# REACTIVITY AND MECHANISMS IN AQUEOUS ORGANOMETALLIC CHEMISTRY: C-H BOND ACTIVATION IN WATER CATALYZED BY MOLYBDOCENES

by

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A DISSERTATION

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The chemistry of three organometallic systems in water was studied with the goal of understanding more fully the reactivity of organometallic complexes in aqueous environments.

Molybdocene complexes were found to catalyze C-H bond activation reactions in water. The catalytically active solutions were prepared from the molybdocene dimer $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ ($Cp' = \eta^5\text{-}C_5H_4CH_3$), which was characterized crystallographically. This compound was shown to exist in a monomer-dimer equilibrium at pD 6.9 in $D_2O$. At elevated temperatures, the Cp*Me* hydrogens were exchanged intramolecularly by deuterium with the activation parameters $\Delta H^{\neq} = 25.0$ kcal mol$^{-1}$ ± 0.68 kcal mol$^{-1}$ and $\Delta S^{\neq} = -5.3$ cal mol$^{-1}$ K$^{-1}$ ± 0.47 cal mol$^{-1}$ K$^{-1}$. Primary alcohols selectively exchange α-hydrogens intermolecularly, and some additional β-hydrogen exchange is observed in secondary alcohols. Formation of chelate complexes, such as the independently synthesized and crystallographically characterized glycolate complex $[Cp'_2MoOCH_2CH_2OH](OTs)$, inhibit the H/D exchange in multidentate alcohols. The exchange reaction proceeds via formation of a ketone hydride molybdocene intermediate $[Cp'_2Mo(OCR_1R_2)H]^+$, which can reversibly dissociate the ketone ligand. The molybdocene hydride complex that results from ketone dissociation was identified by independent synthesis and crystallographic characterization of the hydride complex $Cp'_2MoH(OTf)$. The H/D exchange reaction proceeds stepwise, with the active catalyst being derived from the monomeric complex $[Cp'_2Mo(OH)(OH_2)]^+$. The activation parameters were determined as $\Delta H^{\neq} = 19.4$ kcal mol$^{-1}$ ± 0.2 kcal mol$^{-1}$ and $\Delta S^{\neq} = -22.7$ cal mol$^{-1}$ K$^{-1}$ ± 0.7 cal mol$^{-1}$ K$^{-1}$, and a primary kinetic isotope effect of $k_{H,\, pD6.4}/k_{D,\, pH6.5} = 2.2$ was observed.

In addition to C-H bond activation, the molybdocene catalyst also promotes ester and nitrile hydrolysis, aldehyde disproportionation, ether cleavage and reduction of olefins in water under the appropriate conditions.

Photochemical studies of $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ and chemical and electrochemical oxidation studies of $(CO)_3Fe(TPPTS)_2$ showed that the 17-electron organometallic radicals generated from these precursors exhibit the same reactivity as their organic-soluble analogs. The iron carbonyl complex was characterized crystallographically.

This dissertation contains previously published, co-authored materials.

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# DEDICATION

Meinen Eltern

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# CHAPTER I

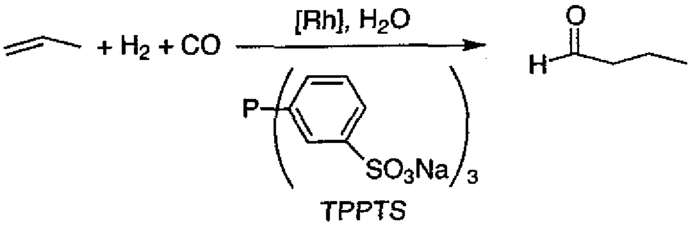
# INTRODUCTION

## Aqueous Organometallic Chemistry

The ubiquitous solvent water has been neglected by organometallic chemists for years. The reason for this neglect is that organometallic compounds and reactions are traditionally known for their sensitivity toward water or even traces of moisture. For example, a recent textbook on inorganic synthesis notes that "most organometallic compounds are oxygen or moisture sensitive,"[1] and in response to a news article on advances in aqueous organometallic chemistry,[2] a reader comments that "at first, the idea of performing organometallic reactions in water might seem ridiculous, since it goes against the traditional belief that most organometallics are extremely sensitive to traces of air and moisture and rapidly decompose in water."[3]

The characteristic feature of organometallic complexes is the presence of one or more metal-carbon bonds.[4] In water, these bonds between the metal and the ligand may be broken, and a number of possible hydrolysis products, including aquo, hydrido, hydroxy and oxo compounds, as well as a variety of ligand-derived products may be formed. Examples of hydrolytically unstable organometallic compounds and their reaction products are discussed in the latter part of this introduction.

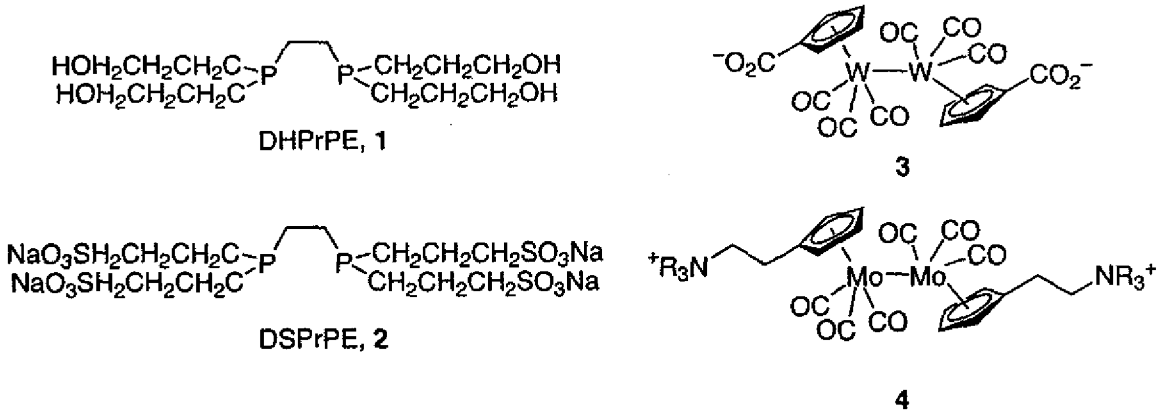
Not all organometallic compounds, however, are unstable in water, and over the past 25 years or so, aqueous organometallic chemistry has received increased attention. This has been well documented in a number of books and review articles.[5] Three main reasons may be given for the interest in water as a solvent for organometallic reactions. First, water is abundant, cheap, and environmentally benign. This is appreciated both in the laboratory as well as in industry,[5d] where organometallics are used as catalysts in a number of important reactions and processes.[5b,c,e,h] Second, the use of organometallic catalysts in an aqueous phase may lead to easy workup procedures. In aqueous biphasic reaction systems, catalysts and products can easily be separated.[6] 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. The first and most prominent example of a reaction catalyzed by an organometallic compound that has found application in industry and that outperforms other well established processes with respect to selectivity and yield shall not remain unmentioned: In the so-called Ruhrchemie/Rhône-Poulenc process, butyraldehyde is produced in quantities of 300,000 tons/year, utilizing a Rh catalyst and the water-soluble phosphine TPPTS (triphenylphosphinetrisulfonate, sodium salt) or derivatives thereof under biphasic conditions (eq 1).[7]



