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Aqueous organometallic chemistry. 3. Catalytic hydride transfer reactions with ketones and aldehydes using $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ as the precatalyst and sodium formate as the hydride source: Kinetic and activation parameters, and the significance of steric and electronic effects

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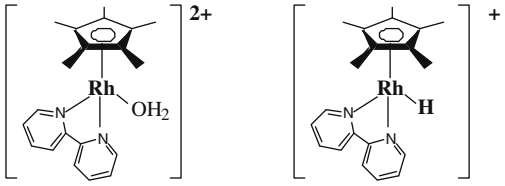
ABSTRACT

The reaction of a precatalyst, $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ (**1**), with sodium formate provided the hydride complex, $[Cp^*Rh(bpy)(H)]^+$ (**2**), *in situ*, at pH 7.0, which was then evaluated in an aqueous, catalytic hydride transfer process with water soluble substrates that encompass 2-pentanone (**3**), cyclohexanone (**4**), acetophenone (**5**), propionaldehyde (**6**), benzaldehyde (**7**), and *p*-methoxybenzaldehyde (**8**). The initial rates, r_i, of appearance of the reduction product alcohols at 23 °C provided a relative rate scale: **8** > **7** ≈ **6** > **5** > **4** > **3**, while the effect of concentration of substrate, precatalyst, and sodium formate on r_i, using **7** as an example, implicates $[Cp^*Rh(bpy)(H)]^+$ formation as the rate-limiting step. The experimental kinetic rate expression was found to be: $d[\text{alcohol}]/dt = k_{cat}[\mathbf{1}][HCO_2Na]$; substrate being pseudo zero order in water. The steric effects were also analyzed and appeared to be of less importance intra both the ketone and aldehyde series, but an inter series comparison appeared to show that the aldehydes had less of a steric effect on the initial rate, i.e., **7** > **4** by a factor of 3.6, while the aldehyde series appeared to have some moderate electronic influence on rates, presumably via electron donation to increase binding to the Cp*Rh metal ion center, in accordance with these proposed concerted binding/hydride transfer reactions. A proposed catalytic cycle will also be presented.

1. Introduction

Recently, we demonstrated the usefulness of the [η^5-pentamethylcyclopentadienyl)rhodium(η^2-(N,N)-2,2′-bipyridine)(aqua)] $(OTf)_2$ complex, $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ (**1**), as a precatalyst for the regioselective reduction of *N*-benzylnicotinamide triflate, an NAD^+ model, in the presence of sodium formate as the hydride source, using 1:1 H_2O/THF as one solvent system, as well as an aqueous NAD^+ model, β-nicotinamide ribose-5′-methyl phosphate, at pH 6.5, to exclusively provide the kinetic 1,4-dihydro product [1,2]. An extensive kinetic and mechanistic study also showed that the 1,4-dihydro regioselectivity was a consequence of binding of the 3-amide carbonyl group to the Cp*Rh metal ion center [2]. In an effort to extend the scope of aqua complex **1** in catalytic reactions, we have studied its reactivity to ascertain whether the *in situ* generated hydride, $[Cp^*Rh(bpy)(H)]^+$ (**2**), formed by reaction of **1** with sodium formate, would have utility in other aqueous, catalytic hydride transfer reactions, and furthermore, to test our recently published mechanism that demonstrated the importance of coordination of the substrate to the η^5-Cp*Rh metal center during the concerted hydride transfer process [2].



1 **2**

Previous studies of organometallic hydride complexes in aqueous, and/or biphasic media reduction reactions with water soluble/insoluble substrates, such as substituted olefins, aldehydes, ketones, and halogen substituted carboxylic acids, have been reported by various groups, with a focus on structure-activity relationships, while the evaluation of kinetic, thermodynamic, steric, and electronic parameters were still aspects that needed further scrutiny [3]. We also preface our remarks about the previous studies with the fact that

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[1] RHF would like to dedicate this contribution on aqueous organometallic chemistry to Ferenc Joó, friend and colleague, in honor of his 60th birthday.

