 1.40, 1.12 ppm) corresponding to the ring protons, of which the olefinic signal occurs the furthest downfield (cf., the ethylene resonance for the complex $[Os(NH_3)_5(\eta^2\text{-}C_2H_4)](OTf)_2$ occurs at 3.22 ppm).[13] When the reduction of **1** is repeated using D_2 and CD_3OD, NMR data for **3**-d_4 reveal a dramatic loss of intensity at 2.68 and 1.52 ppm indicating that the dominant isomer is a product of cis hydro-

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(8) Though pentaammineruthenium(II) fails to form a complex with benzene analogous to **1**, the binuclear complex $[Os(NH_3)_5Ru(NH_3)_5(\eta^2\text{:}\eta^2\text{-}\mu\text{-}C_6H_6)](OTf)_4$ is readily prepared. See: Harman, W. D.; Taube H. *J. Am. Chem. Soc.*, accepted for publication.

(9) Control reaction run in CD_3OD for 7 h at 50 psi.

(10) Synthesis of **3**. All reactions are carried out under rigorously anaerobic conditions. 28 mg of 5% Pd on C is suspended in 5 mL of degassed methanol and stirred under 1 atm of H_2 for 15 min. (The ratio of Os to Pd is 20:1). **1** (85 mg) is added to the slurry, and the mixture is stirred under H_2 for 15 h. The solution is filtered to remove the catalyst and then added slowly to 50 mL of Et_2O upon which a light yellow precipitate is formed. Final yield: 89%.

(11) Characterization of **3**: Anal. Calcd for $C_8H_{25}OsS_2F_6O_6N_5$: C, 14.66; H, 3.84; N, 10.70. Found: C, 14.10; H, 3.76; N, 10.78. ^1H NMR (acetone-d_6, ppm vs TMS) 3.40 (m, 2 H), 2.68 (m, 2 H), 1.52 (m, 2 H), 1.40 (m, 2 H), 1.12 (m, 2 H), 2.88 (b, 12 H), 3.95 (b, 3 H); cyclic voltammetry (100 mV/s; CH_3CN; 1.0 M TBAH; E_λ = 1.40 V; −1.40 V): $E_{1/2}$ = 0.55 V, NHE.

(12) Complex **3** can be generated from cyclohexene directly utilizing synthetic procedures previously described. See ref 18.

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genation in which the osmium–olefin stereochemistry is conserved.[14] Presumably, hydrogenation occurs exo to the metal center (Figure 1). The observance of residual spin density at 2.68 and 1.52 ppm could be a result of either proton scrambling or interconversion of the metal–olefin bond.

Although an acetonitrile solution of **3** fails to surrender a significant amount of cyclohexene over a 36-h period,[15] its oxidation by $[Fe(Cp)_2]^+$ results in the rapid formation of $[Os(NH_3)_5(CH_3CN)]^{3+}$. The liberation of the olefin is experimentally confirmed by repeating this oxidation in acetone-d_6.[16] Over an 18-h period, an *N*,*N*-dimethylacetamide (DMA) solution of the complex $[Os(NH_3)_5(\eta^2\text{-}C_6H_{10})](OTf)_3$, generated from **3** and AgOTf, quantitatively converts to the solvent complex[17] which is then reduced in the presence of benzene to regenerate **1**. Thus a cycle is completed (Figure 2), in which benzene is hydrogenated to cyclohexene with negligible loss of the pentaammineosmium metal center.

The benzene ligand in the complex $[\{Os(NH_3)_5\}_2(\eta^2{:}\eta^2\text{-}\mu\text{-}C_6H_6)]^{4+}$ has a single olefinic site which is not ligated to osmium.[3] However, attempts to hydrogenate **2** under the reported conditions failed to produce detectable amounts of any reduction product. The catalyst recovered from this reaction was shown still to be active toward hydrogenation of **1**. The expected compound $[\{Os(NH_3)_5\}_2(\eta^2{:}\eta^2\text{-}\mu\text{-}C_6H_8)](OTf)_4$ can readily be generated by conventional methods[18] and is stable in solution for hours. The inert nature of **2** toward hydrogenation under the present conditions is attributed to steric crowding from the metal centers which prevents effective π overlap between the organic ligand and the metal surface (Figure 1).

Although the metal center is conserved in the cycle shown in Figure 2, the process is not catalytic: due to the inert nature of **3**, the removal of cyclohexene is conservatively achieved[19] only through oxidation of the metal. However, the cogener to **3**, $[Ru(NH_3)_5(\eta^2\text{-}C_6H_{10})](OTf)_2$, can be prepared[20] and readily surrenders its organic ligand in MeOH ($t_{1/2} \approx 15$ min at 20 °C). Seeking a catalytic route to cyclohexene, we attempted to hydrogenate benzene in a solution of pentaammineruthenium(II). Though the ruthenium analogue to **1** is not known, we hoped to intercept a metastable η^2-coordinated benzene complex. Several reactions were performed in which $Ru(NH_3)_5(OTf)_3$, Pd/C, and excess benzene were slurried in CD_3OD under H_2.[21] ^1H NMR, CV, and GCMS analysis of the resulting filtrates showed complete conversion of benzene to cyclohexane and formation of significant amounts of ammonium ion;[22] thus far our attempts to isolate the proposed intermediate $[Ru(NH_3)_5(\eta^2\text{-}C_6H_{10})]^{2+}$ or any other pentaammineruthenium salt have been unsuccessful.[23]