(1)

One important hurdle in aqueous organometallic chemistry is often the intrinsic insolubility of the metal complexes in aqueous media. Current research efforts in this area therefore include the synthesis of water-soluble ligands that impart solubility to the metal complexes to which they are attached.[5h,i] The importance of ligand design and synthesis for aqueous organometallic chemistry is underlined by the fact that an entire chapter of a recent volume of *Inorganic Synthesis* is dedicated to the preparation of water-soluble ligands.[8] The strategies for the design of water-soluble ligands are outlined with the help of examples from this laboratory. Widely used ligands such as phosphines and cyclopentadienyl are rendered soluble through attachment of water-solubilizing groups, such as the polar $-OH$ or the ionic $-COO^-$, $SO_3^-$ (see also TPPTS, eq 1) and $-NR_3^+$ (Scheme 1).[9-13]

The bidentate phosphines **1** and **2**[11-13] have been used in aqueous biphasic hydrogenations of olefins, with $[Rh(COD)Cl]_2$ as the catalyst precursor.[13] The polar and ionic endgroups on the alkyl sidechains render the transition metal complexes prepared from these phosphine ligands water-soluble.



Scheme 1. Examples of ligands used in aqueous organometallic chemistry: Functionalized phosphine- and cyclopentadienyl ligands.

For investigations of organometallic radicals in aqueous solutions the metal carbonyl dimers **3** and **4** were synthesized.[9,10] In these cases, side chains with ionic functionalities were attached to the cyclopentadienyl rings.

Some organometallic complexes are intrinsically water-soluble. Among those are compounds containing aquo and hydroxy ligands in their coordination sphere, such as the $[Cp^*Rh(OH_2)_3]^{2+}$ dication[14] ($Cp^* = \eta^5\text{-}C_5(CH_3)_5$) and the $[Cp'_2Mo(OH)(OH_2)]^+$ complex ($Cp' = \eta^5\text{-}C_5H_4CH_3$), the latter of which is the subject of the investigations described in Chapters II-V. The aforementioned complexes are soluble by virtue of their ionic charge and their hydrogen-bonding ability through the aquo or hydroxy ligands. The chemistry of these types of water-soluble organometallics has been reviewed recently.[5g,15]

Previous work carried out in this laboratory in the area of aqueous organometallic chemistry has focussed on both gaining an understanding of the fundamental chemistry of organometallic compounds in water, such as water-soluble organometallic radicals,[16] and the application of water-soluble organometallic catalysts.[17] In this dissertation, the results of mechanistic and chemical studies of water-soluble transition metal complexes are discussed which contribute to the understanding of aqueous organometallic chemistry. The goal of the studies on $(CO)_3Fe(TPPTS)_2$ and $[(CpCH_2CH_2NMe_3)Mo(CO)_3]_2$ described in Chapter VI and Chapter VII, respectively, was to obtain quantitative information on the reactivity of water-soluble organometallic radicals with respect to reaction rates and mechanisms. Detailed introductions precede both chapters, and the reader is referred to these chapters for further information.

The major part of this dissertation describes the chemistry of water-soluble molybdocene complexes. The initial preparation of the dimeric $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ (**5**) was motivated by the idea that OH-bridged transition-metal complexes may be involved in the photocatalytic production of $H_2$ and $O_2$ from water.[18,19] Hydroxy-bridged transition-metal complexes are known to release $O_2$ under the appropriate conditions,[20,21] and consequently complex **5** was prepared to investigate its role in a potential photochemical, molybdocene-catalyzed water-splitting cycle.[22,17]

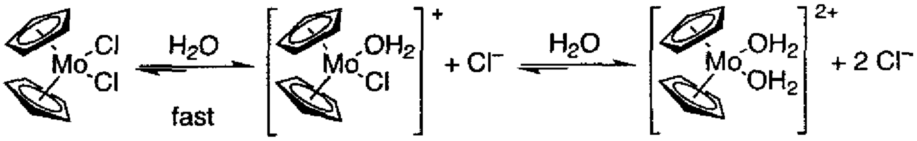
During the investigation of the hydrolysis behavior of **5** it was found that the aqueous solutions of **5** catalyzed C-H bond activation (Chapter II). This exciting result motivated the more detailed investigations on the hydrolysis of molybdocenes (Chapter III), on the intimate mechanism of intermolecular C-H bond activation (Chapter IV), and the reaction chemistry toward a variety of organic substrates (Chapter V). The following sections of this introduction elaborate on the background on aqueous molybdocene chemistry and catalytic C-H bond activation.

## Aqueous Molybdocene Chemistry

Metallocenes of the group VI metals have received a lot of attention since the first report of the dihalides $Cp_2MCl_2$ ($Cp = \eta^5\text{-}C_5H_5$, M= Mo, W) by Cotton and Wilkinson in 1954.[23] A vast number[24] of theoretical,[25] physicochemical[26] and chemical[27] studies on molybdocenes[28] have been carried out since then. However, only a few of the early reports have commented on the chemistry of group VI metallocenes in water.[29,30]

It was the discovery of the anti-tumor activity of metallocenes of the type $Cp_2MX_2$ (M = Ti, V, Mo, X = halides/pseudohalides)[31,32] that has led to numerous detailed investigations of their hydrolytic chemistry. Over the past 15 years, the aqueous chemistry of metallocenes containing Ti, Zr, Hf ,V, Nb, Cr, and Mo has been explored (Table 1). In most cases, hydrolysis of the coordinated halide or pseudo-halide ligands afforded aquated metallocene complexes, with OH or $OH_2$ ligands replacing X. The exact structure of the hydrolysis products is highly dependent on the pH and is often inferred only from titration studies. The hydrolysis chemistry is typically complex, with formation of a number of dimeric and oligomeric species. In a few cases, aquo and hydroxy complexes could be isolated by controlled hydrolysis of the metallocene precursors.[33,34]

The initial step in the hydrolysis of a metallocene is typically the rapid loss of the halide ligands. In the case of $Cp_2MoCl_2$, the first chloride dissociated before complete dissolution of the complex (eq 2).[35]



(2)

The half-life for loss of the second ligand was estimated to be 6.7 min (the pH of the aqueous solution drops to ~3.5 during the hydrolysis).[35] For the metallocene dichlorides of Ti ($k_{d2} = 0.84\ h^{-1}$), Zr ($k_{d2} = 1.31\ h^{-1}$) and V ($k_{d2} = 1.73\ h^{-1}$), the rate of dissociation of the second chloride is much smaller than for Mo.[37]