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precatalyst **1** had been tested in the direct reduction of phenethylmethyl ketone in water, in the presence of sodium formate as the hydride source, by Steckhan and coworkers [4a]. However, in those reported studies, the ketone reduction reaction was actually a "*control experiment*" for the main enzymatic reactions using *in situ* generated 1,4-NADH, from the reduction of natural NAD^+ with **2** [4b], to affect ketone reduction reactions in the presence of the enzyme, horse liver alcohol dehydrogenase (HLADH), and provide chiral alcohols. This latter study [4a] showed that the direct ketone reduction with **2** was not favored in the presence of the better Cp*Rh binding substrate, NAD^+, and that HLADH enzymatic ketone reductions to chiral alcohols prevailed (>99% ee); significant direct reduction of the ketone substrate by **2** would have compromised the % enantioselectivity, but these authors found no significant direct hydride reduction of their ketone substrate (<7% with phenethylmethyl ketone) in their control experiments, and thus, no further experiments on any direct hydride reductions with *in situ* generated **2** and aldehydes/ketones in water were reported by those authors.

More importantly, in our own independent studies using biomimetic model NAD^+ compounds with *in situ* generated **2** in water, in similar chiral reductions of ketones with HLADH [5], we found that the direct reduction "*control experiments*" of a variety of ketones *were in fact favored in the absence of NAD$^+$ or their biomimetic models*. Therefore, as stated, we wanted to expand the scope of aqueous reduction chemistry of **2** by evaluating structure-activity relationships, mechanistic details, and determine kinetic, thermodynamic, steric, and electronic parameters, in this example, by studying a variety of aldehydes and ketones in water at pH 7.0, and at RT.

Moreover, several earlier reports, for example, with *in situ* formed $[(Cp^*Ir)_2(\mu\text{-}H)(\mu\text{-}OH)(\mu\text{-}HCOO)]^+$ showed catalytic ketone and aldehyde substrate reduction ability [3f–h]. These initial studies by Ogo et al. were conducted at a low pH (3.2) [3f,g], where protonation of the *in situ* formed Cp*Ir-μ or η^1-H to produce H_2 could possibly compete with hydride transfer to substrate, thereby mitigating the carbonyl reduction reaction, as well as, from further pH mediated equilibria with, for example, a catalyst precursor, such as $[Cp^*Ir(H_2O)_3]^{2+}$. Moreover, those initial studies were not conducted at high concentrations of formate ion (saturation kinetics), which further limited catalytic activity, and inhibited mechanistic interpretations, including understanding the importance of binding of the substrate to the Cp*Ir metal ion center [1,2]. More recently, Ogo et al. [3i,j] did study various parameters mentioned above with both $[\eta^6\text{-}C_6Me_6)Ru(bpy)(H)]^+$ and $[Cp^*Ir(bpy)(H)]^+$ hydride complexes, and various ketones at pH 4.0 and 2.0, respectively, from 25 to 70 °C, where the higher temperatures caused turnover numbers to be greater, and steric and electronic effects were not dominant. These authors preferred a mechanism where the substrate was not directly binding to the Cp*Ir metal ion center; but rather, acid promoted transfer hydrogenation with no metal–substrate involvement. Furthermore, previous studies by Darensbourg et al. with an aqueous phase soluble $(PTA)_4RuCl_2$ precatalyst, for reductions (sodium formate) of aromatic and aliphatic aldehydes (biphasic reaction conditions) also showed no apparent steric or electronic effects, including other data on inhibition by CO of the reduction reaction, which to our thinking, may have a potential mechanism that included binding of the carbonyl substrate to the Ru(II) metal ion center [3k]. Kuo et al. have studied $[Cp_2MoH(OTf)]$ in aqueous reductions of acetone and substituted derivatives [3n]. In their postulated mechanism, binding of the ketone to the Mo metal ion center occurred with hydride transfer, while electron-withdrawing groups on the acetone nucleus structure facilitated hydride transfer to the carbonyl carbon atom. An excellent overview on transition metal carbonyl hydride mechanisms and applications was published by Bullock and coworkers [6].

