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ARTICLE

Alcohol-assisted base-free hydrogenation of acetophenone catalyzed by $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$

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Abstract: The hydrido–amido complex $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (**1**) catalyzes the base-free hydrogenation of ketones in benzene. Kinetic studies using acetophenone revealed that the system has an induction period, after which the rate of the reaction increases. A constant rate was observed when a critical amount of the product alcohol was added, indicating that the reaction is autocatalytic in 1-phenylethanol. Varying the initial conditions showed that the reaction rate is dependent on hydrogen and catalyst concentration and independent of ketone concentration. Above the critical concentrations of 1-phenylethanol, the reaction rate is independent of alcohol concentration. The rate law for pressures up to 5 atm was found to be rate = $d[alcohol]/dt = -d[ketone]/dt = k[Os][H_2]$, with $k = 30$ mol L^{-1} s^{-1} at 293 K and the temperature dependence provided energy of activation parameters. Therefore, the heterolytic splitting of dihydrogen is rate determining under these conditions. Only small kinetic isotope effects were measured in contrast with the analogous ruthenium system. Complex **1** reacts with the product alcohol 1-phenylethanol and is partially converted into the dihydride complex *trans*-$OsH_2(NH_2CMe_2CMe_2NH_2)(PPh_3)_2$ and acetophenone; with excess alcohol, an osmium alkoxide is observed at low temperature. As expected from these results, **1** is a ketone transfer hydrogenation catalyst in isopropanol.

Key words: catalytic hydrogenation, hydride, ketone, autocatalysis, isotope effect, osmium complex.

Résumé : Le complexe d'hydrure et d'amidure $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (**1**) catalyse l'hydrogénation non basique des cétones dans le benzène. Des études cinétiques réalisées en présence d'acétophénone ont révélé que le système réactionnel présentait une période d'induction après laquelle le taux de la réaction augmente. Un taux constant a été observé lorsque qu'une quantité importante d'alcool est ajoutée, ce qui montre que la réaction est autocatalytique en présence de 1-phényléthanol. En faisant varier les conditions initiales, on montre que le taux de la réaction est indépendant de la concentration en cétone et qu'il dépend des concentrations en hydrogène et en catalyseur. Lorsque l'on dépasse des valeurs de concentration élevées en 1-phényléthanol, le taux de la réaction devient indépendant de la concentration en alcool. Pour des pressions allant jusqu'à 5 atm, on a constaté que la loi de vitesse de la réaction est la suivante : vitesse = $d[alcool]/dt = -d[cétone]/dt = k[Os][H_2]$, où $k =$ 30 mol L^{-1} s^{-1}, à 293 K. La relation de dépendance entre k et la température a permis d'obtenir les paramètres liés à l'énergie d'activation de la réaction. Ainsi, la rupture hétérolytique influe sur la vitesse de réaction dans ces conditions. Seuls de faibles effets isotopiques cinétiques ont été mesurés, en comparaison à ceux du système analogue comportant du ruthénium. Le complexe **1** réagit avec l'alcool 1-phényléthanol et se transforme partiellement en le complexe de dihydrure *trans*-$OsH_2(NH_2CMe_2CMe_2NH_2)(PPh_3)_2$ et en acétophénone. Lorsque l'alcool est en excès, on constate à basse température la présence d'un alcoolate d'osmium. Comme on peut s'y attendre au vu de ces résultats, **1** est un catalyseur de l'hydrogénation de cétone par transfert dans l'isopropanol. [Traduit par la Rédaction]

Mots-clés : hydrogénation catalytique, hydrure, cétone, autocatalyse, effet isotopique, complexe d'osmium.

Introduction

The mechanisms of the homogenous H_2 hydrogenation under base-free conditions of ketones catalyzed by well-defined ruthenium complexes has been studied previously by our research group. These complexes include *trans*-RuH_2(*R*-binap)(tmen), where tmen is $(NH_2CMe_2CMe_2NH_2)$,[1,2] $RuH(NHCMe_2CMe_2NH_2)(PPh_3)_2$,[1] (*S,S*)-$RuHCl(PPh_2C_6H_4CH_2NHC_6H_{10}NHCH_2C_6H_4PPh_2)$/KO*i*Pr,[3] and RuH(app)(*S*-binap), where app is the amide version of the ligand 2-amino-2-(2-pyridyl)-propane.[4] An essential catalytic structure contains a ruthenium–amido bond that causes the heterolytic splitting of H_2 producing a dihydride and an amine group on ruthenium. The diamine ligands tmen and app used in these studies do not possess β-hydrogen atoms to protect the amido form of the ligand from β-hydride elimination and thus preventing the catalyst from converting to a dihydride with an imine form of the ligand. The concept of metal–ligand bifunctional catalysis, first proposed by Noyori, applies well to these catalytic systems.[5,6] That is, both the metal and the ligand, in this case an amido group, participate in the heterolytic splitting of H_2, the rate-determining step of the reaction. Noyori's group studied the mechanism of hydrogenation of the benchmark substrate acetophenone in isopropanol using a well-defined precursor $RuH(BH_4)$(*S*-tolbinap)(*S,S*-dpen) and found that under basic conditions, it also proceeded via rate-determining splitting of dihydrogen across the ruthenium–amido bond with a kinetic isotope effect (KIE) k_{H2}/k_{D2} of 2.0.[7] We reported a k_{H2}/k_{D2} of 2.1 ± 0.1 for the hydrogenation of ace-

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tophenone in benzene catalyzed by our *trans*-RuH_2(tmen)(*R*-binap) catalyst.[2] The use of KIE in the study of organometallic reaction mechanisms has recently been reviewed.[8]

To further explore the reactivity of the group 8 metal triad, the osmium(II) hydrido–amido complex $OsH(HNCMe_2CMe_2NH_2)(PPh_3)_2$ (**1**) and the *trans*-dihydride complex $OsH_2(H_2NCMe_2CMe_2NH_2)(PPh_3)_2$ (**2**) were examined as catalysts in the hydrogenation of acetophenone to 1-phenylethanol in benzene. Initial experiments using **1** as a catalyst revealed an increase in the rate of reaction as the reaction proceeded.[9] Such behaviour could indicate the operation of autocatalysis as first proposed for the system RuH(app)(*S*-binap),[4] that is, the product alcohol speeds up the reaction by lowering the activation barrier for the rate-determining step.

