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Review

Organometallic chemistry in aqueous solution: Reactions catalyzed by water-soluble molybdocenes

Kerry L. Breno, Takiya J. Ahmed, Michael D. Pluth, Christoph Balzarek, David R. Tyler*

Department of Chemistry, University of Oregon, Eugene, OR 97403, USA

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Contents

Abstract

The aqueous chemistry of molecules containing the Cp_2Mo^{2+} unit (referred to as "molybdocenes" in this paper) is reviewed. Aqueous molybdocenes are generated by hydrolysis of the Mo–X bonds in Cp_2MoX_2 complexes (X = halide or pseudo-halide) or by dissolving isolable dimers of the form $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2^{2+}][OTs^-]_2$ in water. The nature of the molybdocene species in solution is pH dependent: $Cp_2Mo(H_2O)_2^{2+}$ has $pK_{a1} = 5.5$ and $pK_{a2} = 8.5$; thus, at neutral and physiological pH, $Cp_2Mo(OH)(OH_2)^+$ is the dominant monomer in aqueous solution. This monomer is in equilibrium with $[Cp_2Mo(\mu\text{-}OH)]_2^{2+}$ ($K_{eq} = 3.5 \times 10^{-2}$ M $\pm$ 1.3×10^{-3} M at pD 3.5). $Cp_2Mo(OH)(OH_2)^+$ and $Cp_2Mo(H)(OH_2)^+$ (and the Cp′ analogs) are catalysts for a variety of reactions in aqueous solution, including H/D exchange reactions that proceed through C–H bond activation pathways, transfer hydrogenation reactions of ketones and aldehydes, nitrile hydration, and the hydrolysis of ethers, carboxylic esters, phosphate esters, and thiophosphinates. In these reactions, the molybdenum center acts as a Lewis acid, activating substrates toward intra- or intermolecular nucleophilic attack by a bound hydroxo ligand or a free water molecule. Mechanistic evidence suggests that the intramolecular hydration and hydrolysis reactions proceed via strained, four-membered ring intermediates.

Keywords: Catalytic hydration; Catalytic hydrolysis; Water-soluble metallocenes; *ansa*-Molybdocenes

1. Introduction

Water has traditionally not been used as a solvent in organometallic chemistry because the M–C bonds in organometallic complexes are frequently susceptible to hydrolysis. Depending on the organometallic complex, a variety of aqua, hydrido, hydroxo, and oxo products may be formed as a result of the reactions with water. However, not all organometallic complexes degrade when exposed to water, and over the past 15 years, aqueous organometallic chemistry has received increased attention. This chemistry has been well documented in a number of books and review articles [1,2]. Three main reasons may be given for the interest in water as a solvent for organometallic reactions. First, water is abundant, cheap, environmentally

* Corresponding author. Tel.: +1 541 3464649; fax: +1 541 3460487.
E-mail address: dtyler@uoregon.edu (D.R. Tyler).

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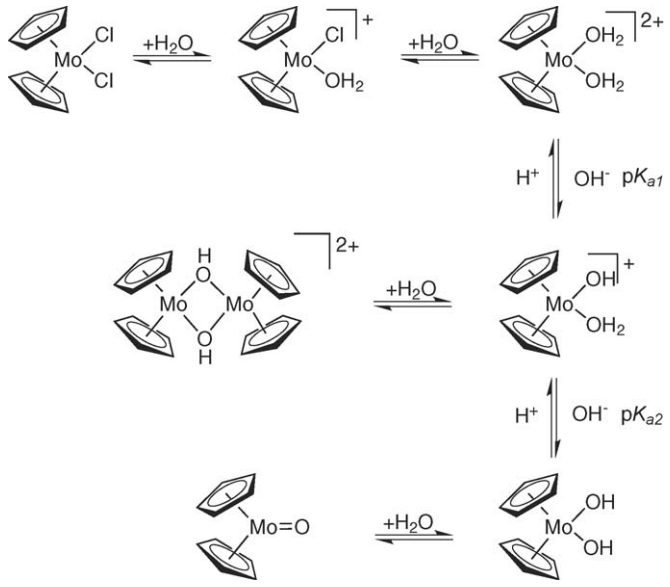
benign, and it has a high heat capacity. This is appreciated both in the laboratory as well as in industry [3], where organometallics are used as catalysts in a number of important reactions and processes [4–7]. Second, the use of organometallic catalysts in an aqueous phase may lead to easy workup procedures. For example, in aqueous biphasic reaction systems, catalysts and products can be easily separated [8]. The third promising aspect of aqueous organometallic chemistry is the possibility of finding reactions that outperform their analogs, or are even unprecedented, in organic solvents [9] (a classic example being the Ruhrchemie/Rhône-Poulence process for the production of butyraldehyde under biphasic conditions [10]).

The insolubility of organometallic complexes in water is often an important hurdle in doing aqueous organometallic chemistry. To deal with this problem, a variety of new water-soluble ligands have been synthesized [2,7,11,12]. When incorporated into metal complexes, these ligands impart water-solubility to the complexes. However, it is often overlooked that many organometallic complexes are intrinsically water-soluble. Among these compounds [13,14] are those containing aqua and hydroxo ligands in their coordination sphere such as $Cp'_2Mo(OH)(H_2O)^+$. These types of complexes are soluble by virtue of their ionic charge and their hydrogen-bonding ability through the aqua or hydroxo ligands.

Because of the emerging importance of water as a solvent in organometallic chemistry and because an extensive aqueous chemistry has developed for the $Cp'_2Mo(OH)(H_2O)^+$ complex, this paper reviews the aqueous chemistry of this molecule and that of its related molybdocene derivatives. Particular emphasis is placed on the homogeneous catalytic reactivity of molybdocene species and the pathways of these catalytic reactions. Initial investigations of the *ansa*-effect on the catalytic reactivity are also discussed. (Note that, as used in this review, molybdocene refers to the Cp_2Mo^{2+} unit and not just to Cp_2Mo^0.) The bioorganometallic chemistry of molybdocenes was recently reviewed and will not be covered here [15].

2. Molybdocenes in aqueous solution

Metallocenes of the group VI metals have received considerable attention since the first report of the Cp_2MCl_2 complexes ($Cp = \eta^5$-C_5H_5, M = Mo, W) by Cotton and Wilkinson in 1954 [16]. A vast number of theoretical, physicochemical, and chemical studies on molybdocenes have been carried out since then [17,18]. However, only a few of the early reports commented on the chemistry of the group VI metallocenes in water [19,20]. It was not until the discovery of the anti-tumor activity of metallocenes of the type Cp_2MX_2 (M = Ti, V, Mo; X = halide or pseudo-halide) that researchers began to focus on the aqueous chemistry of these species [21,22], and over the past 15 years, the aqueous chemistry of metallocenes containing Ti, Zr, Hf, V, Nb, Cr, and Mo has been explored in considerable detail. The hydrolysis chemistry of these compounds is complex, typically involving the formation of a number of dimeric and oligomeric species. The structure of the hydrolysis products is highly dependent on the pH and is often inferred only from titration studies. In most cases, hydrolysis of the coordinated



Scheme 1. Equilibria of the various molybdocene species in aqueous solution.

halide or pseudo-halide ligands occurs first and affords aquated metallocene complexes, with OH or OH_2 ligands replacing X (Scheme 1). In a few cases, aqua and hydroxo complexes can be isolated by controlled hydrolysis of the metallocene precursors [23,24]. In the specific case of Cp_2MoCl_2, the first chloride dissociation is rapid, and by the time of complete dissolution [25], the $[Cl^-]/[Mo]$ ratio is already 1.2.