Table 1. Rates of Cyclopentadienyl Ligand Hydrolysis in Metallocene Dichlorides[a]

| Compound | Rate of Cp Hydrolysis | ref. |
|---|---|---|
| $Cp_2TiCl_2$ | pD ~ 2.0-2.1, 24 h, < 2% Cp hydrolysis | 36 |
| | pD ~ 6.1-6.2, 24 h, > 90% Cp hydrolysis | |
| | 25°C | |
| | 0.318 M $KNO_3$: $6.4\times10^{-3}$ $h^{-1}$ | 37 |
| | 0.103 M NaCl: $1.2\times10^{-3}$ $h^{-1}$ | |
| | ('ambient pH', 37°C) | |
| $(CpMe)_2TiCl_2$ | pD ~ 1.8-2.0, 24 h, < 2% Cp hydrolysis | 36 |
| | pD ~ 7.5-7.9, 24 h, < 5% Cp hydrolysis | |
| | 25°C | |
| $Cp_2ZrCl_2$ | 0.318 M $KNO_3$: $3.8\times10^{-2}$ $h^{-1}$ | 37 |
| | 0.103 M NaCl: $3.8\times10^{-2}$ $h^{-1}$ | |
| | ('ambient pH', 37°C) | |
| $Cp_2HfCl_2$ | 'too fast to measure' | 38 |
| | 25°C | |
| $Cp_2VCl_2$ | 0.318 M $KNO_3$: $\leq 3\times10^{-3}$ $h^{-1}$ | 37 |
| | 0.103 M NaCl: $\leq 3\times10^{-3}$ $h^{-1}$ | |
| | ('ambient pH', 37°C) | |
| $Cp_2NbCl_2$ | pH 1.8: $\tau_{1/2} = 3$ d | 39 |
| | pH 4.8: $\tau_{1/2} =$ 1-2 h | |
| | pH 6.6: $\tau_{1/2} <$ 15 min | |
| | '$Cp_2NbCl_2$(aq)' exists as μ-O dimer | |
| $Cp_2Cr$ | soluble only in conc. acid | 30 |
| | $Cp_2Cr \rightarrow CpCr(OH_2)_n$, < 24 h | |
| | second Cp: $1\times10^{-2}$ $h^{-1}$ | |
| $Cp_2MoCl_2$ | no detectable Cp hydrolysis over several weeks(no $O_2$, pD 7.6) | 35 |
| | ~7 0% Cp hydrolysis, $O_2$, pD = 7 | 40 |

[a]This data was typically obtained by $^1H$ NMR spectroscopy, following the decrease in signal intensity for the Cp-containing species and comparing it to the signal arising from free cyclopentadiene (CpH is soluble in water up to about 4 mM[37]).

The other important hydrolytic process in aqueous metallocene chemistry is the loss of the cyclopentadienyl ligands. The rate of Cp hydrolysis is very pH dependent and varies significantly within the group of metals examined. Table 1 gives an overview of metallocene Cp hydrolysis for different metals under a variety of conditions. It is interesting to note that for the heaviest group VI metallocene dichloride, $Cp_2WCl_2$, only very little is known about its hydrolysis chemistry.[41]

Molybdocene stands out from the list of metallocenes in Table 1 in that it is surprisingly stable with respect to Cp hydrolysis (when oxygen is excluded).[42] This stability allowed the detailed investigation of the molybdocenes' hydrolysis and reaction chemistry (Chapters II-V). Unlike for many of the other metallocenes in Table 1, the hydrolysis products of molybdocene were found to be well defined (Chapter III). This was significant with respect to their reaction chemistry. Molybdocene-catalyzed reactions such as phosphoester hydrolysis,[43,44] pesticide degradation,[45] and C-H bond activation (Chapter IV) can be better understood based on the knowledge of the $[Cp_2Mo(OH)(OH_2)]^+$-$[Cp_2Mo(\mu\text{-}OH)_2MoCp_2]^{2+}$ monomer-dimer equilibrium in water. The latter reaction, the activation of carbon-hydrogen bonds catalyzed by aqueous solutions of molybdocenes, is remarkable. It is one of only a few examples of metal systems that can facilitate this reaction. Catalytic C-H bond activation, which as been called a 'Holy Grail' in chemistry,[46] is discussed in the following section.

## Carbon-Hydrogen Bond Activation

As mentioned above, one of the most interesting features of molybdocenes in water is their ability to catalyze C-H bond activation reactions.[46,47] The activation of carbon-hydrogen bonds is one approach to the functionalization of the chemically rather inert saturated hydrocarbons, such as alkanes (which make up about 50 % of petroleum) and methane. Typically, their reactivity is dominated by partial or complete oxidation (formation of acids or complete combustion to $CO_2$ and $H_2O$), high temperature dehydrogenation ('cracking') or unselective radical halogenation. The lack of reactivity is often attributed the high bond strength of alkane C-H bonds (90-100 kcal/mol) and the low C-H acidity ($pK_a = 45\text{-}60$).[46]

The goal of the many studies in the area of C-H bond activation[48] is to find mild ways of utilizing alkanes in chemical synthesis.[49] One approach is the use of transition metal complexes that undergo oxidative addition reactions with alkanes to give the corresponding alkyl hydride complexes (eq 3).

(3)

Further reaction of the alkyl hydride with appropriate reagents may then result in the formation of the functionalized alkane.[47d,e,g]

One of the first examples of intermolecular alkane functionalization was reported by Shilov and et al. in the early 1970s.[50] In this reaction, alkanes were converted to alkyl halides and alcohols in the presence of $[PtCl_6]^{2+}$ in water at 120 °C. The intermediacy of alkyl hydride complexes (eq 3) was inferred from the observed reaction products. (Note that it was later found that this reaction is not catalytic, but stoichiometric in Pt(IV).[47d]). The feasibility of intermolecular oxidative addition of alkanes to transition metal complexes was first demonstrated by Janowicz and Bergman, who reported that photolysis of $Cp^*Ir(PMe_3)H_2$ in cyclohexane or neopentane solution resulted in the formation of a (cyclohexyl)iridiumhydride complex and a (neopentyl)iridiumhydride complex, respectively.[51]

In addition to intermolecular activation of alkane C-H bonds, numerous examples of both intra- and intermolecular C-H activation reactions involving transition metal compounds are known.[47e] Tungstenocene was one of the first organometallic compounds that were reported to undergo insertion reactions with carbon-hydrogen bonds.[52] Irradiation of $Cp_2WH_2$ in benzene gave $Cp_2W(Ph)H$, and the permethylated analog $Cp^*_2WH_2$ was shown to insert intramolecularly into the C-H bond of a Cp*-methyl group upon irradiation to afford $Cp^*(\eta^5,\eta^1\text{-}C_5Me_4CH_2)WH$.[53-55] Similarly, the dimethylsilyl-bridged molybdocene $[Me_2Si(C_5Me_4)_2]MoH_2$ was just recently reported to also undergo insertion reactions into benzene and the ring-methyl group.[27b] The latter examples show that C-H bond activation is feasible with group VI metallocenes.