The autocatalytic behaviour of our RuH(app)(*S*-binap) system was attributed to the phenylethanol product assisting in the splitting of the H–H bond by inserting its –OH moiety into the four-membered ring of the Ru(H_2)(amido) transition state structure to produce a lower energy six-membered transition state, as shown in Fig. 1, IV.[4] Noyori and co-workers found that isopropanol was the best solvent for the H_2 hydrogenation of ketones. They had previously proposed a similar transition state structure.[7] Alcohol-assisted transition states for other ruthenium-based bifunctional H_2 hydrogenation catalysts were also suggested by Ikariya[10] and Casey.[11]

We describe here our investigation of the kinetics of catalysis by the $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (**1**) complex.

Experimental details

General

Unless otherwise stated, all manipulations were carried out under argon using standard Schlenk and glovebox techniques. $OsHCl(tmen)(PPh_3)_2$ and $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ were prepared as described.[9] All solvents were distilled under argon using sodium/benzophenone ketyl. Acetophenone was purchased from Sigma Aldrich, dried over P_2O_5, and distilled under argon. Acetophenone-CD_3 (99% CD_3) was purchased from Aldrich and was freeze–thaw degassed and dried over 4 Å molecular sieves. Toluene-d_8 was purchased in ampoules from Aldrich, dried with activated 3 Å molecular sieves, and stored under argon. NMR spectra were recorded on Agilent 600 and Varian 400 and 300 MHz spectrometers. The ^{1}H NMR spectra were recorded at 600, 400 or 300 MHz, the ^{13}C NMR spectra at 100 or 75 MHz and the ^{31}P NMR spectra at 242, 161 or 121 MHz. The ^{1}H NMR and ^{13}C NMR spectrum peaks were referenced relative to partially deuterated solvent peaks (mostly benzene-d_6), and the ^{31}P NMR chemical shifts were measured relative to the external reference 85% H_3PO_4.

Attempted reaction of $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (1) with acetophenone

$OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (20 mg, 0.0230 mmol) and acetophenone (11 mg, 0.0916 mmol) were added to an NMR tube and dissolved in C_6D_6. An orange-red solution was observed. The ^{1}H and ^{31}P{^{1}H} NMR spectra were obtained and only the presence of the starting materials was detected.

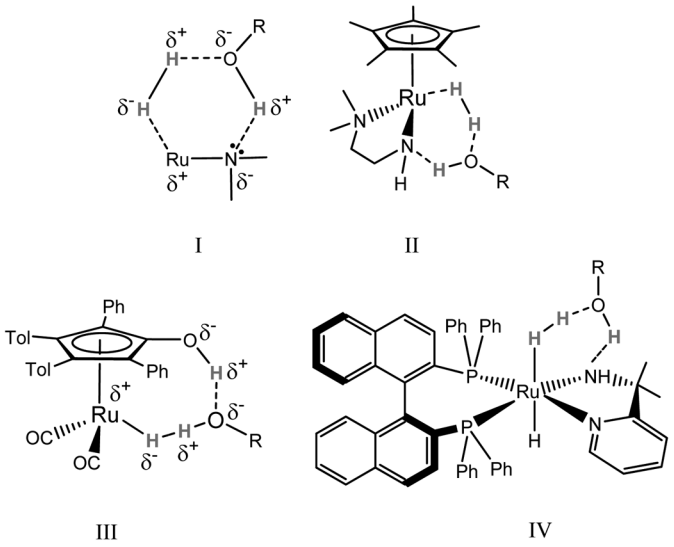
Reaction of $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ with 1-phenylethanol

(*a*) Under argon, $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (20 mg, 0.0230 mmol) and 1-phenylethanol (10 mg, 0.0819 mmol, ~3.6 equiv.) were added to an NMR tube and dissolved in C_6D_6. An orange-red solution was observed. The ^{1}H and ^{31}P{^{1}H} NMR spectra were obtained. The presence of **1** (^{1}H NMR (OsH) –24 ppm, br; ^{31}P{^{1}H} NMR 29 ppm, br) and 1-phenylethanol were detected as well as the presence of *trans*-OsH_2(tmen)$(PPh_3)_2$ (**2**) (^{1}H NMR (OsH) –7.1 ppm; ^{31}P{^{1}H} NMR 37 ppm) and acetophenone. Integration of the hydride peaks in the ^{1}H NMR spectrum of **1** and **2** provided a 1:1 hydride ratio, indicating a 2:1 ratio of **1** to **2**.

(*b*) Under argon, $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (9 mg, 0.0108 mmol) and 1-phenylethanol (26 mg, 1.21 mmol, 20 equiv.) were added to a J. Young NMR tube and dissolved in C_6D_6 to give an orange solution. ^{1}H NMR (600 MHz) and ^{31}P{^{1}H} NMR spectra were measured at 10 min, 7 h, and 24 h at 25 °C and were found to be identical apart from the appearance of some minor peaks in the last spectrum. In each case, resonances assigned to **1** (0.005 mol L^{-1}), **2** (0.005 mol L^{-1}), acetophenone (0.005 mol L^{-1}), and 1-phenylethanol (0.2 mol L^{-1}). The reaction was repeated with wet 1-phenylethanol. In this case, broad hydride resonances were also present at –20 and –21 ppm and these are thought to be associated with $OsH(OH)(tmen)(PPh_3)_2$ solvated with alcohol. After 6 h, the J. Young NMR tube was filled with hydrogen gas (~1 atm) and ^{1}H NMR spectra were obtained again immediately and after several hours. A significant decrease in the signals of **1** was observed, leaving the dihydride **2** as the major species. The signals due to the hydroxide species disappeared more slowly. The acetophenone resonance disappeared leaving only **2** and 1-phenylethanol.

(*c*) Observation of $OsH(OCHPhMe)(tmen)(PPh_3)_2$ (**3**). The toluene-d_8 solution of *b* was cooled to –80 °C and spectra were collected. The concentrations of species observed are reported in the calculation in entry 3 of Table 1 (see below). **3**: ^{1}H NMR: –22.5 br (OsH), 0.51, 0.60, 0.87, 0.88 (br, diastereotopic methyl of tmen due to chiral alkoxide), 1.42, 2.30, 4.27, 5.30 (br, four inequivalent NH), 5.18 (br, OCHMePh), 6.8–8.1 ppm (Ph). ^{31}P{^{1}H} NMR: 25.0 (br), 13.3 ppm (br).