The dissociation rate of the second X^- from the metallocene is dependent on the metal but the reaction typically occurs in 5–45 min. For the metallocene dichlorides of Ti ($k_2 = 0.84\,h^{-1}$), Zr ($k_2 = 1.31\,h^{-1}$), and V ($k_2 = 1.73\,h^{-1}$), the dissociation rate constant (k_2) of the second chloride is much smaller than for Mo [26], for which the half-life for loss of the second chloride ligand was estimated to be 6.7 min [25]. This hydrolysis behavior is independent of X in Cp_2MoX_2, as X = NCS, F, Br, I, Cl, N_3, or OC(O)R all shows similar activity [27,28]. In the case of Cp_2MoCl_2, the pH of the aqueous solution drops to ~3.5 during the hydrolysis due to the acidity of the coordinated H_2O ligand (Scheme 1) [25].

The other important hydrolytic process in aqueous metallocene chemistry is the loss of the cyclopentadienyl ligands. Table 1 gives an overview of metallocene M–Cp hydrolysis for different metals under a variety of conditions. Note that the rate of M–Cp hydrolysis is again pH dependent and varies significantly with the metal. Also note that molybdocene stands out from the other metallocenes in Table 1 in that it is surprisingly stable with respect to Cp hydrolysis. (In fact, if oxygen is excluded, no Mo–Cp hydrolysis can be detected in aqueous solutions of molybdocenes over a period of several weeks.) Thus, while hydrolysis and subsequent degradation of the Cp_2M core are observed with most metallocenes in aqueous solution, the molybdocene core (Cp_2Mo^{2+}) remains intact in water.

The behavior of bis(aqua)molybdocene is noteworthy in at least one other regard: it is the least acidic of the bis(aqua)metallocenes, with $pK_{a1} = 5.5$ and $pK_{a2} = 8.5$. In contrast, titanocene is the most acidic of the aqueous-stable metal-

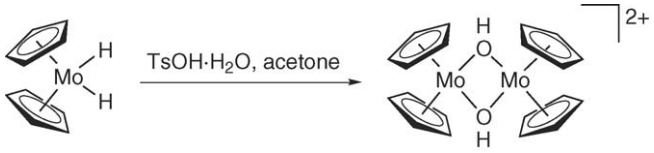
Table 1
Hydrolysis of cyclopentadienyl ligands from metallocenes in aqueous solution

Metallocene	Half-life (h)	Reference
Cp_2TiCl_2	57.0 ± 0.9[a]; 114 ± 11[b]	[26]
Cp_2ZrCl_2	14.1 ± 0.6[a]; 12.7 ± 1.4[b]	[26]
Cp_2HfCl_2	0, immediately upon dissolving[c]	[27]
Cp_2VCl_2	>10 days[a,b]	[26]
Cp_2MoCl_2	Several weeks[d]	[25]
Cp_2NbCl_2	3 days[e], 1–2 h[f], 15 min[g]	[29]

[a] 37 °C, 0.318 M KNO_3.
[b] 37 °C, 0.103 M NaCl.
[c] 25 °C.
[d] No O_2, pD 7.6.
[e] pH 1.8.
[f] pH 4.8.
[g] pH 6.6.

locene species with $pK_{a1} = 3.51$ and $pK_{a2} = 4.35$. Therefore, at neutral and physiological pH, titanocene and most other metallocenes exist as the neutral species, $Cp_2Ti(OH)_2$, while molybdocene exists as $Cp_2Mo(OH)(OH_2)^+$ or $[Cp_2Mo((-OH)]_2^{2+}$. The charged nature of molybdocenes in aqueous solution is important in biological studies because the charged species do not cross biological membranes as well as neutral metallocenes do [30].

In aqueous solution, Cp_2Mo^{2+} exists as both a hydroxo-aqua monomer, $Cp_2Mo(OH)(OH_2)^+$, and the μ-hydroxo dimer, $[Cp_2Mo(\mu\text{-}OH)]_2^{2+}$ ($K_{eq} = 3.5 \times 10^{-2}$ M $\pm$ 1.3×10^{-3} M at pD 3.5, Scheme 1). These water-soluble molybdocenes are accessible either by the hydrolysis of Cp_2MoCl_2 [31] as shown in Scheme 1 or by direct synthesis of $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2^{2+}][OTs^-]_2$ using the route described by Ren et al. (Scheme 2) [32,33]. The monomer–dimer equilibrium for aqueous molybdocenes can be adjusted by varying the pH or changing the substituents on the cyclopentadienyl ligands. As an example of the latter phenomenon, the addition of a methyl substituent to the cyclopentadienyl rings to give $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'^{2+}_2]$ $[OTs^-]_2$ caused the monomer–dimer equilibrium to shift in favor of the monomer ($K'_{eq} = 7.9 \times 10^{-2}$ M $\pm$ 1.0×10^{-3} M at pD 7) [31]. With these molecules, it was suggested that the monomer is favored due to unfavorable steric interactions between the methyl substituents on the cyclopentadienyl ligands in the dimer [31]. Electronic factors may influence the equilibrium as well. For example, methyl substituents increase the electron density on the metal center in the dihydride complex Cp'_2MoH_2 [34] and a similar effect can be postulated for $Cp'_2MoOH(OH_2)^+$. This increased electron density decreases the need to share an electron rich ligand with a second molybdocene center.



Scheme 2. Preparative route to the $[Cp_2Mo(\mu\text{-}OH)]_2[OTs]_2$ complex.

Scheme 3. Synthesis of $Cp_2Mo(H)(OSO_2CF_3)$.

In addition to $Cp_2Mo(OH)(OH_2)^+$, other derivatives of molybdocene have been synthesized and shown to have catalytic properties, both in water and in non-aqueous solvents. A notable example is the hydride complex $Cp_2Mo(H)(OSO_2CF_3)$, synthesized by the route in Scheme 3 [35]. Finally, for completeness, it is noted that Cp_2MoH_2 reacts with strong base in aqueous solution to form Cp_2MoO [36,37]. This species likely forms by sequential deprotonation and dehydration of the $Cp_2Mo(H_2O)_2^{2+}$ species. This reaction and the other equilibria and reactions described above are summarized in Scheme 1.

Finally, note that studies showed that the $Cp_2Mo(OH)(OH_2)^+$ species is the active catalyst in the reactions reported below that involve $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2^{2+}]$ as the starting material. This species is the dominant species at pH 7, and therefore the reactions were carried out at or about neutral pH.