Finally, it is important to point out that the C-H bond activation in transition-metal alkoxide complexes, which is the crucial step in the molybdocene catalyzed H/D exchange of alcohols (see Chapter IV), is well known in organic solvents. It has been utilized in the preparation of metal-hydride complexes,[56] and it is the rate-determining step in the alcohol epimerization catalyzed by Re complexes.[57]

The aqueous chemistry of molybdocenes discussed in this dissertation contributes to the large field of C-H bond activation. It is a unique example of *catalytic* C-H bond activation, and it is one of only a few that occur in water.

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# CHAPTER II

## INTRA- AND INTERMOLECULAR H/D EXCHANGE IN AQUEOUS SOLUTION CATALYZED BY MOLYBDOCENES

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The promotion of organic transformations in aqueous solution by organometallic compounds is an area of intense investigation. Research in this field has led to exciting developments in homogeneous and aqueous biphasic catalysis.[1] As part of our studies in this area[2] we are investigating the catalytic behavior of molybdocenes in aqueous solution. Several detailed investigations of $Cp_2MoCl_2$ ($Cp = \eta^5\text{-}C_5H_5$) have been reported, chiefly because of its potential as an anti-tumor agent,[3] yet the identity of the molybdocene species present in aqueous solution remains somewhat ambiguous. The recent report of the dimeric molybdocene complex[4] $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2][OTs]_2$ (OTs = *p*-toluenesulfonate) led us to investigate how the aqueous chemistry of this dimeric species relates to that of aqueous $Cp_2MoCl_2$. Consequently we prepared the complex $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs]_2$ (Cp', CpMe = $\eta^5\text{-}C_5H_4CH_3$) (**1**) and studied its hydrolysis behavior. Surprisingly we found that H/D exchange occurred with the $D_2O$

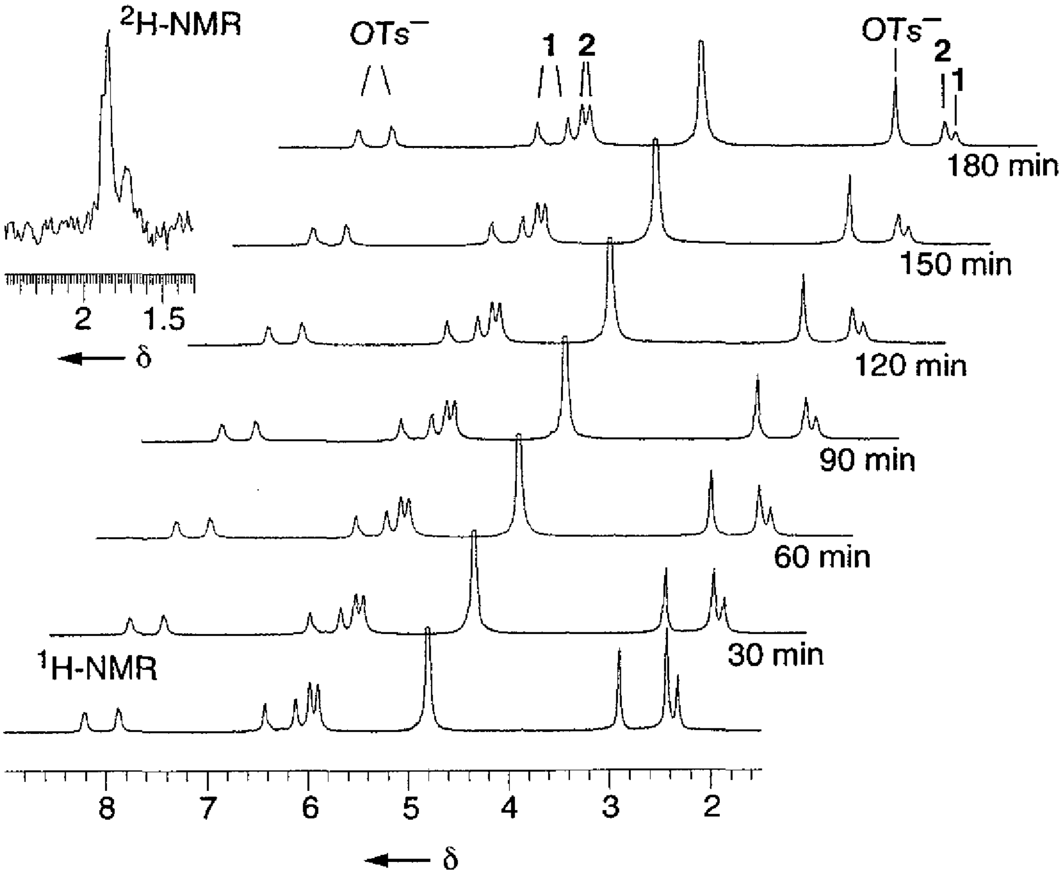
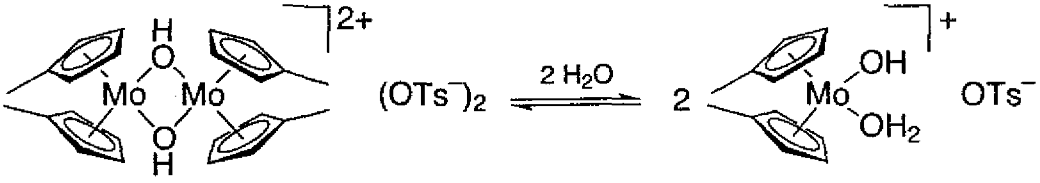


Figure 1. $^1$H NMR spectra of a solution of **1** in $D_2O$ at 75 °C recorded over a period of 3 h. *The inset shows the* $^2$H NMR *of the reaction solution after cooling to* 25 °C.

solvent for the hydrogen atoms on the Cp*Me* groups of the molybdocene. Further investigation showed that H/D exchange also occurred with alcoholic substrates in aqueous solution containing catalytic amounts of **1**. These reactions represent examples of C-H bond activation in aqueous solution.[5]

The molybdocene dimer **1** was prepared from $Cp'_2MoH_2$[6] and HOTs in aqueous acetone. The complex dissolves rapidly in water ($D_2O$) at room temperature to give a mixture of two main hydrolysis products as indicated by NMR (Figure 1). The pH of a 5 mM solution of **1** in $H_2O$ stabilizes at 6.7 after 3 h and remains stable over a period of several days. The $^1$H NMR of $Cp'_2MoCl_2$[6] in $D_2O$ adjusted to pD 6.7 is identical to that of **1** in $D_2O$. Work by Kuo et al. suggests that the predominant species in an aqueous solution of $Cp_2MoCl_2$ at this pH is the hydroxy-aquo complex **2**.[3b] The hydrolysis reaction is therefore proposed to proceed according to Scheme 1. In addition, we found the concentration dependence of the two species present in aqueous solution to be consistent with a monomer-dimer equilibrium.