Fig. 1. Alcohol-assisted transition states proposed by Noyori and co-workers (I), Ikariya and co-workers (II), Casey and co-workers (III), and Morris and co-workers (IV).



Hydrogenation of acetophenone using $OsHCl(tmen)(PPh_3)_2$ and base

Under nitrogen, $OsHCl(tmen)(PPh_3)_2$ (5 mg, 0.00494 mmol), potassium *tert*-butoxide (10 mg, 0.0891 mg), and acetophenone (1.000 g, 8.323 mmol) were added to a Schlenk flask resulting in an orange solution. The solution was purged with hydrogen and stirred under 1 atm hydrogen gas at room temperature for 3 h. After this time, an aliquot was dissolved in $CDCl_3$ and the ^{1}H NMR spectrum was taken. Integration of the methyl peaks of acetophenone and 1-phenylethanol was used to determine a conversion of 16%.

Transfer hydrogenation

Under argon, $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (13 mg, 0.01565 mmol) and acetophenone (104 mg, 0.8656 mmol) were dissolved in 2-propanol (1.005 g, 1.280 mL) and stirred in a round-bottom flask. The catalyst and substrate concentrations were 0.01223 and 0.676 mol L^{-1}, respectively, giving a substrate to catalyst ratio of 55:1. An orange suspension formed due to the insolubility of the

Table 1. Equilibria by adding dry 1-phenylethanol to complex **1** in benzene-d_6 or toluene-d_8 under argon in a sealed NMR tube as observed by ^{1}H and ^{31}P NMR.

Entry	Equilibrium	Equation[a]	Temperature (°C)	K (mol L^{-1})
1	**1** + ROH = **2** + AC	K_4 = ([**2**][AC])/([**1**][ROH]) = ((0.005)(0.005))/((0.005)(0.2))	25	0.03
2	**1** + ROH = **3**	K_3 = [**3**]/([**1**][ROH]) = (0.005)/((0.0005)(0.2))	−80	50
3	**1** + ROH = **3**	K_3 = [**3**]/([**1**][ROH]) = (0.0004)/((0.005)(0.2))	25	0.4

[a]AC, acetophenone; ROH, 1-phenylethanol.

osmium complex in isopropanol. The orange suspension gradually became a yellow solution with a small amount of suspended yellow solid. After 3.5 h, the reaction mixture was filtered through celite in air and diluted to twice the volume with acetone. The sample was analyzed by GC to determine an 80% conversion of acetophenone to 1-phenylethanol.

Preparation of racemic 1-phenylethanol-d_5

1-Phenylethanol-d_5 was prepared by deuterating 5 mL of neat acetophenone-CD_3 catalyzed by50 mg of RuH($NHCMe_2CMe_2NH_2$)(PPh_3)$_2$ at 15 atm of D_2 at 25 °C for 24 h. The resulting mixture was then distilled at reduced pressure under argon and stored over molecular sieves. Attempts to prepare $CH_3CD(OD)Ph$ from protio acetophenone using the same conditions resulted in deuterium scrambling into the methyl group of the product alcohol. The ^{1}H NMR spectrum using C_6D_6 and ^{2}H NMR spectrum using C_6H_6 of nondeuterated 1-phenylethanol was compared to the synthesized 1-phenylethanol-d_5 to confirm that the correct protons had been labelled.

Kinetics: concentration dependence studies

The hydrogenation reactions were carried out in a 50 mL Parr reactor fitted with a glass sleeve and magnetic stirrer. Standard solutions of **1**, acetophenone, and 1-phenylethanol in benzene were made to concentrations of 2.407×10^{-3}, 0.8323, and 0.8210 mol L^{-1}, respectively. Stock solutions were diluted by the required amount of benzene to achieve the desired concentrations. Catalyst solutions were made up to 2 mL separately from the ketone–alcohol solutions that were made up to 3 mL and drawn up into separate syringes. The reactor was degassed and pressurized to the desired pressure with hydrogen gas. The reactor was kept at a desired constant temperature with a Fischer Scientific Isotemp constant temperature bath. The ketone–alcohol solution was injected into the reactor under a flow of hydrogen followed by the catalyst solution, totaling 5 mL. Samples were removed at intervals by temporarily venting the reactor and drawing up a small aliquot by syringe and exposing it to air. The ratio of 1-phenylethanol to acetophenone in each aliquot was determined by GC.

Isotope effect studies

All of the hydrogenations were carried out at constant pressures of H_2 or D_2 using a stainless steel 50 mL Parr hydrogenation reactor fitted with a glass sleeve and a magnetic stirrer. The reactor was modified such that in one of the ports, a stainless steel sampling tube was added. The tubing was 30 cm in length with an inner diameter of 0.01 in. The tube was inserted to the bottom of the reaction vessel and then secured in place using a gas-tight compression fitting. A swing valve was then attached to the other end of the sampling loop. Samples were taken during the reaction by opening the swing valve, allowing an aliquot of the reaction mixture to be sampled.[2] For each data point, two aliquots of equal volume were removed from the reactor, the first of which was discarded. The hydrogenation kinetic study described above utilized a different sampling method that required the pressure in the reactor to be dropped to atmospheric pressure so that an aliquot of the reaction mixture could be extracted via syringe. Utilizing this newly developed sampling tube method, the data points could be obtained at smaller time intervals and also closer to the start of the reaction with minimal changes to the pressure. As well, the new sampling method allowed for double the number of data points to be obtained, leading to more accurate results. This setup minimized the loss of precious deuterium gas. Standard solutions of catalyst, acetophenone, and 1-phenylethanol in benzene were prepared by dissolving the desired amount in 10 or 5 mL volumetric flasks in an argon-filled glove box. Reaction mixtures were prepared by pipetting the appropriate amount of substrate and alcohol solutions into a 3 mL volumetric flask and catalyst solution into a 2 mL volumetric flask and diluting with benzene to give a total volume of 5 mL upon mixing. The substrate–alcohol solution and catalyst solution were taken up in a single 10 mL syringe and then injected into the reactor against a flow of gas. Samples were taken every 2 min. Concentrations of 1-phenylethanol were determined via GC. To ensure proper stirring, a specialized neodymium stirring bar was utilized and the stirring was checked before each reaction by placing the bottom of the reactor over the stir plate to ensure proper alignment of the stir plate and stir bar.