3. Reactions catalyzed by molybdocenes

3.1. H/D exchange through C–H bond activation

During a study of the behavior of molybdocenes in aqueous solution, Balzarek et al. noted that H/D exchange occurred between the D_2O solvent and the hydrogen atoms on the Cp′ methyl groups in a solution of $[Cp'_2Mo(\mu\text{-}OH)]_2^{2+}$ and $[Cp'_2Mo(OH)(OH_2)]^+$ (Fig. 1) [38]. It was proposed that the H/D exchange occurred via the formation of a tucked-in complex formed by C–H bond activation of the methyl group on the cyclopentadienyl ligand (Scheme 4). The molybdenum hydride thus formed would be acidic and will exchange H^+ for D^+ in

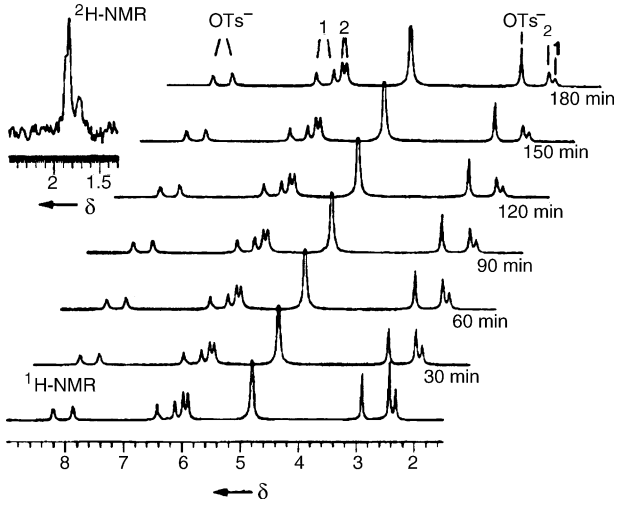
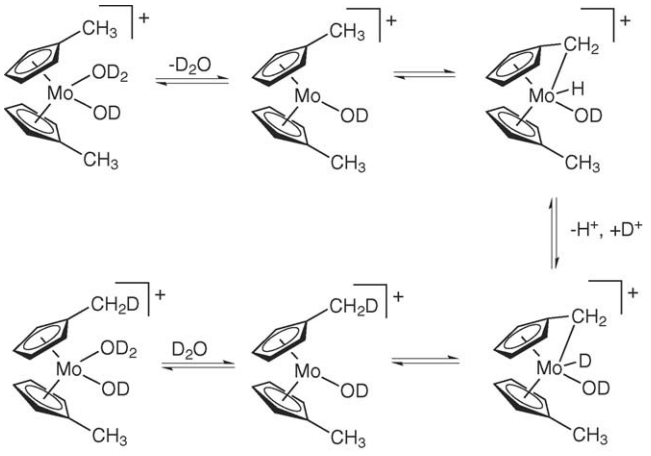


Fig. 1. ^1H NMR spectra of a solution of $[Cp'_2Mo(OH)(OH_2)]^+$ in D_2O at 75 °C recorded over a period of 3 h. The inset shows the ^2H NMR of the reaction solution after cooling to 25 °C. The $[Cp'_2Mo(\mu\text{-}OH)]_2^{2+}$ and $[Cp'_2Mo(OH)(OH_2)]^+$ complexes are labeled **1** and **2**, respectively, in the figure. Reprinted with permission from [38]. Copyright 1999 Wiley VCH Verlag GmbH.



Scheme 4. Proposed mechanism for H/D exchange on the methyl groups of Cp′ in the $[Cp'_2Mo(OH)(OH_2)]^+$ molecule in D_2O.

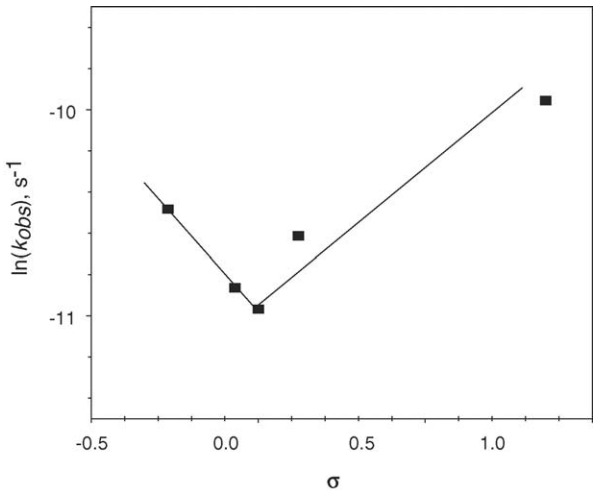
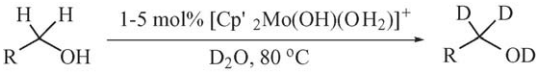


Fig. 2. Hammett plot for the H/D exchange in substituted benzyl alcohols. Reprinted with permission from [42]. Copyright 2001 American Chemical Society.

water. Incorporation of D into the methyl groups on the Cp′ ring then occurs by the microscopic reverse reaction (reductive elimination) to reform the starting molybdocene [38].

It was also found that $[Cp'_2Mo(OH)(OH_2)]^+$ is a catalyst for the H/D exchange at the α carbon in alcohols (Eq. (1)) [38]. The proposed mechanism is shown in Scheme 5. In this pathway, the initial step is dissociation of an H_2O ligand followed by the coordination of the alcohol. The alcohol is deprotonated by H^+ transfer to the hydroxo ligand and an alkoxide complex, **3**, is formed. (Note that a similar step was proposed for the coordination of nucleobases to molybdocenes [30].) Upon dissociation of the remaining aqua ligand, the coordinatively unsaturated molybdocene inserts into the C–H bond of the alkoxide, forming a keto-hydride intermediate (**4**-h). As with the tucked-in hydride in Scheme 5, the keto-hydride complex can undergo reversible protonation (H^+/D^+), which leads to the observed isotope exchange upon dissociation of the coordinated alcohol. (For analogous reactivity, see Refs. [39,40]).

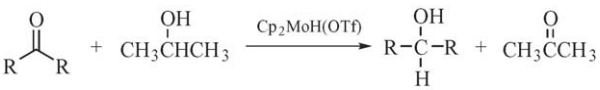


(1)

Detailed studies on the kinetics and mechanism of H/D exchange in alcohols supported the proposed pathway [41,42]. Thus, a kinetic isotope effect ($k_H/k_D = 2.2$) was observed for the reaction with benzyl alcohol, indicating that a C–H bond is broken during the rate-limiting step. In addition, the activation parameters ($\Delta H^{\ddagger} = 19.4 \pm 0.2$ kcal mol^{-1}, $\Delta S^{\ddagger} = -22.7 \pm 0.7$ cal mol^{-1} K^{-1}) suggested that the transition state of the rate-determining step involves an increase in order, such as an associative process [41]. Breno and Tyler further demonstrated that the rate-determining step is facilitated by electron-withdrawing and electron-donating groups, as determined from the Hammett plot in Fig. 2 [42]. The unusual (because it is not inverted) V-shaped biphasic Hammett plot indicated that the rate-determining step is sensitive to electronic effects and that the mechanism of the rate-determining step changes with the electron donating/withdrawing properties of the substrate. Specifically, the rate-determining step in H/D exchange in alcohols was proposed to be C–H bond activation (step **3** → **4**-h, Scheme 5) with the coordination mode of the ketone or aldehyde (σ or π) dependent on the electronic nature of the substrate (Scheme 6). Electron-donating groups stabilize the σ-coordination and the partial cationic character in this type of bonding. In contrast, electron-withdrawing groups encourage π-coordination to stabilize the central carbon (Scheme 7) [42]. It is noteworthy that the molybdocene-catalyzed H/D exchange reaction is one of the few examples of catalytic C–H bond activation reactions in *aqueous* solution.