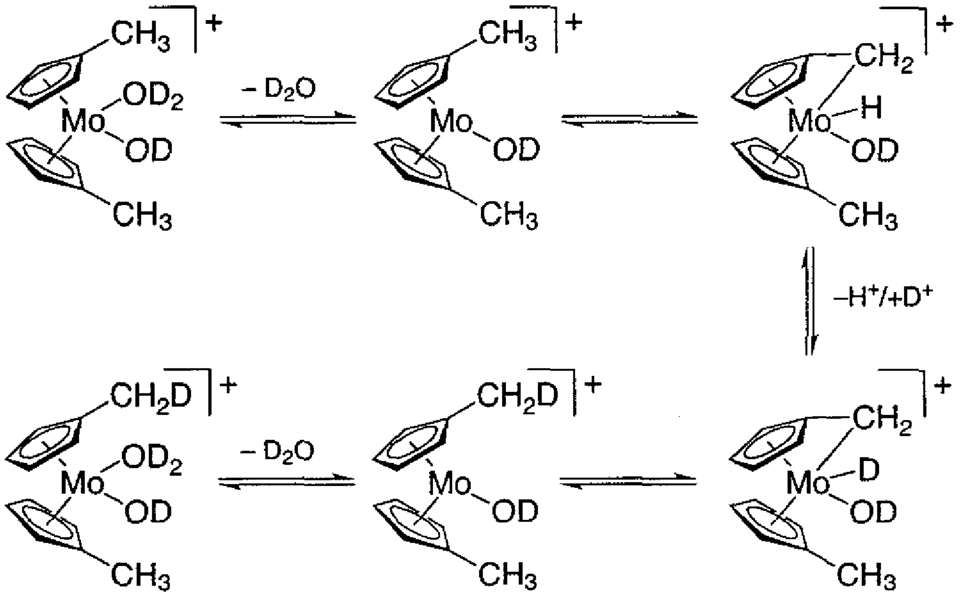


**1** **2**

Scheme 1. Hydrolysis mechanism of **1**.

In an experiment designed to study the temperature dependence of the hydrolysis reaction, a solution of **1** in $D_2O$ was heated to 75 °C and monitored by $^1$H NMR (Figure 1). Over a period of three hours, the resonances for the Cp*Me* groups ($\delta = 2.43$, 2.31 at 75°C) disappeared without any significant change in the signal intensities of the other resonances, while the pD remained unchanged. The $^2$H NMR spectrum[7] of this sample after cooling to room temperature revealed that the protons on the Cp*Me* group had undergone H/D exchange with the $D_2O$ solvent (Figure 1).[8]

A possible mechanism for the H/D exchange involves the intramolecular insertion of the molybdenum center into a C-H bond of the Cp*Me* group (Scheme 2). This



Scheme 2. Proposed mechanism for the intramolecular H/D exchange.

pathway is analogous to the intramolecular C-H activation in $[Cp^*_2W]$ ($Cp^* = \eta^5$-$C_5Me_5$) in which, upon thermolysis or photolysis of appropriate precursors, the tucked-in complex $Cp^*(\eta^5,\eta^1$-$C_5Me_4CH_2)WH$ is formed.[9] The hydride ligand in the activated, tucked-in molybdenum complex can then exchange with the water by a protonation/deprotonation reaction. Conversion of the deuteride complex back to the hydroxy-aquo complex results in a species now containing deuterium in the Cp*Me* group.

Alternatively, the H/D exchange could proceed by a simple proton exchange without participation of the metal center if the Cp*Me* hydrogens were sufficiently acidic. An experiment in which the aqueous molybdocene solution was adjusted to pD 12.8 and heated at 85°C showed that the H/D exchange is slow, with only 17% conversion after 3h. This result is not consistent with a simple proton exchange.

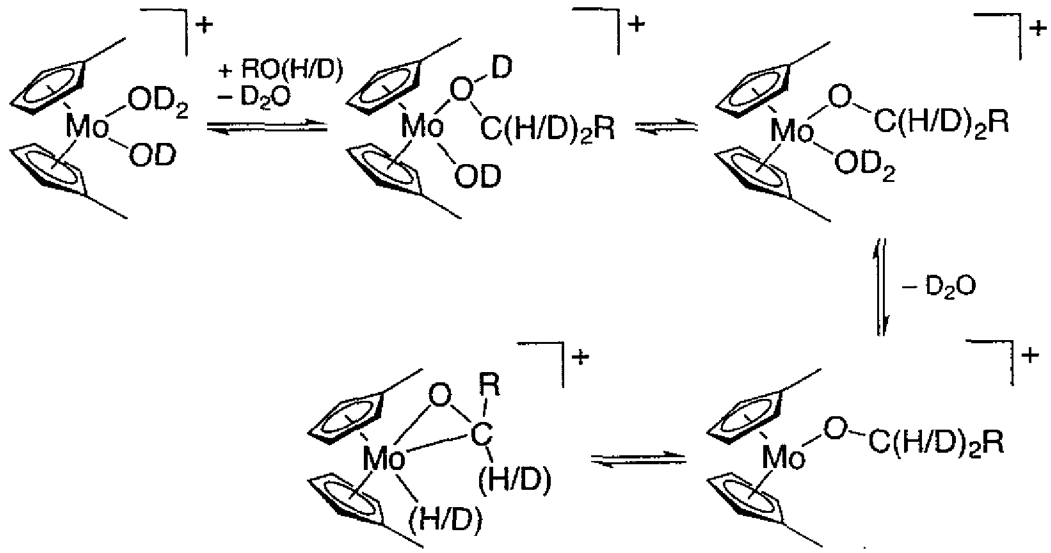
Table 1. Intermolecular H/D Exchange With Alcoholic Substrates

| Substrate | $c$(ROH) (mol $L^{-1}$) | mol % **1** | T (°C) | $t$ (h) | % H/D Exchange |
|---|---|---|---|---|---|
| MeOH | 1.02 | 0.9 | 102 | 39 | 67 |
| EtOH | 0.71 | 2.6 | 102 | 39 | 30 |
| $^n$PrOH | 0.55 | 3.2 | 85 | 68 | 48 |
| $^n$BuOH | 0.45 | 3.7 | 85 | 22 | 33 |
| $HOCH_2CH_2OH$ | 0.38 | 3.6 | 88 | 29 | 6 |

Likewise, a radical pathway as an alternative to the C-H activation mechanism seems thermodynamically unreasonable because it would necessitate the homolytic cleavage of the very strong H-O bond of water in the H(D) atom abstraction step.

In order to test the scope of the H/D exchange reaction, various alcoholic substrates and a catalytic amount of **1** were heated to 85-100 °C for several hours and the reaction monitored by $^1$H and $^2$H NMR. The results of these experiments are summarized in Table 1.

With primary alcohols, incorporation of deuterium is observed on the α-carbon atom. No H/D exchange occurred with the ethers $Et_2O$ and THF. A reasonable mechanism for the intermolecular exchange reaction requires the coordination of the alcohol to the metal center in the first step (Scheme 3). Rapid proton exchange then results in formation of an alkoxy-aquo complex. Upon dissociation of the aquo ligand the metal center inserts into the α-C-H bond to form a hydrido species.[10] Exchange of the hydride ligand in the molybdenum complex by D and reversing the reaction path then leads to the α-labeled alcohol.



Scheme 3. Mechanistic proposal for the intermolecular H/D exchange in an alcoholic substrate.