Therefore, we present our recent results on the use of *in situ* generated **2** in catalytic hydride transfer reactions that provided a structure-activity relationship with regard to ketone and aldehyde substrates, and delved into factors such as steric and electronic parameters to observe any conceivable effects on the initial rates of reduction. We also studied the kinetics and activation parameters of this reaction with regards to concentrations of substrate, precatalyst **1**, and sodium formate, on the initial rates of reaction, to provide insights into the mechanism of reduction, and to present a plausible catalytic cycle for the reduction of the ketone and aldehyde substrates.

2. Results and discussion

2.1. Structure-activity relationships: steric and electronic effects

The reactivity of *in situ* generated **2** in catalytic hydride transfer reactions was evaluated in aqueous solution at pH 7.0 (buffered) at 23 °C with various water soluble ketone and aldehyde substrates that encompassed: 2-pentanone (**3**), cyclohexanone (**4**), acetophenone (**5**), propionaldehyde (**6**), benzaldehyde (**7**), and *p*-methoxybenzaldehyde (**8**) (Chart 1), using GC and GC/MS techniques to follow the initial rates/turnover frequencies, and establish a structure-reactivity relationship (Table 1).

The initial rates of appearance of the reduction product alcohols, r_i ($M\,s^{-1}$), provided a relative rate scale: **8** > **7** ≈ **6** > **5** > **4** > **3**, and thus, it appeared that steric effects were more pronounced with the ketone series in comparison to the aldehyde series, while the electronic effects with aldehydes also appeared to influence their reactivity over the ketones; aldehyde **8**, 6 times faster than ketone **4**, and 1.5 times faster than **7**, presumably due to the electron-donating *p*-methoxy group on the benzene ring that apparently moderately increased carbonyl group binding to the η^5-Cp*Rh metal ion center. This binding phenomena of substrate to the η^5-Cp*Rh metal ion center was also found recently to be crucial for the regioselective reduction of various NAD^+ models, *N*-benzyl-3-substituted pyridium triflate salts in 1:1 THF/H_2O with **2** [1,2], as well as, an aqueous NAD^+ model, β-nicotinamide ribose-5′-methyl phosphate [2].

Furthermore, as stated, aryl aldehyde, **8**, was slightly faster than aryl aldehyde, **7**, as well as alkyl aldehyde, **6**; therefore, aldehydes, **6**–**8**, were ~2 to ~20 times more reactive than the one aryl and two alkyl ketones studied. Moreover, in the ketone series, the relative rate sequence, **5** > **4** > **3**, also defined that steric effects were not significant and that electronic effects were relatively more important, although the sterically less demanding alkyl cyclic ketone, **4**, was somewhat faster in the reduction reaction over alkyl ketone, **3**, by a relative rate factor of 3.6. The electronic effect of the aryl group directly bonded to the carbonyl appeared to moderately affect the relative rates for the series of ketones, which, in our opinion, implies phenyl group donation to increase electron density at the carbonyl oxygen. Thus, this electronic effect was less effective for the aldehyde series in going from **6** to

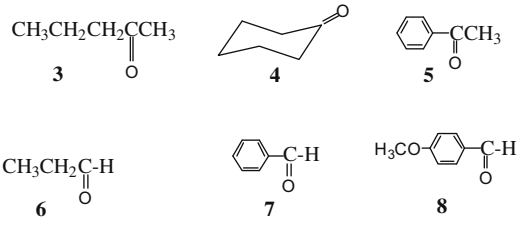
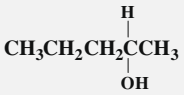
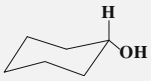
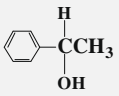
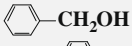
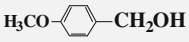


Chart 1.

Table 1
Ketone and aldehyde reduction products, initial and relative rates, and turnover frequencies[a].

