Aqueous "Green" Organometallic Chemistry: Structure of the Molybdocene Monohydride Used for Carbonyl Reduction in Water

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Summary: The compound bis(η^5-cyclopentadienyl)hydridomolybdenum(IV) triflate, which was synthesized from Cp_2MoH_2 and methyl triflate, is water soluble and undergoes hydride deuteride exchange in D_2O. The molybdocene monohydride reduces ketones and aldehydes in water under mild aqueous conditions (pH 7 and 40 °C), which underscores the utility of this metallocene hydride for further organic transformations. Mechanistic features for the ketone → alcohol reduction suggest that either the reduction process is promoted by acid protonation of the carbonyl oxygen or it follows the reverse pathway of the aqueous C−H activation of primary alcohols by $Cp_2MoCl_2(aq)$ reported earlier by Balzarek and Tyler.

Introduction

Metallocene hydrides have been proposed as key intermediates and catalysts in olefin hydrogenation and polymerization reactions, and they have found widespread synthetic utility.[1] However, the lack of aqueous stability and solubility for most metallocene hydrides limits their synthetic utility in aqueous solvents. There are practical advantages for carrying out metallocene hydride chemistry in water. These include the environmental and financial benefits of not working with anhydrous volatile solvents and the convenience of not solubilizing polar molecules (i.e., carbohydates) for work in organic solvents.[2] In terms of organic synthesis, the water medium may provide a new set of selectivity in organic transformations since it has been shown that alterations in solvent polarity give rise to different reactivities.[3] Despite these advantages, there have been only isolated examples of metallocene hydride chemistry in water. Ito and co-workers first reported that the protonated tungstocene and molybdocene dihydrides ($Cp_2MH_3^+$, M = Mo(IV) or W(IV); Cp = η^5-C_5H_5) reduce imines, aldehydes, and ketones under strong acidic

conditions.[4] More recently Balzarek and Tyler have shown that the methylated molybdocene monohydride is an intermediate species in the aqueous C−H activation of primary alcohols.[5] While the aqueous chemistry of molybdocene dichlorides (Cp_2MoCl_2) is well documented,[6] not much is known about aqueous properties of its corresponding monohydride. In this connection, we report the synthesis and aqueous chemistry of the water-soluble molybdocene monohydride, $Cp_2Mo(H)OTf$ (**I**). This metallocene serves as an aqueous analogue of sodium borohydride, and it can carry out reductive chemistry under mild aqueous conditions.

Green and co-workers first reported the aqueous solubility and stability of molybdocene dihydrides under strong acidic conditions, which resulted in the protonated trihydride.[7] Ito and co-workers have used this trihydride to reduce polar functional groups (carbonyls, alkenes, and imines) via hydride attack on the electrophilic carbon[4] under extreme acidic conditions. In addition, Bullock and co-workers have used $Cp(CO)_3WH$ in triflic acid to make $[Cp(CO)_3W(alcohol)]^+OTf^-$ complexes through ionic hydrogenation of ketones and aldehydes.[8] To this end we report that **I** reduces carbonyl functionalities just as effectively as the trihydride $Cp_2MoH_3^+$,[9] but under mild aqueous conditions. This finding represents the reverse chemical step for the aqueous C−H activation by $Cp_2MoCl_2(aq)$ and $Cp'_2Mo(\mu-OH)_2MoCp'_2^{2+}$ reported by Balzarek and Tyler,[5] and it further contributes to the growing list of aqueous organometallic transformations.[10]

Results and Discussion

Complex **I** was made through the reaction of Cp_2MoH_2 with 1 equiv of methyl triflate in benzene. The air-

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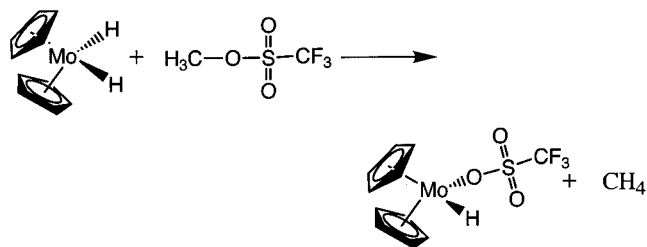* To whom correspondence should be addressed. E-mail: kuo@lclark.edu.