Further information about the reaction pathway in the intermolecular exchange reaction was obtained from an experiment using the bifunctional alcohol ethylene glycol. The H/D exchange with this substrate occurs at a significantly slower rate than with the monofunctional alcohols. In addition, $^1$H NMR spectra showed the formation of a 1:1 complex between the molybdocene fragment and ethylene glycol. These observations can be explained in terms of the chelating ability of ethylene glycol, leading to a molybdocene complex in which the bidentate ligand occupies both coordination sites in the equatorial plane of the bent metallocene, thus inhibiting the α-C-H bond insertion. If the H/D exchange were to proceed by a simple protonation/deprotonation mechanism as a result of a weakened α-C-H bond, there would be no distinct difference in reaction rates for monodentate alcohols in comparison to bidentate alcohols.

Evidence for the intermediacy of the π-carbonyl complex (Scheme 3) was obtained from an experiment in which a mixture of isopropanol and 2-butanone was heated under H/D exchange conditions. Acetone and 2-butanol were observed as the products of this reaction, presumably because of an exchange of the coordinated ketone in the intermediate. Complete details of the mechanistic studies of the intermolecular exchange will be presented elsewhere.

In summary, the $[Cp'_2Mo]^{2+}$ complex is capable of activating C-H bonds in aqueous solution. We are continuing to investigate the mechanism of this H/D exchange and the applicability of this system to other substrates.

## Experimental Section

**1**: A solution of $Cp'_2MoH_2$ (1.04 g, 4.04 mmol) and *p*-toluenesulfonic acid monohydrate (0.74 g, 3.90 mmol) in a mixture of 100 mL acetone/1 mL was refluxed for 8 h under $N_2$. The solution slowly turned green and a gray precipitate separated. The precipitate was separated by filtration and washed with benzene and hexanes to give a microcrystalline, gray powder (1.49 g, 86%). $^1H$ NMR (300 MHz, [D$_6$]DMSO) $\delta$ 7.45 (d, $^3J(H,H) = 8$ Hz, 4 H; *p*-OTs), 7.10 (d, $^3J(H,H) = 8$ Hz, 4 H; *p*-OTs), 5.96 (t, $^3J(H,H) = 2$ Hz, 8 H; *Cp'*), 5.73 (t, $^3J(H,H) = 2$ Hz, 8 H; *Cp'*), 2.28 (s, 6 H; *p*-OTs-*Me*), 1.75 (s, 12 H; Cp'-*Me*), 1.27 (s, 2H, OH). Anal. Calcd. for $C_{38}H_{44}Mo_2O_8S_2$: C, 51.59; H 5.01; Found: C, 51.90; H, 5.48. UV-Vis (DMSO) $\lambda_{max}$= 578 nm.

In a typical deuteration experiment, a solution of 5-10 mg **1** and 20-30 μL substrate in 0.7 mL $D_2O$ was prepared under $N_2$ and transferred into an NMR tube which was subsequently sealed. The sealed tube was heated in an oil bath at constant temperature and the reactions were followed by $^1H$ and $^2H$ NMR.

## Bridge

Chapter II described the initial experimental evidence for the molybdocene-catalyzed C-H bond activation. Subsequent to the publication of this work, the activation parameters for the intramolecular H/D exchange were determined. From the Eyring plot in Figure 2 one obtains $\Delta H^{\neq} = 25.0$ kcal mol$^{-1}$ ± 0.68 kcal mol$^{-1}$ and $\Delta S^{\neq} = -5.3$ cal mol$^{-1}$ K$^{-1}$ ± 0.47 cal mol$^{-1}$ K$^{-1}$. The small negative activation entropy is consistent with an intramolecular mechanism.

In order to understand the detailed mechanisms of the molybdocene promoted

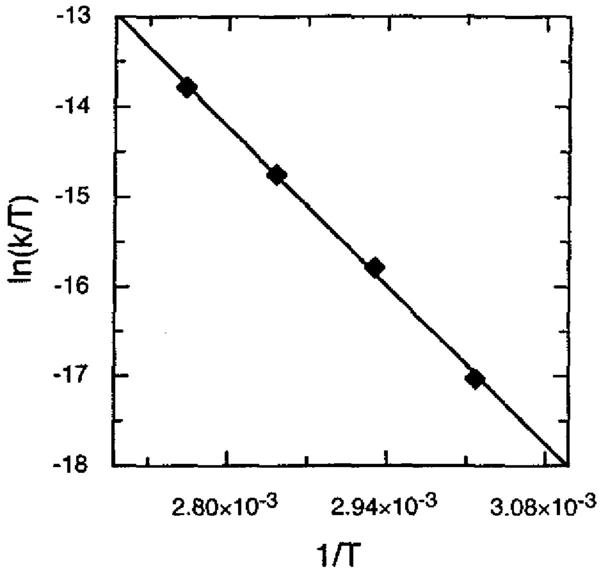


Figure 2. Eyring plot for the intramolecular H/D exchange. Experimental conditions: c([Cp'$_2$Mo($\mu$-OH)$_2$MoCp'$_2$][OTs]$_2$) = 13.3 mM. The decrease of the Cp*Me* resonances in the $^1H$ NMR spectra follows 1st order kinetics. Rate constants were obtained by linear regression of the [Cp*Me* protons] vs. time data. The reaction rates were $1.33\times10^{-5}$ (58.2 °C), $4.74\times10^{-5}$ (68.2 °C), $13.9\times10^{-5}$ (78.7 °C) and $37.2\times10^{-5}$ (88.9 °C) s$^{-1}$, respectively.

H/D exchange in water it was necessary to investigate in detail the hydrolysis chemistry of the catalyst itself. These studies are described in Chapter III, which has been accepted for publication. It was co-authored by Louis Y. Kuo, who carried out the experiments on the non-methylated $Cp_2MoCl_2$ and its corresponding dimer, Timothy J. R. Weakley, who carried out the crystal structure determination, and the author's advisor, David R. Tyler.

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# CHAPTER III

## INVESTIGATION OF THE MONOMER-DIMER EQUILIBRIA OF MOLYBDOCENES IN WATER

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## Abstract

The formation of monomeric and dimeric molybdocene complexes in water was investigated by $^1$H NMR spectroscopy between pD 3.5 and pD 7. The aqueous solutions were prepared from $(CpR)_2MoCl_2$ and $[(CpR)_2Mo(\mu\text{-}OH)_2Mo(CpR)_2](OTs)_2$ (CpR = $\eta^5$-$C_5H_4R$; R=H, $CH_3$). The complex $[(CpCH_3)_2Mo(\mu\text{-}OH)_2Mo(CpCH_3)_2](OTs)_2$ was structurally characterized by X-ray crystallography. The identity of aquated molybdocenes was found to be independent of the precursor used to prepare the aqueous solutions, but dependent on the pH. The solution structures of the molybdocenes at neutral pH are inferred as the monomeric $[(CpR)_2Mo(OH_2)(OH)]^+$ and the dimeric $[(CpR)_2Mo(\mu\text{-}OH)_2Mo(CpR)_2]^{2+}$. The equilibrium constants for the monomer-dimer

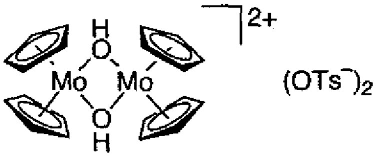
equilibria were obtained from $^1$H NMR dilution studies as $K'_{eq} = 7.9\times10^{-2}$ M ± $1.0\times10^{-3}$ M for R=$CH_3$ at pD7 and as $K_{eq} = 3.5\times10^{-2}$ M ± $1.3\times10^{-3}$ M for R=H at pD 3.5.