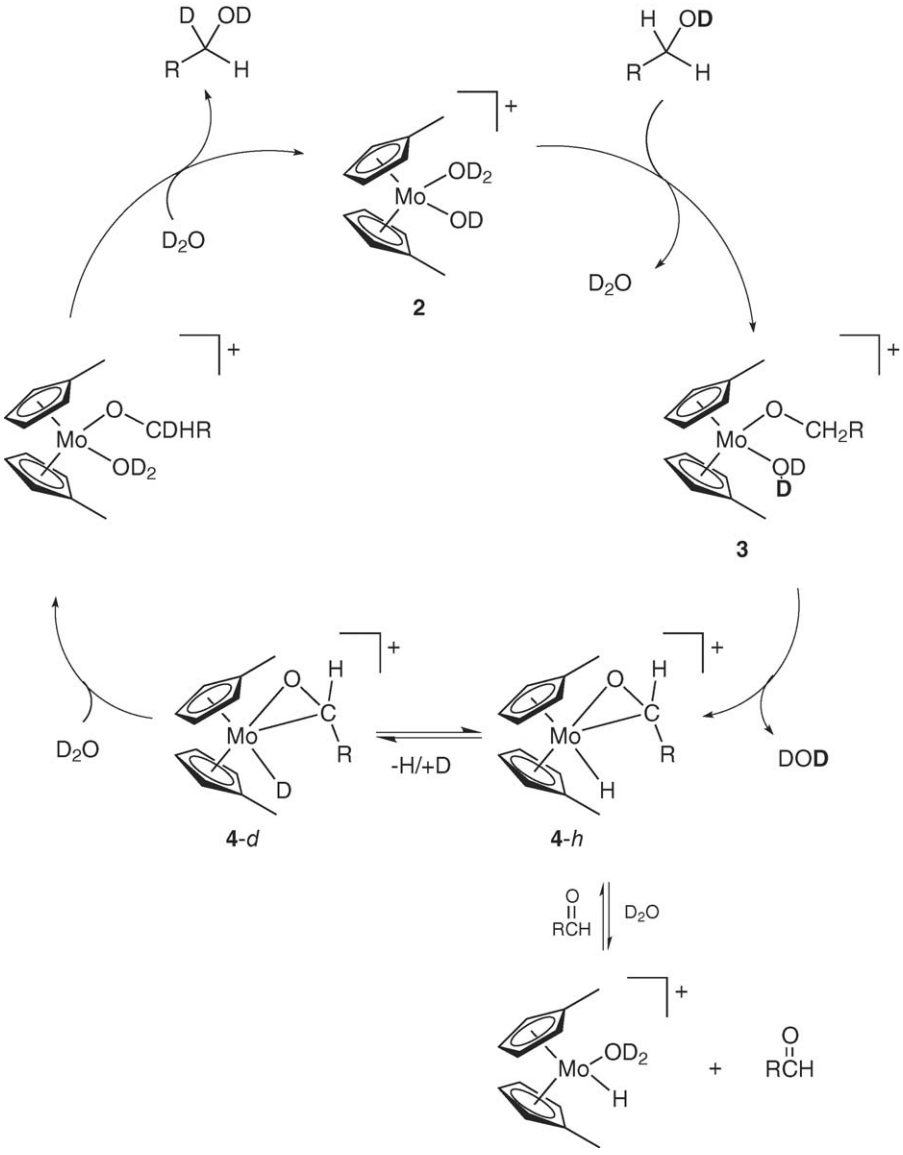
3.2. Transfer hydrogenation

The reversible coordination of alcohols to $Cp'_2Mo(OH)(OH_2)^+$ and of aldehydes and ketones to species **4** (in Scheme 5) has been exploited for transfer hydrogenation reactions. Kuo et al. showed that acetophenone is catalytically hydrogenated by $Cp_2MoH(OTf)$ in the presence of 2-propanol [35,43]. The mechanism of hydrogenation (Scheme 7) is similar to that in Scheme 5 for C–H bond activation in alcohols. Thus, the ketone coordinates to the $Cp_2MoH(OTf)$ species (to give species **4**) and then hydride transfer occurs to form the molybdocene alkoxide **3**. A second hydrogen is transferred from a coordinated aqua ligand and then 1-phenylethyl alcohol dissociates from the molybdocene. $Cp'_2Mo(OH)(OH_2)^+$ is generated and 2-propanol (as a sacrificial reducing agent) serves to regenerate the monohydride **4** by reversing these steps. The net reaction is thus:



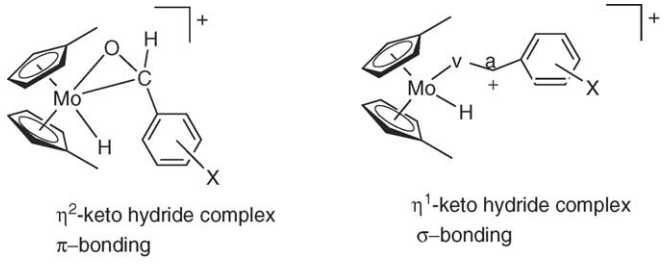
(2)

An alternative mechanism was considered (based on the Meerwein–Ponndorf–Verley mechanism) in which the metal acts as a collecting point for the alcohol and ketone, which is then followed by direct hydrogenation. However, deuterium incorporation in 1-phenylethyl alcohol indicated that the molybdocene hydride takes an active role in hydrogenation by act-



Scheme 5. Proposed mechanism for the H/D exchange in alcohols catalyzed by $[Cp'_2Mo(OH)(OH_2)]^+$.