Substrate	Product	Initial rate (r_i, M s^{-1})	Relative rate	TOF (h^{-1})
3		6.9×10^{-6}	1.0	1.0
4		2.5×10^{-5}	3.6	3.0
5		3.8×10^{-5}	5.6	5.0
6	$CH_3CH_2CH_2OH$	8.3×10^{-5}	12	10.0
7		9.1×10^{-5}	13	11
8		1.3×10^{-4}	20	15

[a] A general procedure for all the kinetic experiments was as follows: a 10 mL aliquot of the sodium formate solution (deoxygenated, 0.31 M in buffer NaH_2PO_4/Na_2HPO_4, 0.1 M, pH 7.01–7.04)) was transferred with a gas-tight syringe into a volumetric flask (25 ml) with a stir bar under N_2. Then, for example, benzaldehyde, **7**, (31.5 μL, 32.9 mg, 0.29 mmol) and 10 μL of ethyl acetate (internal standard) were added to the reaction mixture, followed by 100 μL of a 0.050 M stock solution of [Cp*Rh(bpy)(H_2O)]($OTf)_2$, **1**, via syringe, and the total solution rapidly mixed at 23 °C in a controlled temperature bath. The reaction progress was followed by GC and GC–MS.

8 with a relative rate ratio of **6**/**7** = 1.08, while the steric effect was also apparently not critical in the aldehyde series. To reiterate, any increase in electron density on the carbonyl group; i.e., a better σ-donating carbonyl oxygen, facilitates binding to the η^5-Cp*Rh metal ion center, presumably in concert with hydride transfer. Therefore, the overall picture from the results in Table 1 showed that the steric parameters have a moderate effect on rate, while the electronic effects were evident, but were rather subtle, with a relative rate scale of ketone and aldehyde reactivity, spanning a small range of 1–20.

2.2. Mechanistic aspects: kinetic and activation parameters

The mechanisms for these aqueous, catalytic hydride transfer reactions with ketone and aldehyde substrates, utilizing **2** as the catalyst, would be important to elucidate to adequately describe the reaction pathways for this process in water [3]. Therefore, the effect of concentration of one of the substrates, **7**, precatalyst, **1**, and sodium formate, on the initial rates of reduction, r_i , at low conversions to the alcohol product (~10%), was studied, and indeed, r_i was found to be dependent on the concentrations of precatalyst **1**, and formate ion from the plots of r_i (M s^{-1}) vs. [precatalyst **1**, and formate ion (M)], but not on the concentration of the substrate, **7**. We surmised from the results with substrate **7** that the concentrations of all the ketone or aldehyde substrates studied were all pseudo zero order. Further verification of the reaction order with one representative substrate, **7**, catalyst **2**, and formate ion as determined from plots of ln r_i vs. ln [**7**], ln [**1**], and ln [HCO_2-Na], provided slopes of 0.0, 1.0, and 1.0, respectively.

The experimental rate-law being: $d(\mathbf{CHOH})/dt = k_{cat}[\mathbf{1}][HCO_2\text{-Na}]$ with k_{cat} = 6.81 M^{-1} s^{-1} at 295.6 K.

The lack of significant steric parameters, but subtle electronic effects, on the initial and relative rates of carbonyl reduction shown in Table 1 appeared to implicate both coordination of the substrate ketone or aldehyde to the η^5-Cp*Rh metal ion center with concerted hydride transfer, as we discovered previously for the NAD^+ models [1,2], while the kinetic results showed that [Cp*Rh(bpy)(H)]$^+$, **2**, formation was presumably the rate-limiting step; even though the substrate does not appreciably effect the rate, we surmised that binding of substrate to the Cp*Rh metal ion center was a critical step for hydride transfer to the carbonyl carbon. Therefore, the following equations and equilibria could be established for our mechanistic interpretations of the observed reductions of the ketone/aldehyde substrates, Eqs. (1)–(4), in analogy with the biomimetic NAD^+ reduction with **2** [2]:

$$[\mathrm{Cp*Rh}(\underset{\mathbf{1}}{\mathrm{bpy}})(H_2O)]^{2+} + HCO_2^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} [\mathrm{Cp*Rh}(\underset{\mathbf{A}}{\mathrm{bpy}})(O_2CH)]^+ + H_2O \quad (1)$$