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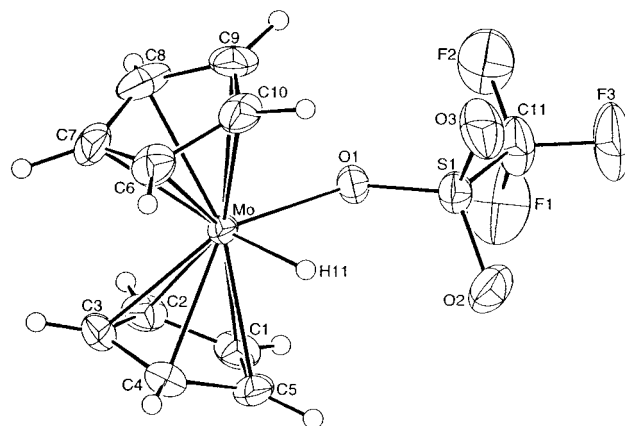
Figure 1. Crystal structure of $Cp_2Mo(H)OTf$ (**I**). Selected bond lengths and angles: Mo–H, 1.63(4) Å; Mo–O1, 2.186(2) Å; O1–Mo–H = 82(1)°, $Cp_{centroid}$–Mo–$Cp_{centroid}$ = 141.7(4)°.

sensitive, red complex can be purified by extraction in water followed by evaporation.[11] The ^1H NMR in D_2O (pH 7.0) is unexceptional in that we see a Cp resonance (10H) and a hydride resonance (1H) at 5.15 and −9.65 ppm, respectively. That this complex showed no interaction with the MOPS (morphinopropanesulfonic acid) buffer allowed us to conduct further aqueous studies on **I** buffered at neutral pH.

X-ray quality crystals[12] of complex **I** could be grown by vapor diffusion of hexane into a benzene solution. The crystal structure of **I** (Figure 1) shows mononuclear $Cp_2Mo(H)OTf$ molecules with eclipsed cyclopentadienyl ligands forming the familiar clamshell geometry about the Mo(IV) ion. The geometry is unexceptional with regard to the average Mo–C bond distance $(2.29 \pm 0.05$ Å) and the O–Mo–H bond angle (82°) when compared to prior Cp_2Mo systems.[13] The ring centroid–Mo–ring centroid angle of 141.7(4)° for **I** falls between that found for most Cp_2MoL_n complexes (130−135°)[13] and Cp_2MoH_2 (145.8°).[14] Such an angle is consistent with the hydride and triflate ligation since Prout and co-workers have seen that reduced ligand–Cp repulsion due to smaller ligands leads to larger ring centroid–Mo–ring centroid angles.[15]