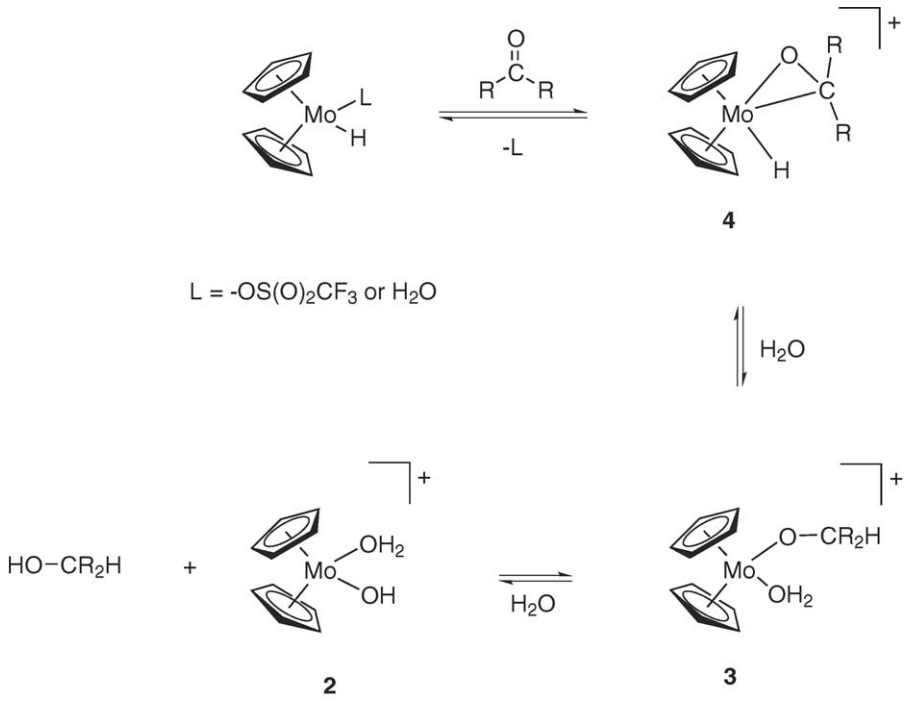
ing as more than a collecting point. The activation parameters ($\Delta H^{\ddagger} = 19$ kcal mol^{-1} and $\Delta S^{\ddagger} = -26$ cal mol^{-1} K^{-1}) measured by Kuo et al. [43] were identical to those observed by Balzarek et al. [41] for H/D exchange in alcohols, suggesting the rate-determining step is the same in each reaction, i.e., C–H bond activation is the rate-determining step.



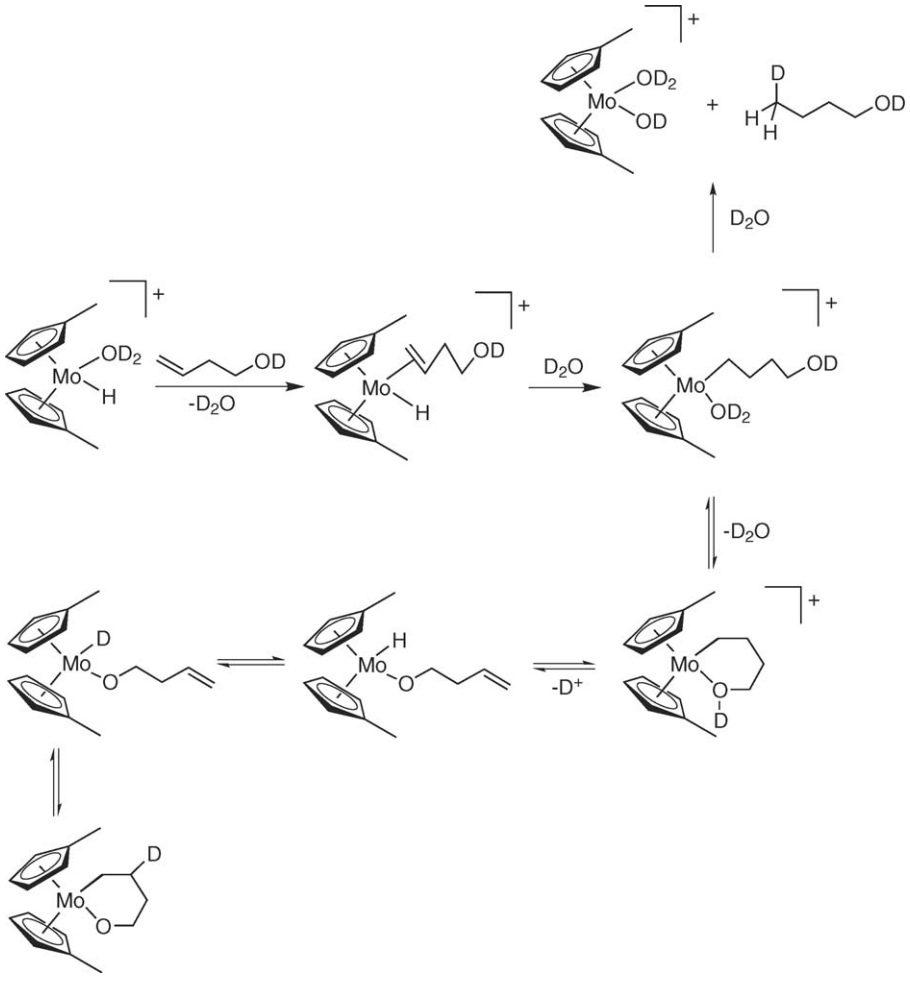
Scheme 6. Coordination of an aldehyde or ketone to an aqueous molybdocene. This species is a key intermediate in the H/D exchange in alcohols. Either σ- or π-type coordination will occur, depending on the electron-donating/withdrawing properties of the substituents on the aldehyde/ketone.

3.3. Stoichiometric hydrogenation of olefins

Breno et al. extended the pathway in Scheme 7 to the hydrogenation of olefins (Scheme 8) [44]. Unsaturated alcohols coordinate to $Cp'_2MoH(OTf)$ and hydrogenation proceeds as in transfer hydrogenations. However, without the sacrificial oxidant the reaction is stoichiometric, producing both a saturated alcohol and $Cp'_2Mo(OH)(OH_2)^+$. Because these reactions take place in water, the olefins typically have water-solubilizing functional groups such as –OH. These functional groups can be non-innocent. For example, the terminal –OH groups in 4-penten-1-ol and 3-buten-1-ol can coordinate to the molybdocene to form an intermediate molybdocenocycle (Scheme 8). (This is a recurring theme in aqueous organometallic chemistry; the functional groups that impart water-solubility to a substrate, lig-



Scheme 7. Proposed mechanism for the catalytic hydrogenation of ketones using $Cp_2MoH(OTf)$. The catalyst is regenerated by following the reverse pathway using 2-propanol.



Scheme 8. Reaction of $Cp'_2MoH(OH_2)^+$ with olefins.

and, or complex are frequently non-innocent and can coordinate to vacant coordination sites on a metal center [41].) Evidence for the formation of this intermediate comes from the observation of D incorporation at an olefinic carbon (Scheme 8).

3.4. Nitrile hydration

In addition to C–H bond activation reactions, aqueous molybdocenes catalyze the addition of water to various substrates (hydration). In particular, $[Cp'_2Mo(OH)(OH_2)]^+$ is a water-soluble, comparatively reactive catalyst for the hydration of nitriles [45]. The hydration reaction (Eq. (3)) is straightforward and no subsequent hydrolysis of the amide product occurs. The hydration of acrylonitrile is of particular interest due to the industrial demand for acrylamide. Note that the molybdocene-catalyzed hydration reaction of acrylonitrile is chemoselective: the nitrile is hydrated but no olefin hydration is observed. In the general case, however, if the nitrile contains ether or ester functional groups then these groups can be hydrolyzed (see below).