$$[\mathrm{Cp*Rh}(\underset{\mathbf{A}}{\mathrm{bpy}})(O_2CH)]^+ \xrightarrow{k_3} [\mathrm{Cp*Rh}(\underset{\mathbf{B}}{\mathrm{bpy}})H]^+ + CO_2 \quad (2)$$

$$[\mathrm{Cp*Rh}(\underset{\mathbf{B}}{\mathrm{bpy}})H]^+ + \underset{\mathrm{RCH}}{\overset{\mathrm{O}}{\parallel}} \underset{k_5}{\overset{k_4}{\rightleftharpoons}} [\mathrm{Cp*Rh(bpy)}(\underset{\mathbf{C}}{\eta^1\text{-}O\text{-}OCH_2R})]^{2+})] \quad (3)$$

$$[\mathrm{Cp*Rh(bpy)}(\underset{\mathbf{C}}{\eta^1\text{-}O\text{-}OCH_2R})]^{2+})] + H_3O^+ \xrightarrow{k_6} 1 + RCH_2OH \quad (4)$$

Since the concentration of the intermediate **A** was not zero, but had very little change with time, and that of intermediates **B** and **C** never in appreciable quantities, it was appropriate to apply the steady-state approximation to them. Moreover, a Michaelis–Menten saturation kinetic effect, indicative of a pre-equilibrium, was observed experimentally for formate ion (Eq. (1)). In order to obtain a simplified final rate-law equation, the concept of a rate-determining step involved in the mechanism was studied (see supporting information). Thus, two possibilities were proposed for the putative rate-limiting step: (1) the formation of the [Cp*Rh(bpy)H]$^+$, intermediate **B** in Eq. (2); or less likely, (2) the formation of the substrate-**B** complex, intermediate **C** in Eq. (4), where we have combined the binding and hydride transfer steps to simplify the kinetic interpretation. If indeed the formation of [Cp*Rh(bpy)H]$^+$ was the rate-determining step, then $k_3 << k_4$.

Therefore, the formation of [Cp*Rh(bpy)H]$^+$ was proposed as the rate-limiting step in the reduction of the aldehydes and ketone substrates, and this postulate was in agreement with the experimental rate orders (ln, ln plots, Supporting Information) found in aqueous media: [**1**], 1.0; [HCO_2Na], 1.0 and [**7**] 0.0, respectively. As a result, the initial rate of formation of the alcohol product was independent of the substrate concentration (**3**–**8**) under these aqueous reaction conditions and provided a zero order for substrate, which was consistent with our previous regioselective reduction results with an aqueous NAD^+ model and NAD^+ itself with **2** at pH 6.5 [1,2]. Although the rate-determining step was thought to be [Cp*Rh(bpy)H]$^+$ formation, binding to the Cp*Rh metal center was assumed to be critical for alcohol formation; in the reduction of the biomimetic NAD^+ model, *N*-benzylnicotinamide triflate, with **2**, in 1:1 THF/H_2O, the rate-

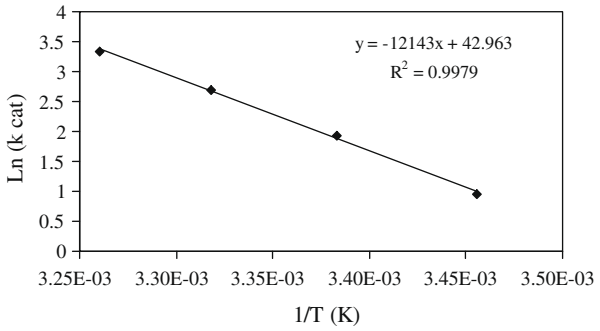


Fig. 1. Arrhenius plot of ln k_{cat} vs. $1/T$ for substrate **7**.

determining step was found to be the binding of the amide carbonyl of the NAD^+ model to the Cp*Rh hydride complex, **2** [1,2].