Over time (~8 h, unbuffered at pH 5−6) at 45 °C the hydride resonance disappears, and it is replaced by a deuterium signal (Figure 2) at the same chemical shift $(k_{obs} = 0.41$ $h^{-1})$. This is indicative of a hydride–deuteride exchange, which we found to be faster under acidic conditions (unbuffered at pH ~2) and to be relatively temperature independent. Atwood and co-workers have seen the same hydride–deuteride exchange take place in D_2O with the dihydride complex *trans*-Ir(CO)(Cl)(H)$_2$(TPPTS)$_2$ (TPPTS = P(*m*-C$_6$H$_4$SO$_3$-Na)$_3$).[16] Since the molybdocene complex is known to bind
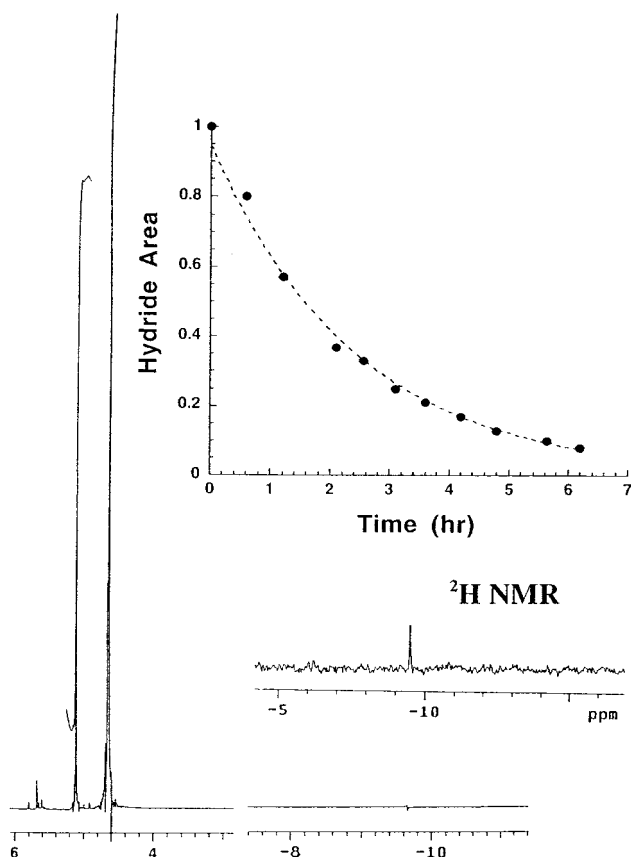
Figure 2. ^1H NMR spectrum of $Cp_2Mo(H)OTf$ in D_2O (unbuffered pH 5−6) after 8 h at 45 °C that shows the disappearance of the hydride resonance at −9.6 ppm. The inset is a ^2H NMR spectrum showing that the hydride has been exchanged for the deuteride, and a kinetics plot of the disappearance of the hydride signal. The disappearance of the hydride area was fit to an exponential decay with a k_{obs} of 0.41 h^{-1}.

phosphates,[6a] sulfates,[17] amines,[18] and alcohols,[5] kinetic studies as a function of pH would be problematic due to the coordination properties of most pH buffers. In addition to this hydride–deuteride exchange, we also

(11) The parent compound Cp_2MoH_2 (190 mg, 0.83 mmol) was dissolved in 10 mL of C_6H_6. Methyl triflate (180 mg, 1.1 mmol) was added to this stirred solution. After stirring at room temperature for 3 h, the C_6H_6 was removed in vacuo and replaced with H_2O (0.5 mL). The aqueous red solution was filtered and then dried in vacuo to yield 270 mg (0.72 mmol) of the $Cp_2Mo(H)OTf$ monohydride (86% yield). Anal. Calcd for $C_{11}H_{11}F_3MoS \cdot 2.5H_2O$: C 35.39; H 4.29. Found: C 35.34; H 3.85.

(12) The compound **I** crystallized in the $P2_1/c$ space group with the following cell constants: $a = 12.2250(12)$ Å, $b = 8.5082(11)$ Å, $c = 13.1264(7)$ Å, $b = 104.401(7)°$, $V = 1322.3(3)$ Å^3, and $Z = 4$. The R value = 0.038 Å

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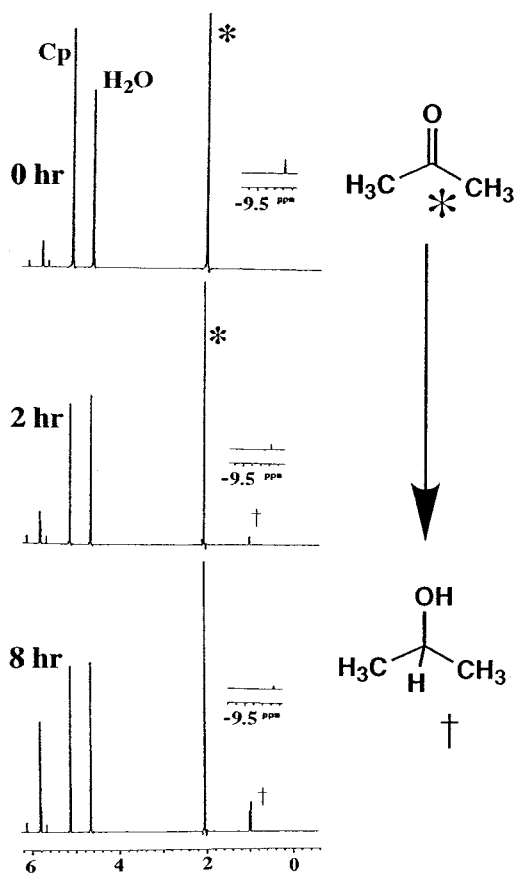(18) Jutzi, P.; Redeker, T. *Eur. J. Inorg. Chem.* **1998**, 663−674.