The kinetics of the nitrile hydration reactions were probed using an iterative kinetics-fitting program. From these fits, it was concluded that the rate of hydration was reversibly inhibited by substrate (nitriles) and irreversibly inhibited by product (amides) [45]. A mechanism consistent with the observed hydration and inhibition postulates an intramolecular attack of hydroxide on a coordinated nitrile leading to a η^2-amidate intermediate (Scheme 9) [45]. Note that this four-membered ring is not unusual because strained four-membered rings formed when nucleobases coordinated to molybdocene [30]. Also note the mechanism is similar to that proposed for the catalytic hydration of nitriles using $[Co(1,4,7,11\text{-tetraazacyclododecane})(OH_2)_2]^{3+}$ [46].

$$N{\equiv}C{-}R \xrightarrow[\text{1-5\% Cp'}_2\text{Mo(OH)(OH}_2)^+]{H_2O} H_2N{-}\overset{\overset{O}{\|}}{C}{-}R \qquad (3)$$

Breno et al. reported that increasing the electron-withdrawing ability of the nitrile (substrate) enhanced the rate of the reaction, as shown by the Hammett plot in Fig. 3. This result suggested that the step involving intramolecular hydroxide attack is rate limiting for nitrile hydration [45].

It is noted that the absence of H/D exchange in the hydration reactions of nitriles indicates that an enolate-type species is not formed, consistent with the proposed intramolecular mechanism (Scheme 10).

3.5. Molybdocene-catalyzed hydrolysis

A variety of substrates including ethers, carboxylic acid esters, phosphate esters, and thiophosphinates can be hydrolyzed using molybdocene catalysts (Scheme 11) [47–49].

Molybdocene-catalyzed hydrolysis was initially reported by Kuo et al. with activated *p*-nitrophenyl phosphate [50]. He found that the catalyzed hydrolysis of activated phosphate esters (such as *p*-nitrophenyl phosphate) occurred 10^5 times faster than aqueous hydrolysis at pH 7. Further studies demonstrated the effective hydrolysis of dimethyl phosphate, the organophosphate pesticides parathion and paraoxon, and thiophosphinates [48,49,51]. For the hydrolysis reactions of the phosphate diesters, significant rate enhancement by a factor of 10^5 to 10^8 over aqueous hydrolysis was noted. However, for the phosphate triesters and thiophosphinates, the rate acceleration was only 10^2 to 10^3 over uncatalyzed aqueous hydrolysis.

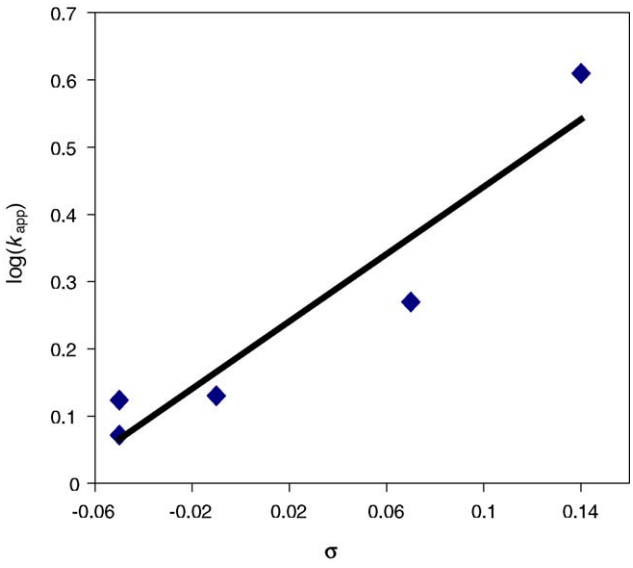
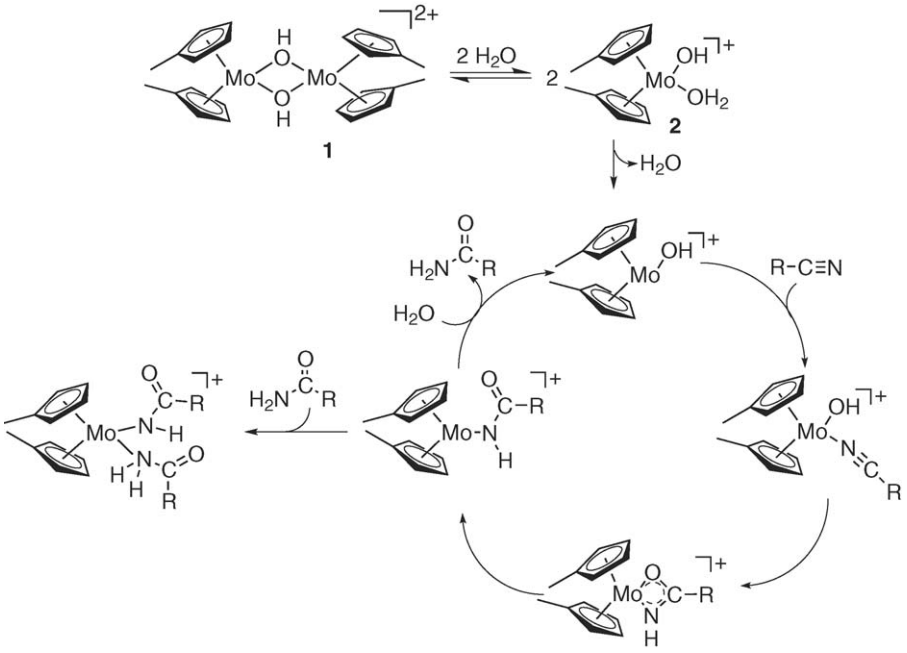


Fig. 3. Hammett plot for the hydration of nitriles. Reprinted with permission from [45]. Copyright 2003 American Chemical Society.

Based on the different rate enhancements and the activation parameters, Kuo proposed two different mechanisms for phosphate hydrolysis [49,50]. In the case of the phosphate diesters, intramolecular attack of a bound hydroxide was proposed to lead to the larger rate enhancements, and the smaller rate enhancements with the phosphate triesters and thiophosphinates were proposed to result from intermolecular water attack. In this latter case, the Mo center serves merely as a Lewis acid to activate the substrates to nucleophilic attack. In parathion, $^{18}O/^{16}O$ isotope studies demonstrated that nucleophilic attack occurred on the carbon rather than on the central phosphate, based on the incorporation of ^{18}O in the leaving alcohol (Scheme 12) [49].

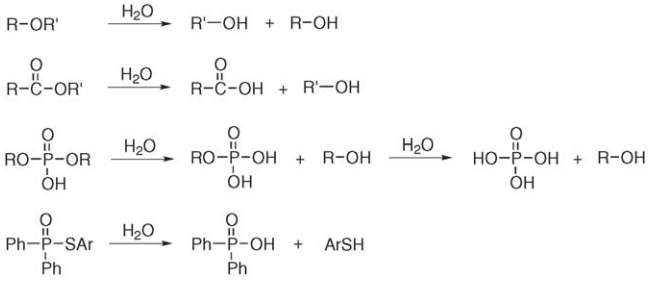
The proposed mechanism for the intramolecular molybdocene-catalyzed hydrolysis of dimethyl phosphate is similar to that proposed for analogous reactions catalyzed by Co(III) coordination complexes [52]. In this case, the mechanism involves both Lewis acid activation of the substrate through coordination and intramolecular hydroxide attack (Scheme 12). In related work, Breno et al. studied the hydrolysis reactions of carboxylic acid esters and ethers [47]. The hydrolysis of the carboxylic acid esters and of ethers was proposed to proceed by a similar mechanism involving intramolecular hydroxide attack. Note in this pathway that intramolecular hydroxide attack leads to the formation of a strained cyclic intermediate. In support of this pathway, it was noted that prior studies suggested that similar, strained four-membered rings formed when nucleobases coordinated to molybdocenes [30]. The activation parameters for the hydrolysis of ethyl acetate with $Cp'_2Mo(OH)(OH_2)^+$ ($\Delta H^{\ddagger} = 5.9$ kcal/mol and $\Delta S^{\ddagger} = -48$ eu) [47] and phosphate