## Introduction

The metallocene dihalide, bis($\eta^5$-cyclopentadienyl)molybdenum(IV) dichloride ($Cp_2MoCl_2$, Cp= $\eta^5$-$C_5H_5$, **1**) has received recent attention with regard to its rich variety of water-based chemistry. The coordination of aquated $Cp_2MoCl_2$ to DNA constituents[1-3] serves to model the fundamental bioinorganic chemistry of metallocene antitumor drugs[4,5] with its putative biomolecular target. The studies in this area subsequently led to the finding that $Cp_2MoCl_2$ effectively promotes the hydrolysis of activated[6] and unactivated phosphate esters[7] with rate accelerations similar to coordination compounds that effect the same chemistry.[8,9] $Cp_2MoCl_2$ has also been studied for its potential as a catalyst in systems for photochemical water-splitting.[10] More recently, aqueous solutions containing hydrolyzed $[Cp'_2Mo]^{2+}$ complexes (Cp' = $\eta^5$-$C_5H_4CH_3$) were shown to catalyze C-H bond activation.[11]

Crucial to the understanding of this metallocene's rich chemistry in water is the fundamental knowledge of its speciation in aqueous solution. To date, the most complete report of $Cp_2MoCl_2$ aqueous chemistry[1] shows that the metallocene rapidly loses both of its chloride ligands ($\tau_{1/2}$ ~ 20 minutes in unbuffered water) while the Cp-ligands remain bound even at neutral pH. Potentiometric measurements yielded two titratable protons with pKa's of 5.5 and 8.5. In a later potentiometric study, a third reproducible equivalence point ($pK_a = 2.8$) was found.[12] No evidence was presented, however, from which the existence of a monomeric, dimeric, or higher oligomeric species could be deduced.

The recent work on molybdocene-promoted phosphate hydrolysis[7] raised the question of a possible monomer-dimer equilibrium for this group VI metallocene. The rate of phosphate hydrolysis was found to be half-order in $Cp_2MoCl_2$,[7] which was interpreted in terms of an active molybdocene monomer that is in equilibrium with a dimeric species. The possibility for dimer formation is reasonable in light of the reports by Ito[13-15] who described a molybdocene complex in which two molybdocene fragments are bridged by two hydroxide ligands (**2**).



**2**

The first investigation of a dimeric molybdocene complex in water was reported in the context of C-H bond activation chemistry promoted by water-soluble molybdocenes.[11] The reaction solution, prepared from $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ (**2'**), was found to contain two molybdocene species. These two complexes were proposed to be the dication $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2]^{2+}$ and its hydrolysis product, the catalytically active $[Cp'Mo(OH)(OH_2)]^+$ monomer.

Previous hydrolysis studies of metallocenes include the investigation of titanocenes[16-18] as well as Co[19] and Rh[20,21] pentamethylcyclopentadienyl complexes in water. These complexes were reported to form dimeric or oligomeric compounds in solution. Examples of crystallographically characterized hydroxy-bridged metallocenes with two Cp rings on each metal center include $[Cp_2ZrL(\mu\text{-}OH)]_2$ (with L = $OCOCF_3$,[22] NCPr,[23] or imidazole[24]) and $[Cp_2Y(\mu\text{-}OH)]_2\bullet PhCCPh$.[25] Their water-based chemistry, however, has not been explored further.

In this report we present evidence for the existence of monomer-dimer equilibria in aqueous solutions of the molybdocenes complexes $[(CpR)_2Mo(\mu\text{–}OH)_2Mo(CpR)_2](OTs)_2$ (CpR = $\eta^5$-$C_5H_4R$; R=H, $CH_3$). The chemistry of these molybdocenes in water is shown to be independent of the precursor, whether it is the dihalide or the μ-OH-dimer, and the speciation depends solely on the pH of the solution. These results contribute to a better understanding of aqueous molybdocene chemistry.

## Results and Discussion

### Monomer-Dimer Equilibria at Neutral pH

In our studies on water-soluble molybdocenes,[11] we found that solutions of $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ (**2'**) in $D_2O$ contain two metallocene species, based on $^1$H NMR spectra (Figure 1a). After dissolving **2'** in $D_2O$ at 23 °C, the initial resonances in the Cp' region of the spectrum at $\delta = 5.9$ ppm and 5.65 ppm (**D'**)[26] decreased over a period of 3 hours, while new resonances appeared at $\delta = 5.4$ ppm (**M'**).[26] No free methylcyclopentadiene could be detected, indicating that the Cp' ligands remained metal-bound. The pH of a 10.6 mM solution of **2'** in $H_2O$ changed only slightly from pH 6.2, measured immediately after preparation, to pH 6.9, once the monomer-dimer equilibrium was established. No change in the chemical shifts of **M'** and **D'** were observed during the

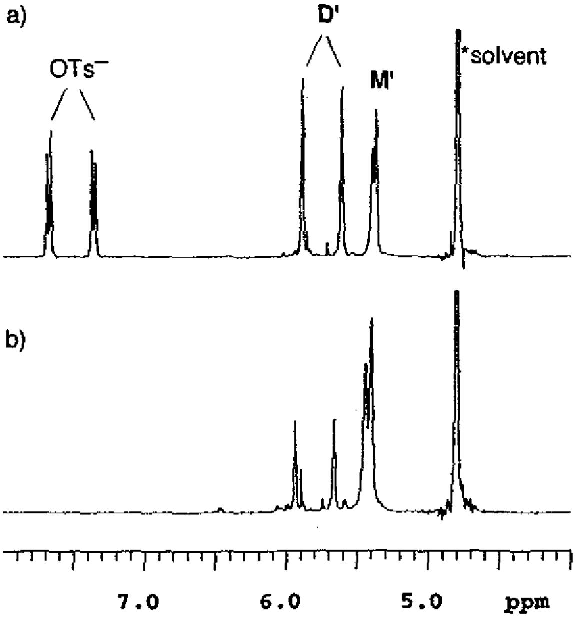


Figure 1. $^1$H NMR spectra of a) [Cp'$_2$Mo(μ-OH)MoCp'$_2$](OTs)$_2$ (**2'**, 15 mM, $D_2O$) and b) Cp'$_2$MoCl$_2$ after adjusting the pD to 6.9 (**1'**, 10 mM, $D_2O$).

hydrolysis process. The molybdocene solutions then remained stable for weeks with regard to pH, monomer-dimer equilibrium, and Cp-ligand hydrolysis.