Figure 3. Reduction of 15 mM acetone (*) at 2.0 ppm to 2-propanol († at 1.0 ppm) with **I** (5 mM) in D_2O (pH 3−4) as observed by ^1H NMR spectroscopy. Inset figure is the upfield region (−9.5 to −10 ppm) showing the disappearance of the hydride. Note the appearance of a new cyclopentadienyl peak at ∼5.8 ppm that is attributable to the aquated Cp_2Mo as confirmed by addition of Cp_2MoCl_2(aq).

found that **I** is converted to a new complex with a Cp signal at 5.7−5.8 ppm. This hydrolytic process, which has a k_{obs} < 0.03 h^{-1}, is much slower than the hydride−deuteride exchange and therefore represents a negligible transformation in water. However, during the synthesis of **I**, an aqueous extraction of the monohydride is involved that always results in a small amount of this byproduct. Addition of Cp_2MoCl_2(aq), which exists as $Cp_2Mo(OH)(OH_2)^+$, to an aqueous solution of **I** resulted in an increase in this new Cp signal at 5.8 ppm. This suggests $Cp_2Mo(H)OTf$ slowly hydrolyzes to $Cp_2Mo(OH)(OH_2)^+$ [6b] in water.

The water solubility of this metallocene hydride prompted us to see if it could reduce carbonyl functionalities to alcohols in water. The ^1H NMR spectra of **I** (5 mM) with acetone (∼ 3 equiv) in D_2O (unbuffered, pH 5−6) showed a clean transformation to 2-propanol.

In the time required for the acetone reduction (∼8 h), a significant amount of the original hydride would be converted to the deuteride. As a result, acetone would be reduced by both hydride and deuteride, which explains why the 2-propanol product signal at 1 ppm is not a clean doublet (Supporting Information figure). A similar acetone → 2-propanol transformation was also observed when the reaction was done in D_2O buffered at pH 7.0 with MOPS. While the coordination properties of most buffers to $Cp_2Mo(OH)(OH_2)^+$ precluded a careful
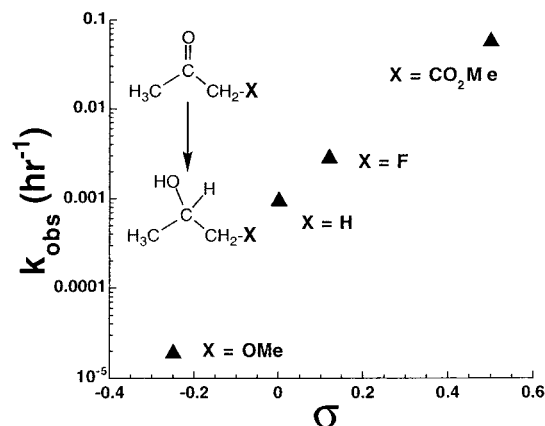

Figure 4. Rates of acetone derivative ($CH_3-CO-CH_2-X$) reduction as a function of substituent (**X**). Reductions were done in a 10 mM MOPS (pH 7, 40 °C) buffer with 5 mM of **I** and ketone, and only the initial (∼10%) rates of reduction were recorded.