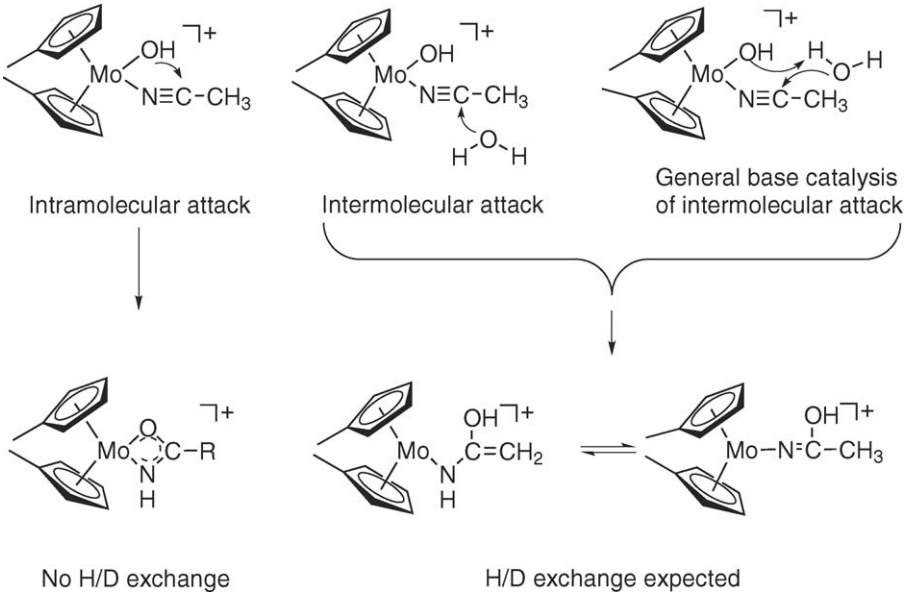
Scheme 9. Proposed mechanism for the hydration of nitriles with $Cp'_2Mo(OH)(OH_2)^+$.

ester hydrolysis with Cp_2MoCl_2 ($\Delta S^{\ddagger} = -16$ eu) [50] are consistent with a geometrically constrained transition state, as proposed in the mechanism in Scheme 12.

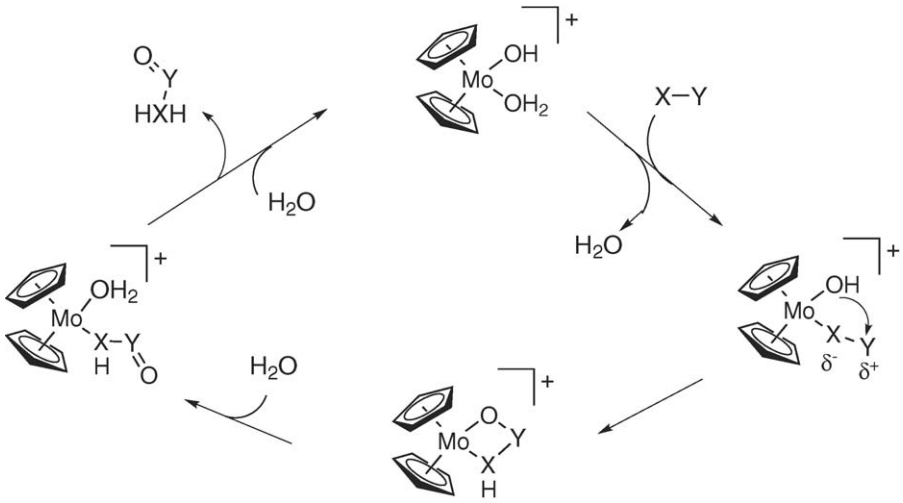
Overall, aqueous molybdocenes are highly effective hydrolysis catalysts that, depending on the substrate, increase the hydrolysis rate by a factor of 10^2 to 10^8. The hydrolysis of organophosphate pesticides and thiophosphinates are the first examples of such reactions mediated by an organometallic complex in aqueous medium. In addition, the hydrolysis of thiophosphinates affords benign degradation products relative to base-catalyzed hydrolysis and may have implications for the remediation of persistent organophosphate pollutants.



Scheme 11. Hydrolysis reactions catalyzed by aqueous molybdocenes.



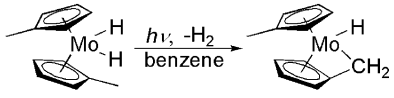
Scheme 10. Predicted H/D exchange for various hydrolysis mechanisms.



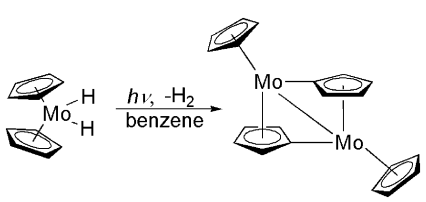
Scheme 12. Generalized mechanism for hydrolysis catalyzed by molybdocenes.

4. Water-soluble *ansa*-molybdocene catalysts

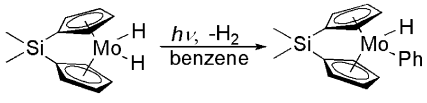
In order to impart more activity to the $Cp'_2Mo(OH)(OH_2)^+$ catalyst and its related derivatives, we are investigating the synthesis and reactivity of selected water-soluble *ansa*-molybdocene complexes. Previous studies have documented that *ansa* ligands can have a dramatic effect on the reactivity of Group VI metallocenes. For example, non-bridged metallocenes react photochemically to form intramolecular tucked-in complexes as shown in Eq. (4) [53] or bridged species as in Eq. (5) [54,55]. However, on introduction of a silane-bridge, the corresponding *ansa* complexes exhibit very different reactivity. Rather than forming tucked-in complexes, the silyl-bridged molybdocenes activate exogenous C–H bonds (for example, in the solvent; Eq. (6)) [53]. Remarkably, these molecules also activate C–C bonds, as observed in the oxidative addition of acetonitrile (Eq. (7)) [53]. The methylene-bridged molybdocene dihydride complex reacts similarly to the silyl-bridged complexes, promoting C–H bond activation (Eq. (8)). Thermal reactivity also changes substantially when *ansa*-bridges are incorporated into the metallocene. For example, the non-bridged dihydride complex reacts with the C–H bond in thiophene to give $Cp_2Mo(\eta^1\text{-}C\text{-}SC_4H_3)H$, but C–S bond activation is observed when the Cp ligands are bridged with Me_2Si (Eq. (9)) [56].