Our investigation of monosubstituted benzene derivatives of **1**[3b] indicates that pentaammineosmium(II) displays a high regioselectivity in many of these complexes with activation barriers to tautomerization as high as 17 kcal/mol. It may therefore be possible to achieve stereoselective partial hydrogenation of substituted arenes, in which the facilitating metal center can be conveniently recycled. We hope to extend our investigation to include the selective hydrogenation of other pentaammineosmium(II) complexes of η^2-bound aromatic ligands such as pyridines,[5f] pyrroles, and furans.[24]

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(14) ^1H NMR of **3**-d_4 (acetone-d_6, ppm vs TMS) 3.40 (m, 2 H), 2.68 (m, 0.2 H), 1.52 (m, 0.2 H), 1.40 (m, 1.8 H), 1.12 (m, 1.8 H), 2.88 (b, 12 H), 3.95 (b, 3 H). Exclusive cis hydrogenation of **1** would conserve the mirror plane in the product (**3**-d_4), and the corresponding NMR would feature only three cyclohexene resonances, provided that the metal center was confined to a single side of the hexene plane.

(15) After 36 h at 30 °C an acetonitrile solution of **3** was shown by cyclic voltammetry to contain less than 10% of the complex $[Os(NH_3)_5(CH_3CN)]^{2+}$.

(16) An acetone-d_6 solution of **3** is treated with 1 equiv of $[Fe(Cp)_2]PF_6$. A ^1H NMR of the reaction mixture shows the formation of free cyclohexene (5.75, 2.05, 1.71 ppm).

(17) $[Os(NH_3)_5(\eta^2\text{-}C_6H_{10})](OTf)_3$ is generated from the oxidation of **3** by AgOTf in acetone. The solvolysis of this material in DMA is monitored by cyclic voltammetry.

(18) The complex $[\{Os(NH_3)_5\}_2(\eta^2{:}\eta^2\text{-}\mu\text{-}C_6H_8)](OTf)_4$ was prepared by using synthetic procedures outlined in the following: Harman, W. D.; Taube, H. *Inorg. Chem.* **1987**, *26*, 2917.

(19) I.e., without the subsequent decomposition of the metal center.

(20) The complex $[Ru(NH_3)_5(\eta^2\text{-}C_6H_{10})](OTf)_2$ was prepared by the reaction of cyclohexene with a methanol solution of $[Ru(NH_3)_5(CH_3OH)]^{2+}$.

(21) In a typical reaction $Ru(NH_3)_5(OTf)_3$ (200 mg) and benzene (1.0 mL) are slurried with 5% Pd^0/C (25 mg) in CD_3OD (4.0 g) under 50 psi of hydrogen gas for 1.5–7 h. Under similar conditions $[Ru(NH_3)_6]^{3+}$ is readily reduced by H_2 to $[Ru(NH_3)_6]^{2+}$; the triflate analogue is expected to behave similarly.

(22) A significant amount of partially deuteriated cyclohexanes were also detected.

(23) Efforts are currently directed toward identifying the active form of this ruthenium catalyst.

(24) These complexes have been prepared by using the synthetic procedures outlined in ref 18 and will be reported separately.

Transition-State Structural Features for the Thermolysin-Catalyzed Hydrolysis of *N*-(3-[2-Furyl]acryloyl)-Gly-LeuNH$_2$

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Thermolysin is a metalloendoproteinase isolated from *Bacillus thermoproteolyticus*.[1] Despite extensive kinetic,[2-6] crystallographic,[7-10] and molecular modelling[11] studies, several important mechanistic problems remain unsolved. Resolution of these issues are essential to an accurate description of catalysis by thermolysin and related metalloproteinases. Of central importance is the identification of the rate-determining step and the structural characterization of the rate-limiting transition state.

In this communication, I report results of experiments that probe structural features of the rate-limiting transition state for the thermolysin-catalyzed hydrolysis of the chromogenic substrate, *N*-(3-[2-furyl]acryloyl)-Gly-LeuNH$_2$[12] (FA-Gly-LeuNH$_2$; cleavage occurs at the Gly-Leu bond). Specifically, β-deuterium isotope effects (β-DIE; ratio of rate constants for the hydrolysis of FA-Gly-LeuNH$_2$ and FA-Gly(d_2)-LeuNH$_2$) and solvent deuterium isotope isotope effects (SIE; ratio of rate constants for the hydrolysis of FA-Gly-LeuNH$_2$ in light and heavy water) were determined for the kinetic parameter, k_{cat}/K_m (k_E). Together, these isotope effects suggest that the rate-limiting step is decomposition of a zwitterionic tetrahedral intermediate.

Thermolysin, FA-Gly-LeuNH$_2$, and D_2O were from Sigma Chemical Co. and used without further purification. The deuteriated derivative of the substrate, FA-Gly(d_2)-LeuNH$_2$, was prepared by Bachem. The material appeared isotopically and chemically pure as judged by fast-atom bombardment mass spectroscopy and thin-layer chromatography, respectively. "Kinetic purity"[13] of substrates was verified by the lack of a

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