Without adequate stirring, diffusion of H_2 or D_2 into the solution does not occur as efficiently and the rate of the reaction proceeds extremely slowly.

Results

Like the ruthenium analogue RuH($NHCMe_2CMe_2NH_2$)(PPh_3)$_2$, the new osmium–amido complex **1** is an active ketone hydrogenation catalyst. With an acetophenone concentration of 0.17 mol L^{-1} in benzene and a ratio of acetophenone to **1** of 347:1 and the mild conditions of 5 atm of hydrogen and 20 °C, the turnover frequency (TOF) continuously increases, reaching a maximum of 0.4 s^{-1} with 98% conversion to 1-phenylethanol in 20 min. Under the same conditions using RuH($NHCMe_2CMe_2NH_2$)(PPh_3)$_2$, the TOF continuously decreases from an initial maximum TOF of 1 s^{-1}, achieving 99% conversion in 20 min (Fig. 2). The hydrido–chloro complex OsHCl(tmen)(PPh_3)$_2$ is a precatalyst that is activated by reaction with KOtBu. This combination can be used to hydrogenate neat acetophenone to 1-phenylethanol under the mild conditions of 1 atm of dihydrogen and room temperature. Reported osmium catalysts for the hydrogenation of ketones require higher temperatures (>80 °C).[12–18] An initial comparison of the kinetic behaviour of the osmium– and ruthenium–amido catalysts showed a distinct difference in the shape of the kinetic curves (Fig. 2). The major qualitative difference observed between the two different catalysts is that while the RuH($NHCMe_2CMe_2NH_2$)(PPh_3)$_2$ starts with a higher rate and slows down as the reaction progresses, the osmium catalyst **1** displays an induction period with a relatively low rate, which then increases as the reaction progresses. The decrease of the rate observed in reactions using the ruthenium catalyst is due to the increase in alcohol concentration, which reacts with the catalyst to form an alkoxide complex. The decrease in available catalyst is responsible for the decrease in reaction rate. To test whether alcohol concentration was responsible for the increasing rate observed when using the osmium catalyst **1**, the reaction was repeated with an initial concentration of 1-phenylethanol added to the reaction mixture.

The addition of 1-phenylethanol to the reaction mixture resulted in a marked increase in reaction rate compared to the initial reaction with no alcohol added. In Fig. 3, the plots of 1-phenylethanol concentration versus time are given for the reactions with and without alcohol. The observed induction time for the reaction without an

Fig. 2. A comparison of the course of the hydrogenation of acetophenone using the catalysts $RuH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ and $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$. [M] = 4.8×10^{-4} mol L^{-1}, $[acetophenone]_i$ = 0.1665 mol L^{-1}, 5 atm H_2, 5 mL of C_6H_6.

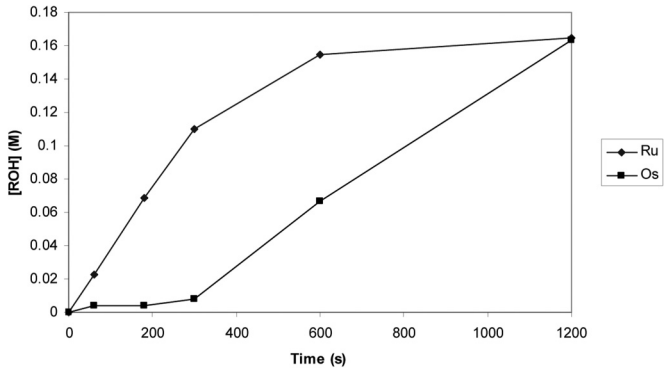
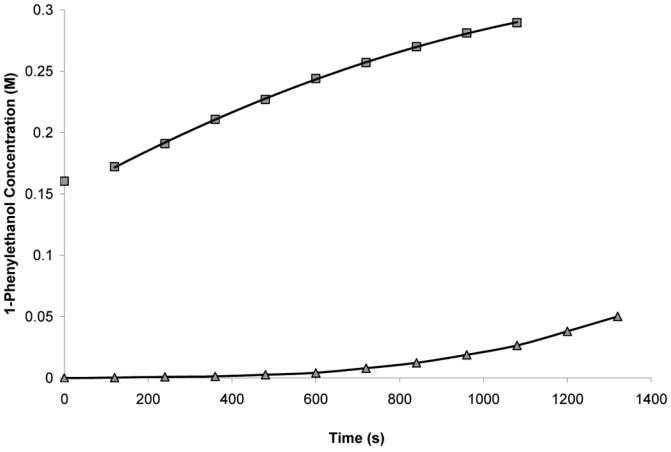


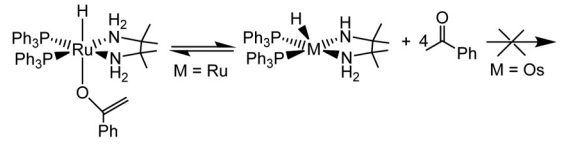
Fig. 3. The effect of 1-phenylethanol concentration on the rate of hydrogenation using complex **1** and acetophenone in benzene. [Os] = 3.19×10^{-4}, [acetophenone] = 0.1634 mol L^{-1}, 5 atm H_2, 20 °C, 5 mL of C_6H_6. $[1\text{-Phenylethanol}]_i$ = 0.1604 mol L^{-1} (squares), no initial 1-phenylethanol added (triangles).



initial concentration of alcohol has been eliminated in the reaction with alcohol added.