Thus, the reaction rate (v) would approach a maximum value (v_{max}) at high concentrations of formate ion: $v_{max} = k_3[\mathbf{1}]_0$. Therefore, a plot of $1/v$ vs. $1/[HCO_2^-]$, at a given $[\mathbf{1}]_0$ concentration (3.2×10^{-2} M), is shown to be a straight line (Fig. 7, Supporting Information), which provided the values of $k_3 = 1.4 \times 10^{-4}$ (s^{-1}) and $K_m = 3.68 \times 10^{-2}$ (M) for the reactions conducted in water.

The temperature effect on the rate constant, k_{cat}, was studied in the range of 289–306 K (higher temperatures were not feasible) for substrate **7** in water (pH 7.0) at concentrations of 3.1×10^{-2} M, complex **2** at 4.95×10^{-4} M, and HCO_2Na at 0.3069 M. An Arrhenius plot of ln k_{cat} vs. $1/T$ for substrate **7** (Fig. 1) allowed us to determine the activation energy, E_a, while the other parameters, such as the enthalpy, entropy, and free energy of activation were obtained as follows: $\Delta H^{\ddagger}$; $\Delta S^{\ddagger}$ from Eyring plots of ln k_{cat}/T vs. $1/T$; $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S$. (Table 2). All the thermodynamic and activation parameters in Table 2 were consistent with those found for the reduction of NAD^+ and the biomimetic models of NAD^+ with **2** in H_2O [2].

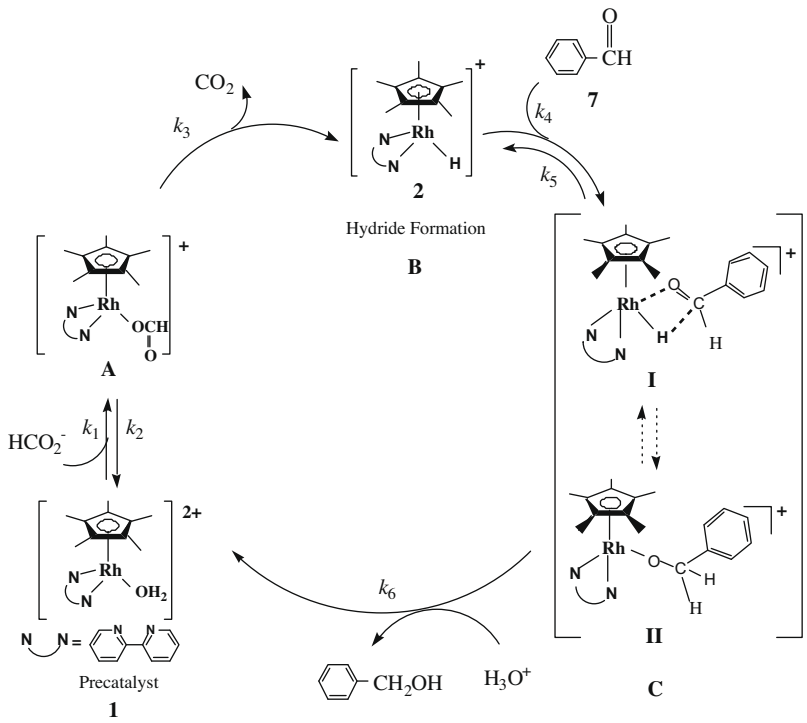
Table 2
Thermodynamic and activation parameters for substrate **7**.

$\Delta H^{\ddagger}$ (kcal/mol)	23.6 ± 1.0
$\Delta S^{\ddagger}$ (eu)	24.9 ± 1.4
$\Delta G^{\ddagger}$ (kcal/mol) @ 25°C	16.1
E_a (kcal/mol)	24.1 ± 1.01

Thus, our above-mentioned kinetic analysis, and the data in Table 1, allowed us to propose a plausible catalytic cycle for the reduction of the ketone/aldehyde substrates, **3–8**, with **1** as the precatalyst, and sodium formate as the hydride source (Scheme 1). The reaction of **1** with HCO_2Na provided the $[Cp^*Rh(bpy)(O-C(O)H)]^+$ complex, **A**, which decomposed to the hydride complex, $[Cp^*Rh(bpy)(H)]^+$, (**B**), via a β-hydrogen elimination reaction to produce CO_2 [1,2]. The important role of the carbonyl functionality of substrates **3–8** was to coordinate to the Cp*Rh metal ion center. It should be emphasized that even though the rate-limiting step was found to be $[Cp^*Rh(bpy)(H)]^+$ formation, we proposed, from the results in Table 1, that substrate binding to the Cp*Rh metal ion center was still crucial for product formation. This was further substantiated by reaction of a 1:1 mixture of substrate **4** and its reduction product, cyclohexanol, which showed no effect on the initial rate of reduction, and therefore, no effect on hydride formation, nor apparently, the binding of substrate **4** to **2**.