pH study of this reduction process, we have seen that in unbuffered acidic solution (pH 3−4), such as the one in Figure 3, the rates of acetone reduction are ∼50-fold faster than at pH 7 in MOPS. In addition, we found **I** reduces benzaldehyde to benzyl alcohol almost instantaneously and is unreactive toward esters. Ito and coworkers have seen a similar reactivity pattern in carbonyl reduction by Cp_2MoH_2.[4] However, the mild aqueous conditions (pH 7.0 and 40 °C) for the reduction process by **I** makes this transformation distinct from Cp_2MoH_2. In the case of Cp_2MoH_2, excess protic acid was necessary for the reduction to occur stoichiometrically at room temperature (∼7 h). In fact the reactions were run with acetic acid as the solvent, and when 1 equiv of acid was used, the reduction was successful only in methanol at 50 °C.

Our interest in understanding the mode of hydride reactivity by **I** prompted us to examine the relative reduction rates of acetone derivatives ($CH_3C(O)CH_2-X$) with both electron-donating (X = OMe) and -withdrawing (X = F, CO_2Me) substituents. Ideally this type of study would be suited for benzaldehyde derivatives, but the parent aldehyde underwent instantaneous reduction by **I** in D_2O. In addition, chloro- and iodoacetone instantaneously reacted with the hydride of **I** through probably a halogenation reaction. When the initial rates (first 10%) of ketone reduction (5 mM) by an equimolar amount of **I** in D_2O are plotted against the Hammet constant of the substituent, we see a strong correlation indicating that carbonyl reduction by **I** is favored by electron-withdrawing substituents. This behavior is consistent with a mechanism for carbonyl reduction that proceeds through hydride attack on the electropositive carbonyl carbon. It should be noted that in all these cases the rate of alcohol production corresponded with the rate of $Cp_2Mo(OH)(OH_2)^+$ production (new Cp singlet at 5.8 ppm). This suggests that the fate of **I** upon reduction of the ketone is conversion to the $Cp_2Mo(OH)(OH_2)^+$ complex. That the thermochemistry for ketone reduction by **I** is similar to that found in borohydride is underscored by the Arrhenius plot of fluoroacetone reduction by $Cp_2Mo(H)OTf$ in D_2O (pH 7). This transformation goes through an ordered transition state with an entropy of activation of −36 ± 5 eu, which is within the experimental ∆S of activation for boro-

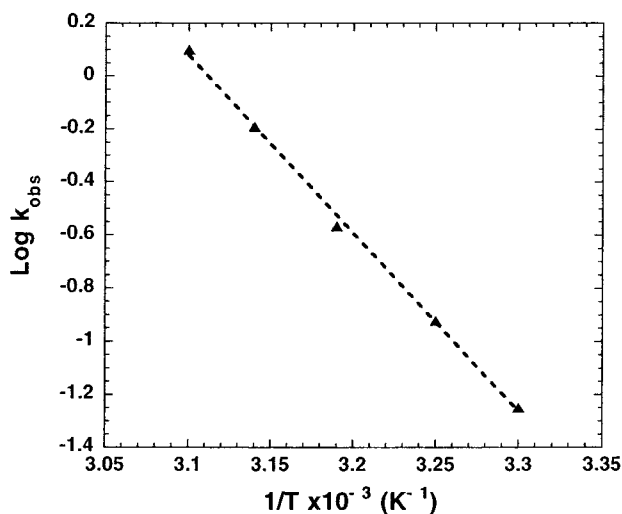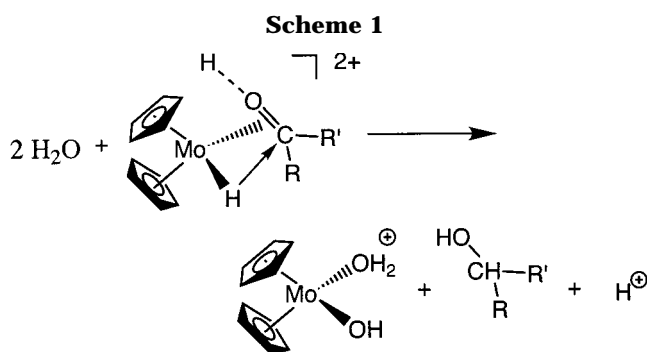**Figure 5.** Arrhenius plot of fluoroacetone reduction by **I** under the same conditions as that described in Figure 4.
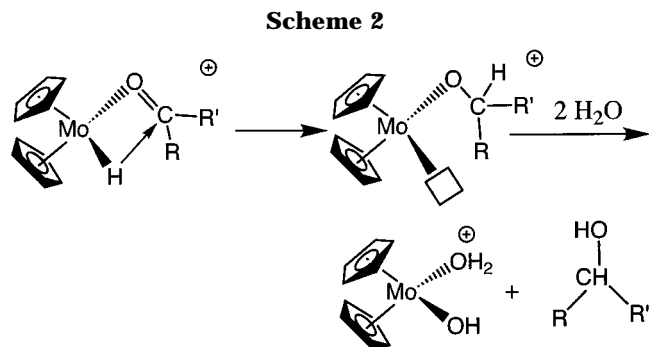
Scheme 1