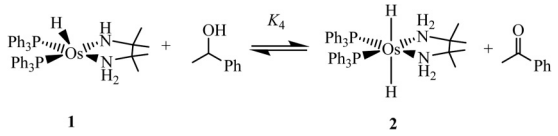
To examine the effects of the substrate and product on the catalyst, stoichiometric reactions of the amido–hydrido complex **1**, and product 1-phenylethanol and the substrate acetophenone were conducted. The results were unlike those of the analogous ruthenium complex $RuH(NHCMe_2CMe_2NH_2)(PPh_3)_2$, which resulted in alkoxide and enolate complexes.[1] Instead, no reaction was observed between acetophenone and **1**:

(1)



When **1** was reacted with 4 equiv. of 1-phenylethanol in C_6D_6, as in eq. 2, an equilibrium was established where some 1-phenylethanol was dehydrogenated to produce the dihydride **2** and acetophenone. Integration of the hydride peaks of **1** and **2** in the ^1H NMR spectrum indicate a 2:1 ratio of **1** to **2**. While the $^{31}P\{^1H\}$ signal at 37.1 ppm for **1** was sharp, the amido peak at 29.3 ppm was broadened. The experiment was performed in a closed NMR tube, which prevented any loss of hydrogen gas from **2** from leaving the system. Free hydrogen gas could not be detected in the ^1H NMR spectrum due to overlap with the methine hydrogen of 1-phenylethanol. No hydrogen is expected because the calculated concentration of acetophenone equals that of the concentration of the dihydride **2** within experimental error:

(2)



When 20 equiv. of 1-phenylethanol was added to **1** in C_6D_6 or toluene-d_8, the equilibrium shifted toward the dihydride **2**, now in a ratio of 1:1 with **1**. A broad resonance of the amido hydride is shifted downfield to –23.75 ppm from –23.85 in the absence of alcohol. This is actually the weighted average of the hydride chemical shifts of the amido complex **1** at –23.85 and a small amount of the alkoxide complex $OsH(OCHMePh)(tmen)(PPh_3)_2$ **3** at –22.5 ppm, which are in fast exchange. The last resonance can be observed when the solution is cooled to –80 °C. In fact, the equilibrium shifts dramatically toward the alkoxide complex at low temperature, as indicated by the equilibrium constants reported in Table 1. These were determined from the integration of proton resonances and relating these to the starting concentrations of **1** and alcohol. The alkoxide complex **3** has spectra very similar to those of $RuH(OR)(tmen)(PPh_3)_2$,[1] RuH(OCHMePh)(*R*-binap)(tmen),[1] and RuH(OCHMePh)(*R*-binap)((*R*,*R*)-$NH_2CHPhCHPhNH_2$)[19] reported previously. The reaction of the osmium–amido complex with water to produce a hydride hydroxide complex $OsH(OH)(tmen)(PPh_3)_2$ has also been reported but this is only observed when the added alcohol contains water.[20]

The ability of **1** to dehydrogenate 1-phenylethanol implied its activity as a transfer hydrogenation catalyst. To test its effectiveness as a transfer hydrogenation catalyst, **1** and acetophenone were stirred in 2-propanol under argon in a ratio of 55:1. After a period of 3.5 h, 80% conversion of acetophenone to 1-phenylethanol was achieved with a TOF of 13 h^{-1}. It is of note that this is much slower than the TOF of 0.4 s^{-1} achieved for the preliminary H_2 hydrogenation described above (Figs. 2 and 3). Turnover frequencies of 120 and 60 h^{-1} were achieved for the transfer hydrogenation of acetophenone using $OsH_2Cl_2(P^iPr_3)_2$ and $OsH_2Cl_2(PMe^tBu_2)_2$, respectively, as catalysts in Werner's group.[17] Although both reported TOF are higher, it should be noted that they performed their reactions at 83 °C, while we performed ours at room temperature.

Kinetics

Kinetic experiments were performed to determine the effect of the catalyst, substrate, and hydrogen concentrations on the rate of hydrogenation of acetophenone to 1-phenylethanol using **1** as a catalyst. Previous results from preliminary hydrogenation experiments using **1** indicated that the rate of hydrogenation was increased by the presence of the product alcohol (Fig. 3). Therefore, kinetic experiments were needed with an alcohol present at the start. The fact that **1** is also a transfer hydrogenation catalyst precluded the use of 2-propanol as a solvent due to competing transfer and H_2 hydrogenation processes. Instead, the kinetic experiments were performed in benzene as the solvent, and nearly equal concentrations of the substrate acetophenone and the product 1-phenylethanol were added before beginning the hydrogenation. The faster alcohol-assisted rate (Table 2) was thereby achieved throughout the hydrogenation and any transfer hydrogenation from 1-phenylethanol to acetophenone had no net effect on the concentration of the substrate or product.

The effect of the catalyst concentration on the rate of the reaction can be seen in Fig. 4. As the concentration of **1** is increased, keeping the hydrogen pressure and initial substrate and alcohol

Table 2. Dependence of the rate of production of alcohol catalyzed by **1** on the concentrations of **1**, H_2, acetophenone, and temperature.

Run	[**1**] (mol L^{-1})	Pressure H_2 (atm); [H_2] (mol L^{-1})	[Ketone] (mol L^{-1})	Temperature (K)	Rate r (mol L^{-1} s^{-1})	$k = r/([Os][H_2])$ (mol L^{-1} s^{-1})
1	9.6×10^{-5}	5.0; 1.32×10^{-2}	0.1665	293	4.6×10^{-5}	36
2	4.8×10^{-5}	5.0; 1.32×10^{-2}	0.1665	293	2.1×10^{-5}	33
3	1.4×10^{-4}	5.0; 1.32×10^{-2}	0.1665	293	8.3×10^{-5}	45
4	9.6×10^{-5}	5.0; 1.32×10^{-2}	0.1332	293	4.5×10^{-5}	36
5	9.6×10^{-5}	5.0; 1.32×10^{-2}	0.1998	293	5.8×10^{-5}	46
6	1.4×10^{-4}	2.0; 5.28×10^{-3}	0.1665	293	4×10^{-5}	26
7	1.4×10^{-4}	5.0; 1.32×10^{-2}	0.1665	293	6.0×10^{-5}	32
8	1.4×10^{-4}	9.0; 2.38×10^{-2}	0.1665	293	9×10^{-5}	26
9	1.4×10^{-4}	14.0; 3.8×10^{-2}	0.1665	293	10×10^{-5}	26
10[a]	2.7×10^{-4}	5.0; 1.32×10^{-2}	0.1665	293	9.3×10^{-5}	26
11[a]	2.7×10^{-4}	5.0; 1.36×10^{-2}	0.1665	298	1.03×10^{-4}	28
12[a]	2.7×10^{-4}	5.0; 1.39×10^{-2}	0.1665	303	1.16×10^{-4}	31
13[a]	2.7×10^{-4}	5.0; 1.24×10^{-2}	0.1665	288	7.4×10^{-5}	22
14[a]	2.7×10^{-4}	5.0; 1.19×10^{-2}	0.1665	283	6.1×10^{-5}	19

Note: Initial 1-phenylethanol concentration = 0.164 mol L^{-1}.
[a]Temperature varied; different setup and catalyst batch.