We further suggest that this binding process of carbonyl substrate to the Cp*Rh metal ion center occurred in concert with hydride transfer (Scheme 1, **C I**, transition state). It should also be noted that hydride transfer, **I** to **II** in **C**, could possibly be a reversible process as was recently found in the regioselective reduction of NAD^+ models [2].

Finally, displacement of the alcohol product and recycling **1**, via another hydride $[Cp^*Rh(bpy)(H)]^+$ molecule, completes the plausible catalytic cycle, with substrate **7** as an example.



Scheme 1. Plausible catalytic cycle for the reduction of all the substrates, **3–8**, with **7** as an example.

3. Conclusions

The significant results in the aqueous reductions of the carbonyl substrates, **3**–**8**, with $[Cp^*Rh(bpy)H]^+$ (**2**), to exclusively form the kinetic product alcohols, were the rate-limiting formation of $[Cp^*Rh(bpy)H]^+$, and the proposed binding of the carbonyl substrates to the η^5-Cp^*Rh metal ion center, in concert with hydride transfer. This crucial binding step (Scheme 1, **C1**) appeared to be moderately dominated by steric effects in an inter comparison to both the ketone and aldehyde series, while electronic effects, although subtle, were epitomized by the results with substrates **4** and **8**. The ketone series, **3**–**5**, showed a slight steric effect during the reduction reaction for the alkyl ketone substrates, **5** > **3**, while the aryl ketone showed a moderate electronic effect, with **5** > **4** > **3**, where the electron-donating effect of the benzene ring directly bonded to the carbonyl group appeared to increase binding to the Cp^*Rh metal ion center.

The aldehyde series, **6**–**8**, which appeared to also minimize steric effects during the reduction reaction, emphasized a subtle electronic effect, where placing further electron density on the carbonyl oxygen; i.e., comparing substrate **7** to **8**, increased the initial rate of reduction by a moderate factor of ~1.5. It was also important to note that the rate-limiting step in these aqueous carbonyl reduction reactions, the formation of $[Cp^*Rh(bpy)H]^+$, was the same in aqueous solution for the regioselective reduction of natural NAD^+ and the aqueous NAD^+ model, β-nicotinamide ribose-5′-methyl phosphate, at pH 6.5 [1,2].

These reported results can be best compared with the previous findings by Ogo et al. [3i,j], which utilized $[Cp^*Ir(bpy)(H)]^+$, an analog of **2**, and $[\eta^6\text{-}C_6Me_6)Ru(bpy)(H)]^+$ in an acidic water medium, with several similar ketone substrates. Firstly, the results with the hydride complex, $[\eta^6\text{-}C_6Me_6)Ru(bpy)(H)]^+$, at pH 4.0 under saturation kinetics with sodium formate, were compared for steric and electronic effects [3i]. From our perspective, the steric effects have a minimal consequence on the reported TOF, in agreement with the similar ketone substrates in Table 1. The electronic effect results were more difficult to compare, but the fact that e-withdrawing groups on the carbonyl group should possibly limit the protonation step on the carbonyl oxygen, Ogo et al′s. mechanism of choice, does bode better, in our opinion, for direct bonding of the carbonyl to η^6-$(C_6Me_6)Ru$ metal ion center. For comparison to the Ogo et al. $[Cp^*Ir(bpy)(H)]^+$ results [3j], again with several similar ketones, the steric effects seemed to moderately affect the TOF, while the electronic effects appeared to be less important, but binding of the substrate ketone to the Cp^*Ir center can not be overlooked. Moreover, to reiterate, the $(PTA)_4RuCl_2$ results of Darensbourg et al. [3m], while difficult to compare to the presented results because the aldehyde substrate reactions were conducted in a biphasic mode, did have an important inhibition result with benzaldehyde (**7**), in the presence of CO, which quenched the reduction reaction, and intimated that binding of the carbonyl group to the Ru metal ion center was possibly important for the reduction to proceed. Kuo et al. [3n] also proposed binding of the substrate ketone to the $[Cp_2MoH(OTf)]$ metal ion center during transfer of the hydride to the carbonyl of the ketone substrate.