hydride reduction of ketones in THF (-28 to -37 eu).[19] These results are reminiscent of the acetone reduction by [Ru(bipy)$_2$(CO)H]PF$_6$ in water.[20] In such a process, it was proposed that a fast acetone + acid (HA) pre-equilibrium occurs to form a [(CH$_3$)$_2$CO- - -HA] complex. This is then followed by the slower step in which the Ru-hydride reduces the protonated acetone to form 2-propanol. Although we are unable to carry out a systematic study of how acetone reduction by **I** is affected by pH, the fact that we see a faster rate under acidic conditions is consistent with a general acid-catalyzed pathway. In such a scheme (Scheme 1), the poorly coordinating triflate ligand of **I** is replaced by the ketone that is protonated in water. This protonated ketone is set up for nucleophilic attack by the hydride to form 2-propanol. It is reasonable to propose that water can protonate the coordinated acetone while the carbonyl is reduced by the hydride of **I**, for it was found that the hydroxyl proton of [2,5-Ph$_2$-3,4-Tol$_2$(η^5-C$_4$COH)-Ru(CO)$_2$H] can protonate benzaldehyde with concomitant reduction of the aldehyde by the Ru-hydride.[21] An

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Scheme 2

alternative mechanism for acetone reduction (Scheme 2) by **I** involves the reverse step of the C−H activation of primary alcohols by Cp$_2$Mo(OH)(OH$_2$)$^+$.[5] In such a process (reverse of Scheme 2) the Cp$_2$Mo-alkoxide, which is formed from Cp$_2$Mo(OH)(OH$_2$)$^+$ and alcohol is oxidized to the Cp$_2$Mo(H)-ketone complex. In the reaction described in Scheme 2, the bound ketone-molybdocene hydride complex undergoes a reduction transformation to the CpMo-alkoxide that is subsequently hydrolyzed to the alcohol and Cp$_2$Mo(OH)(OH$_2$)$^+$. The difference between the two proposed mechanisms (Schemes 1 and 2) is rather subtle and can be traced to the role of the acid in water. In fact, both proposed mechanisms proceed with the same rate-determining step, which is hydride attack on the carbonyl carbon.

Conclusion

This report presents crystallographic evidence for a water-soluble metallocene monohydride that functions as a reducing agent of carbonyl functionalities. The striking feature for this metallocene hydride is that the reductive transformations can be done in water under mild conditions. This suggests the metallocene compound and its derivatives could have some practical applications in organic synthesis. This finding augments the synthetic utility of aqueous metallocene complexes, which has spurred us to further expand the synthetic utility of Cp$_2$Mo(H)OTf.

Supporting Information Available: Experimental methods, supporting ^{1}H NMR spectrum, crystallographic information/data (Table 1) for Cp$_2$Mo(H)OTf including tables of hydrogen coordinates (Table 2), anisotropic parameters, bond lengths (Table 3) and angles (Table 4), and additional crystal packing figures. This material is available free of charge on the Internet at http://pubs.acs.org.

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