Fig. 4. The effect of osmium concentration on the initial rate of acetophenone hydrogenation (runs 1–3 in Table 2). [1-Phenylethanol]$_i$ = 0.1642 mol L^{-1}, 5 atm H_2, [acetophenone]$_i$ = 0.1665 mol L^{-1}, 5 mL of C_6H_6. Molar osmium concentrations are given in the legend.

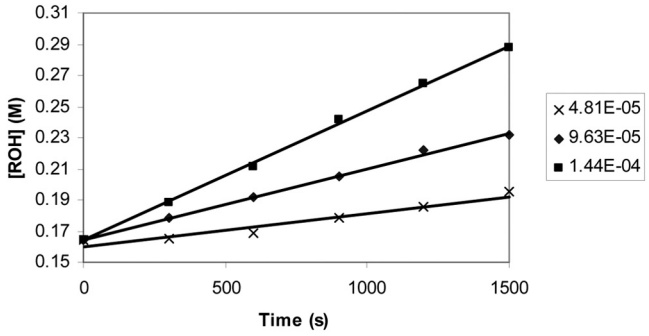
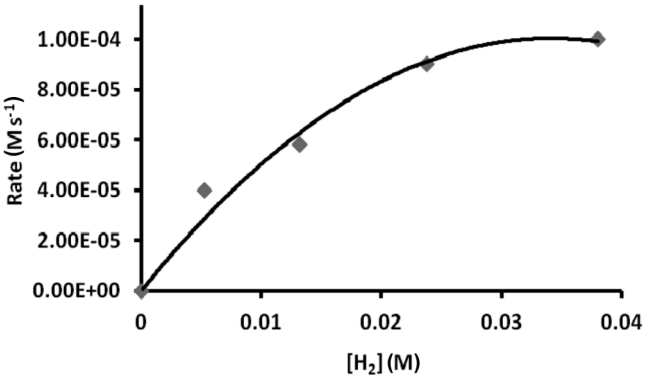


Fig. 5. The effect of hydrogen concentration on the initial rate of acetophenone hydrogenation (runs 6–8 in Table 2). [Os] = 1.44×10^{-4} mol L^{-1}, [acetophenone]$_i$ = 0.1665 mol L^{-1}, [1-phenylethanol]$_i$ = 0.1642 mol L^{-1}, 5 mL of C_6H_6. Hydrogen pressures 2, 5, 9, and 14 atm, respectively.



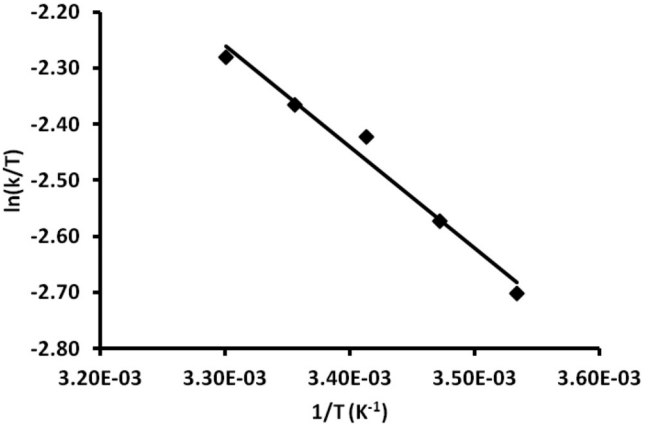
concentrations constant, the rate of hydrogenation increases proportionally.

When the concentration of **1** and the initial concentration of product, along with the pressure of hydrogen, were kept constant and the substrate concentration was varied, no change in the rate of hydrogenation was observed. The straight lines observed in all of the kinetic experiments reinforces the fact that there is no dependence on the substrate concentration. The linearity also means that, although the presence of alcohol increases the rate of reaction compared to the rate of reaction in the absence of alcohol, the reaction is not directly dependent on the concentration of the alcohol. This is consistent with the observation of constant rate to complete conversion. Varying the hydrogen pressure (and thereby the hydrogen concentration) and keeping the catalyst concentration and the initial substrate and alcohol concentrations constant caused an increased rate of hydrogenation with higher hydrogen pressures (Fig. 5). The hydrogen concentration dependence is more complicated than that of previously reported ruthenium systems. At pressures lower than 5 atm, we assume that the rate is first order in hydrogen concentration but that at higher pressures, another step becomes rate determining and the hydrogen pressure dependence levels off.

Thus, the rate law for the alcohol-assisted hydrogenation of acetophenone using **1** as a catalyst at up to 5 atm H_2 is given by

$$(3)\quad \text{Rate} = \mathrm{d}[1 - \text{phenylethanol}]/\mathrm{d}t = -\mathrm{d}[\text{acetophenone}]/\mathrm{d}t = k[1][H_2]$$

Fig. 6. An Eyring plot for temperatures ranging from 283 to 303 K (runs 10–14 in Table 1).



At a temperature of 20 °C, a rate constant k of 34 mol L^{-1} s^{-1} was obtained. By contrast, the analogous ruthenium complex has the same rate law with k of 1.1×10^2 mol L^{-1} s^{-1}.[1] Thus, the ruthenium complex is three times more active under comparable conditions. The temperature dependence (and isotope effect studies) were

Table 3. Average initial reaction rates, rate constants k, and the isotope effects using catalyst **1**.