Finally, we wish to categorize $[Cp^*Rh(bpy)H]^+$ as an example of a hydride that can bind to the substrate functional group, and in that process, has constricted the transition state for hydride transfer, in this example, to the carbonyl carbon atom [1,2]. Thus, there is the potential of forming chiral alcohols from the reduction of achiral ketones with the development of sterically limited chiral ligands on the Cp^*Rh metal ion center, and will be pursued in the future.

4. Experimental

4.1. Materials

$[Cp^*RhCl_2]_2$ was purchased from Colonial Metals and was used as received. $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ was prepared according to the literature method [2], using $[Cp^*Rh(H_2O)_3](OTf)_2$ as the precursor [7]. Water (HPLC grade) was purchased from Aldrich. All the ketones, aldehydes, and alcohols were purchased from Aldrich and used as received after GC/MS analysis.

4.2. Equipment

The pH values were obtained with an Orion 601A pH meter equipped with an Orion semimicro combination electrode. GC or GC/MS analyses were performed on a Hewlett–Packard instrument (HP 5890) with a J&W, DB-Wax column (30 m, film thickness 0.25 μm, I.D. 0.25 mm). A circulating water bath (VWR 1160) was used to control the temperature. For experiments conducted at different temperatures, the circulating water bath was warmed up for at least 1 h before the kinetic studies were initiated.

4.3. Kinetic procedures for the reductions of ketones or aldehydes, 3–8, with precatalyst $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ and sodium formate

The kinetic experiments at 23 °C, which were controlled by a circulating water bath (VWR 1160), were followed using GC and GC–MS techniques. For experiments conducted at different temperatures, the circulating water bath was warmed up for at least 1 h before the kinetic studies were initiated. Stock solutions of $[Cp^*Rh(bpy)(H_2O)]OTf_2$ (0.050 M) and sodium formate (0.31 M in buffer NaH_2PO_4/Na_2HPO_4 0.1 M, pH = 7.01–7.04) were made for the kinetic experiments in H_2O. All the solutions were degassed (N_2) prior to being used. The induced volume change was taken into account for the calculation of the turnover frequency (TOF).

A general procedure for all the kinetic experiments was as follows: A 10 mL aliquot of the sodium formate solution (deoxygenated) was transferred with a gas-tight syringe into a volumetric flask (25 ml) with a stir bar under N_2. Then 31.5 μL of benzaldehyde (0.029 mmol, 32.93 mg), **7**, and 10 μL of ethyl acetate (internal standard) were added to the reaction, followed by 100 μL of a 0.050 M stock solution of $[Cp^*Rh(bpy)(H_2O)](OTf)_2$ via syringe, and the total solution rapidly mixed at 23 °C in a controlled temperature bath. A GC–MS sample was run every 10 min (or 1 h depending on the substrate) until the starting material disappeared. Calibration curves for all substrates were recorded to obtain the GC response factors, and calculate concentrations of substrate reacted and products formed with time. All the kinetic experiments were carried out with constant stirring, while some reactions were followed for more than 24 h. The values of the initial rate (r_i) were obtained from at least 3 runs, using plots of ln C (product) vs. time.

4.4. Activation parameters for benzaldehyde, 7

An analogous procedure with the same amount of **7** (0.031 M) as described above was used, except that the solutions were run at several temperatures. The values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were obtained from plots of ln k_{cat}/T vs. $1/T$ and the E_a was obtained from the plot ln k_{cat} vs. $1/T$. $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2009.10.015.

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