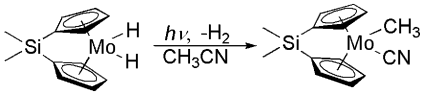
(4)



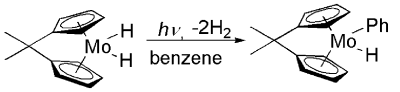
(5)



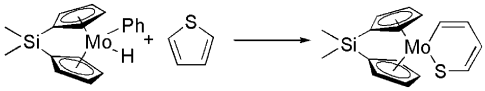
(6)



(7)



(8)



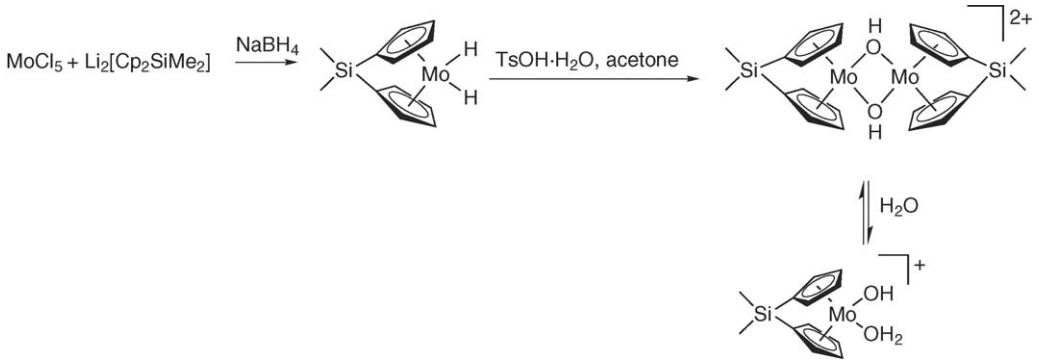
(9)

Although the comparison of the reactivity of the Mo(II) intermediate in the reactions above to the aquated Mo(IV) species (in Cp_2Mo^{2+}) is not exact, we hypothesize that interannular bridges will also lead to increased rates of reactivity in the Cp_2Mo^{2+} complexes, if for no other reason than because the vacant coordination sites are more accessible. In addition, the more electrophilic metal center in the *ansa* complexes may lead to reactivities not observed with the non-bridged catalysts.

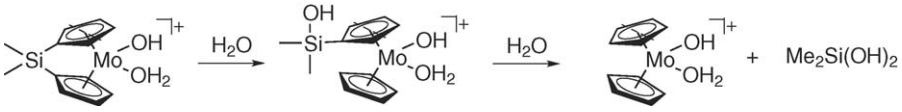
The interesting reactivity of *ansa* complexes, together with the remarkable stability of molybdocenes in water, make *ansa*-molybdocene complexes logical selections to carry out catalytic transformations of organic substrates in aqueous medium. To examine this hypothesis, the $[(Cp_2Si(CH_3)_2)Mo(\mu\text{-}OH)_2Mo(Cp_2Si(CH_3)_2)^{2+}][OTs^-]_2$ complex was synthesized. The synthetic route paralleled the synthesis of the non-*ansa* complexes and is outlined in Scheme 13 [31].

NMR spectroscopy showed that $(Cp_2Si(CH_3)_2)Mo(\mu\text{-}OH)_2Mo(Cp_2Si(CH_3)_2)^{2+}$ was not stable in aqueous solution [57,58], particularly upon heating. Complete hydrolysis occurred in 12 h, and the strained bridging silane hydrolyzed and the non-bridged non-substituted molybdocene was formed, as shown in Scheme 14.

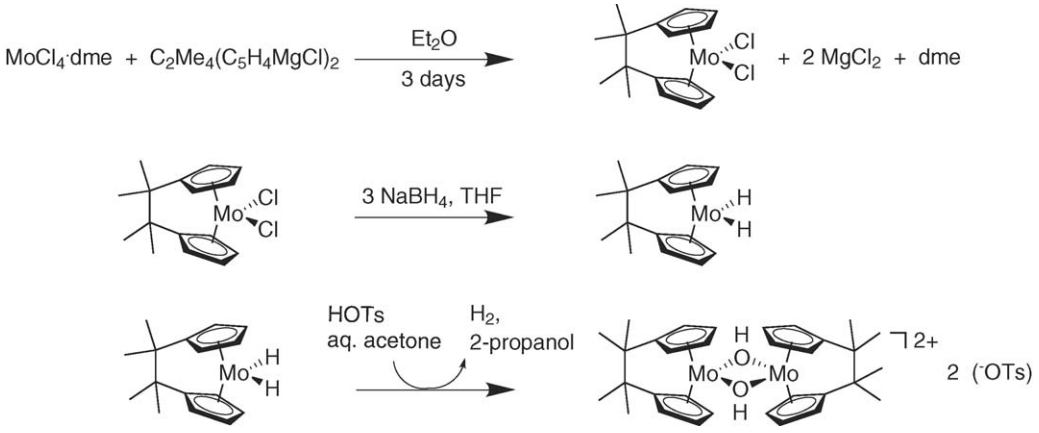
Because the hydrolysis of $(Cp_2Si(CH_3)_2)Mo(\mu\text{-}OH)_2\text{-}Mo(Cp_2Si(CH_3)_2)^{2+}$ precluded further study of this molecule, the water-soluble tetramethylethylene-bridged *ansa*-molybdocene complex $[(Cp_2C_2(CH_3)_4)Mo(\mu\text{-}OH)_2Mo(Cp_2C_2(CH_3)_4)^{2+}][OTs^-]_2$ was synthesized next. The molecule was prepared according to the route in Scheme 15 [57]. In



Scheme 13. Synthetic route to $[(Cp_2Si(CH_3)_2)Mo(\mu\text{-}OH)_2Mo(Cp_2Si(CH_3)_2)^{2+}][OTs^-]_2$.



Scheme 14. Hydrolysis of $(Cp_2Si(CH_3)_2)Mo(OH)(OH_2)^+$.



Scheme 15. Preparation of a water-soluble tetramethylethylene-bridged molybdocene dimer.

water, the complex underwent hydrolysis to afford the monomer $(Cp_2C_2(CH_3)_4)Mo(OH)(OH_2)^+$ and at least one additional species at high concentration. Preliminary data indicate that the tetramethylethylene-bridged complex catalyzes the selective hydration of nitriles. The exact identity of the active catalyst and the mechanism of catalysis are currently under investigation.

5. Summary and conclusions

The coordination chemistry and organometallic chemistry of molybdocenes in water has been investigated extensively over the past 20 years because of the intrinsic solubility and hydrolytic stability of these complexes. In water, the molybdenum center acts as a Lewis acid, activating substrates toward intra- or intermolecular nucleophilic attack by a bound hydroxo ligand or free water molecule. Mechanistic evidence suggests that the intramolecular hydration and hydrolysis reactions proceed through strained, four-membered ring intermediates, which are relatively common to molybdocene chemistry. These investigations have led to rare examples of C–H bond activation in water, as well as organometallic-mediated phosphate and thiophosphinate hydrolysis. The rich aqueous chemistry of molybdocenes may be further enhanced by incorporation of an interannular bridge, which alters the geometry and electronics of the molybdocene system. The more accessible coordination site and the increased electrophilicity of the metal center is expected to lead to enhanced reaction rates and a wide range of interesting reactivity.

Acknowledgment

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