Kinetic run H^*_2/PhCOCH$^*_3$/ROH*	Rate of reaction, ν_0 (10^{-5} mol L^{-1} s^{-1})	Rate constant k = ν_0/([Os][H_2]) (mol L^{-1} s^{-1})	Isotope effect (k_H/k_D)
HHH	11±1	26	
HHD	11±1	26	1.0±0.1
HDD	11±1	26	1.0±0.1
DDD	10±1	24	1.1±0.1

Note: Runs were carried out using a single syringe in which the catalyst, substrate, and alcohol were mixed prior to injection into the reactor. [Os] = 3.18×10^{-4} mol L^{-1}, [acetophenone] or [acetophenone-d^3] = 0.163 mol L^{-1}, [1-phenylethanol] or [1-phenylethanol-d^5] = 0.160 mol L^{-1}, 5 atm of H_2 or D_2 = 1.32×10^{-2} mol L^{-1}, 20 °C, 5 mL of C_6H_6.

determined using a different reactor setup and batch of catalyst. The rate constant in this case was 26 mol L^{-1} s^{-1} at 293 K. The Eyring plot (Fig. 6) used five rates from temperatures spaced 5° apart from 10 to 30 °C. The thermodynamic values for activation enthalpy and entropy are $\Delta H^{\ddagger}$ = 3.7 kcal mol^{-1} and $\Delta S^{\ddagger}$ = –39 cal mol^{-1} with a Gibbs free energy of activation of $\Delta G^{\ddagger}$ (293 K) = 15 kcal mol^{-1}. The values correspond to a transition state that is more ordered than the reactants due to the loss of entropy of the gaseous hydrogen.

Isotope effect measurements

The rate data to probe isotope effects were collected in at least triplicate to improve the accuracy of the data (Table 3). The error in the rates is 10%. The experiments requiring deuterium gas were measured at 5 atm D_2 pressure. A few runs that gave a value that deviated by more than 10%, probably because of leak or impurity, were rejected. The purity of the catalyst was verified weekly by ^1H and ^{31}P NMR and by the standard rate generated by the all-protio system.

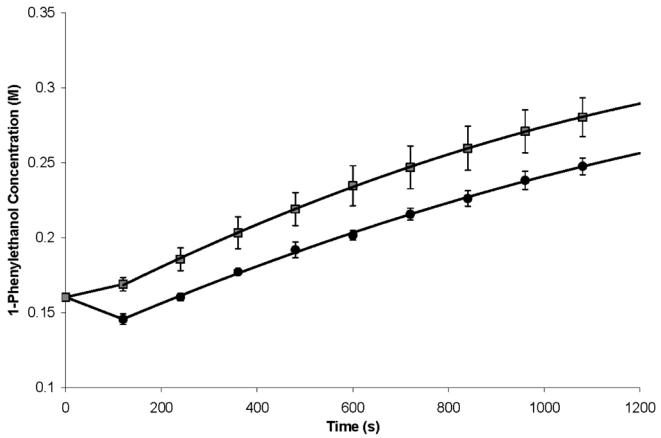
To differentiate between the protio and deutero gas, acetophenone, and 1-phenylethanol for each run, a three-letter designation code was used such that the first letter of the code represents the gas, the second letter the ketone, and the third letter the alcohol that was used in the experiment. H is used for protio species, while D is used for deutero species. For example, a set of runs that used H_2 gas, protio acetophenone, and protio 1-phenylethanol would be designated HHH.

A typical comparison of plots for the HHH and DDD runs is shown in Fig. 7. The slight delay in the first 60 s is likely to be associated with temperature changes when the solution is added to the reactor and dissolution of gas into the solution, slower for deuterium. The lower initial pressure of gas allows the reverse of reaction 4, the dehydrogenation/dedeuteration of the added alcohol, to occur, resulting in an initial drop in alcohol concentration.

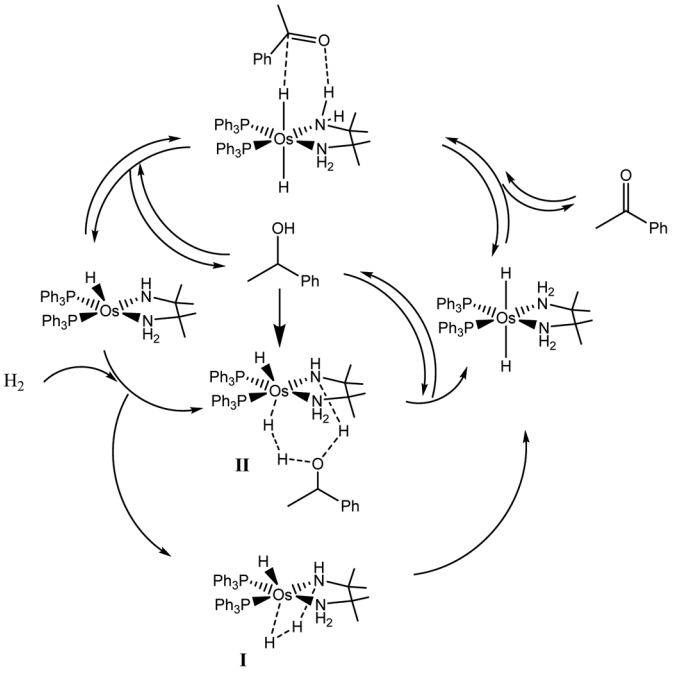
Discussion

The rate law for the hydrogenation of acetophenone catalyzed by **1** in the presence of excess product alcohol with pressures less than 5 atm displays a dependence on the concentration of catalyst and the concentration of hydrogen. This indicates that the rate-limiting step involves the addition of hydrogen to the catalyst, a feature similar to the system using the ruthenium hydrido–amido complex RuH(NHCMe$_2$CMe$_2$NH$_2$)(PPh$_3$)$_2$ as a catalyst.[1] What is not taken into account is the effect of alcohol on the rate. At relatively low concentrations of alcohol (~ <0.02 mol L^{-1}), the rate of hydrogenation is slower than that when higher concentrations of alcohol are present (~ >0.02 mol L^{-1}) (Fig. 3). Yet at higher alcohol concentrations, the rate of hydrogenation is independent of alcohol concentration. The alcohol is changing the nature of the rate-limiting step in such a way as to lower the activation energy of that transition state. At low concentrations of alcohol, the hydrogenation reaction operates by a slow mechanism, and at higher concentrations of alcohol, it operates by a faster "alcohol-assisted" mechanism. The non-alcohol-assisted mechanism (**I** in Scheme 1) is the same as that proposed for the analogous ruthenium system,[1] where hydrogen is heterolytically split across a metal–amido bond generating a metal hydride and amine. The

Fig. 7. Sample plot of the HHH (squares) and DDD (circles) runs. The error bars represent one standard deviation.

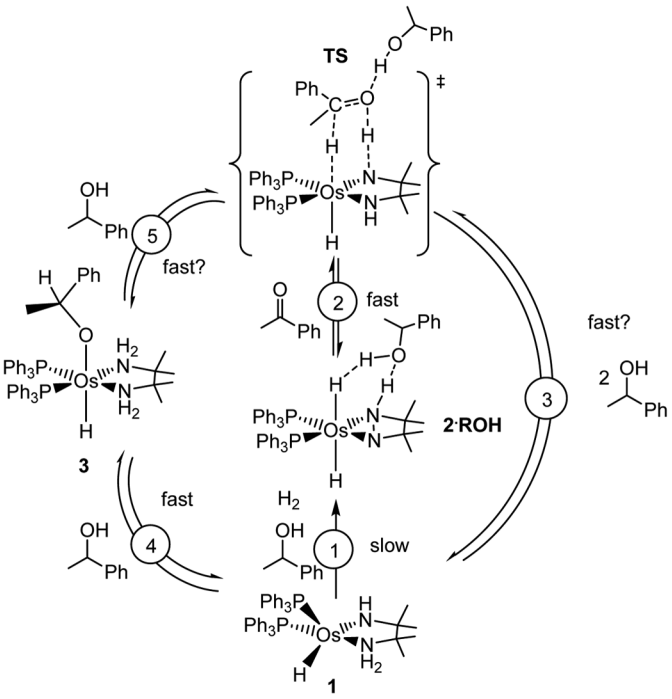


Scheme 1. A possible mechanism for the hydrogenation of acetophenone to 1-phenylethanol using OsH(NHCMe$_2$CMe$_2$NH$_2$)(PPh$_3$)$_2$ as a catalyst: the nonassisted splitting of dihydrogen (I) and the alcohol-assisted splitting of dihydrogen (II).



alcohol-assisted mechanism (**II** in Scheme 1) involves a six-membered ring consisting of the metal center, a molecule of hydrogen, the OH of a molecule of alcohol, and the amido nitrogen (Fig. 1). Rather than splitting hydrogen directly across the osmium–amido bond, the hydrogen is split between the metal and alcohol oxygen, while the amido nitrogen is protonated by the alcohol pro-

Scheme 2. Routes to explain the formation of the alkoxide complex **3**.



ton. This proton shuttle mechanism is proposed to facilitate the addition of hydrogen to the catalyst, thereby raising the rate of hydrogenation. This alcohol effect was not observed for the related ruthenium system,[1] and this likely reflects the higher reactivity of the Ru–N(amido) bond compared to the Os–N bond toward dihydrogen and other small molecules.[9,21]

The observed KIEs are negligible or small, with a value of 1.1 ± 0.1 for the DDD system, comparing the all-protio system with the system using deuterium gas, deuterated acetophenone (at the methyl), and deuterated alcohol (except for the phenyl group) (Table 3). Deuteration of the gas and substrate does not seem to significantly affect the rates (the DDH and DHH systems have a KIE of 1.0 ± 0.1). The value of 1.1 contrasts with the ruthenium system *trans*-RuH_2(tmen)(binap), which has a k_H/k_D of 2.1 ± 0.1 for the direct heterolytic splitting of dihydrogen/dideuterium across the Ru–N(amido) bond in benzene.[2] The proton shuttle mechanism like that shown in Scheme 1 appears to lack a KIE. Density functional theory is currently being applied to further interpret this result and understand this mechanism more deeply.

NMR experiments to examine the reaction of alcohol with complex **1** have revealed several details. The triplet hydride resonance of the dihydride **2** in the presence of alcohol is broadened to a peak width of 18 Hz at 600 MHz at 25 °C. This is attributed to the formation of an OsH···HOR dihydrogen bond (hydridic protonic interaction) as shown in **2**.**ROH** in Scheme 2; this causes a shortening of the T_1 and broadening of the hydride resonance[22–29] A detail still to be determined is the route followed when **1** reacts with alcohol to give the dihydride **2** and the alkoxide **3** (Scheme 2). This is the equivalent question, discussed in the literature, as to whether such dihydride complexes react with acetophenone to give directly the alcohol and the amido complex **1** via H^+/H^- transfer to the ketone in the transition state (path 2 to a polarized **TS**, then path 3 to **1**, and then path 4 to the alkoxide complex **3** of Scheme 2)[1,2,4,5,7,30] or to give an alkoxide complex **3** via an initial hydride transfer (path 2 to an ion pair **TS** that includes a hydrogen-bonded alkoxide and then path 5 to complex **3** in Scheme 2).[19,31–36] Arguments have been made for each pathway depending on the solvent and other conditions. An observation in the current work is that the alkoxide forms quickly from the amido complex and alcohol and is more prevalent at low temperatures. In the low dielectric constant solvent benzene, hydride transfer from **2** to acetophenone to give a transient free alkoxide seems unfavourable, making a concerted H^+/H^- transfer route more likely, as proposed previously for catalysts operating in benzene–alcohol mixtures.

Conclusions

The synthesis of the amino–amido complex of osmium $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ has allowed a detailed study of the (base-free) hydrogenation of acetophenone in benzene catalyzed by this well-defined complex. This osmium complex can split dihydrogen across its metal–amido bond to produce a *trans*-dihydride **2** and this behaviour is somewhat analogous to the ruthenium complex $RuH(NHCMe_2CMe_2NH_2)(PPh_3)_2$. Where the osmium complex differs from the ruthenium complex is in the reactivity of the amido nitrogen. Stronger bonding between osmium and the amido nitrogen makes it less reactive than the ruthenium counterpart.[9] The osmium–amido complex can act as a transfer hydrogenation catalyst as well as a H_2 hydrogenation catalyst. It acts most efficiently as a direct hydrogenation catalyst for acetophenone when alcohol is present.

The kinetic isotope effect has been determined experimentally for the homogeneous hydrogenation of ketones using $OsH(NHCMe_2CMe_2NH_2)(PPh_3)_2$ (**1**) and found to be about 1.1 ± 0.1. The next step will be to use density functional theory calculations to assist in finding a mechanism that explains the lower KIE for osmium than the value of 2.1 found for the related ruthenium system $RuH_2(NH_2CMe_2CMe_2NH_2)$(*R*-binap).

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