To investigate the formation of the second species further, the concentrations of **D'** and **M'** were determined for a series of solutions, prepared from varying amounts of **2'** in $D_2O$. The concentrations of **D'** and **M'** were obtained by integrating the $CpCH_3$ resonances in the $^1$H NMR spectrum at $\delta = 1.81$ ppm and 1.93 ppm, respectively, versus the integral of the $O_3SC_6H_4CH_3$ resonance at $\delta = 2.40$ ppm. The concentration of [**D'**] relative to [**M'**] decreased with decreasing total molybdocene concentration, and the plot of [**M'**]$^2$ against [**D'**] is linear (Figure 2, □). This data is consistent with the existence of a monomer-dimer equilibrium, with **D'** being the dimeric complex and **M'** being the

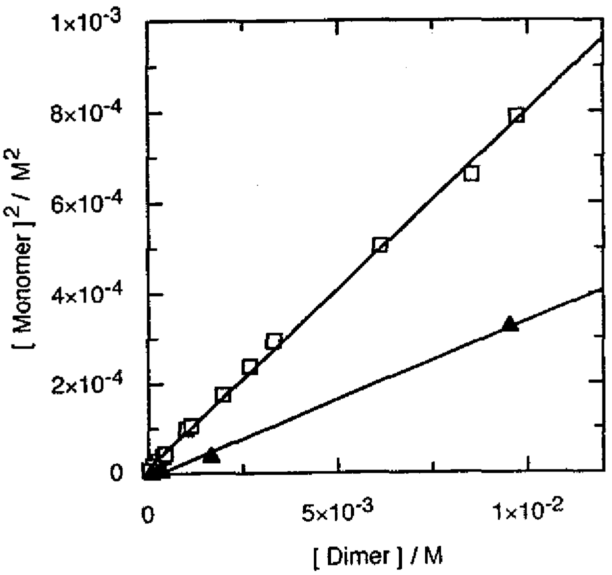
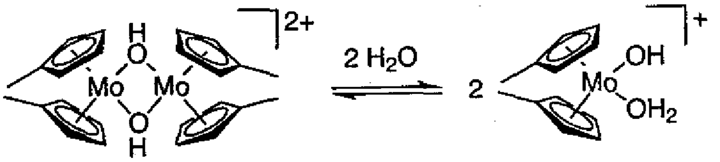


Figure 2. Evaluation of the equilibrium constants: Plots of [Monomer]$^2$ vs. [Dimer]: **2'** in $D_2O$ at pD 7 (□), $K'_{eq} = 7.9\times10^{-2}$ M ± $1.0\times10^{-3}$ M; **1** in $D_2O$ at pD 3.5 (▲), $K_{eq} = 3.5\times10^{-3}$ M ± $1.3\times10^{-3}$ M.

monomer. From a linear regression, the equilibrium constant $K'_{eq} = [\mathbf{M'}]^2/[\mathbf{D'}] = 7.9\times10^{-2}$ M ± $1.0\times10^{-3}$ M was obtained.

The structure of the monomer is inferred as containing one hydroxo and one aquo ligand. This assumption is based on the observation that, upon dissolution of **2'** in $H_2O$, the pH does not change significantly.[27] This is consistent with a hydrolysis process in which no $H^+$ or $OH^-$ is generated, i.e. an aquo ligand simply joins the coordination sphere of the metallocene.[28] The monomer-dimer equilibrium is therefore described by eq 1.



**D'** **M'** (1)

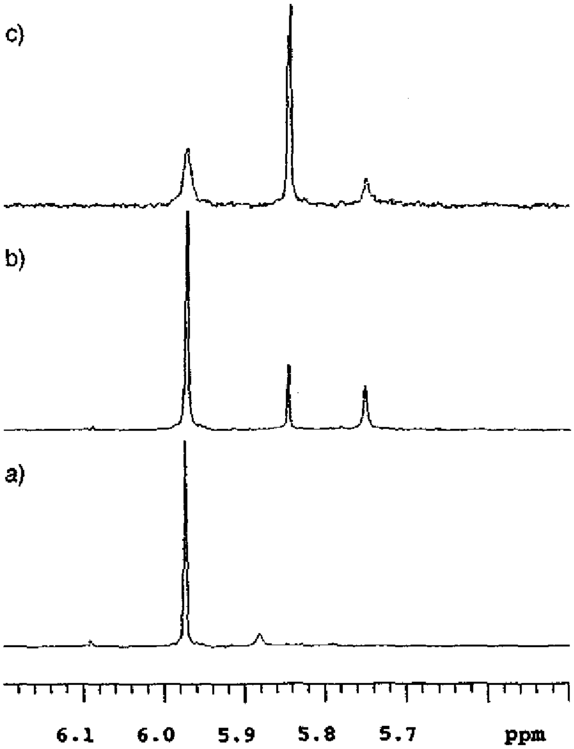


Figure 3. Dilution of $Cp_2MoCl_2$ (pD 7) with $D_2O$ adjusted to pD 7.0. Concentrations for $Cp_2MoCl_2$ are a) 40 mM; b) 0.65 mM; and c) 0.15 mM. The pD remained at 7.0 over the course of the dilution experiment.

Aqueous solutions containing **D'** and **M'** can also be prepared from the dihalide complex $Cp'_2MoCl_2$ (**1'**, 16mM) through pD adjustment by addition of NaOH in $D_2O$ to pD 6.9. As shown in Figure 1b, this results in a solution containing **D'** and **M'**. This result shows that the speciation of molybdocenes in water does not depend on the precursor, but only on the pH of the aqueous solution.

The solution chemistry of the non-methylated analogs of **1'** and **2'** under neutral conditions is more complex in that three species are formed. The $^1H$ NMR spectrum of $Cp_2MoCl_2$ (**1**, 40 mM) in $D_2O$, buffered at pD 7 using MOPS,[29] shows the predominant species at $\delta = 5.97$ ppm (Figure 3a; Table 1). Dilution of this solution to 0.65 mM and

Table 1. Summary of $^1$H NMR Data[a]

| complex | pD | $^1$H NMR (ppm)[b] |
|---|---|---|
| $Cp'_2Mo(OH)(OH_2)$ (**M'**) | 6.9 | 5.46 (m), 5.42 (m), Cp |
| | | 1.95 (s), Me |
| $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2]^+$ (**D'**) | 6.9 | 5.89 (m), 5.61 (m), Cp |
| | | 1.80 (s), Me |
| $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2]^+$ (**D**) | 7.0 | 5.97 (s), Cp |
| $Cp_2MoCl_2$ (aq), monomer | 3.5 | 6.05 (s), Cp |
| $Cp_2MoCl_2$ (aq), dimer | 3.5 | 5.85 (s), Cp |

[a] in $D_2O$. [b]relative to residual HOD.

0.15 mM in molybdocene results in the appearance of two new species at 5.85 ppm and 5.75 ppm. Upon addition of $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2](OTs)_2$ (**2**) to a solution of **1**, adjusted to pD 7, only the resonance at 5.97 ppm increased in the $^1$H NMR spectrum taken immediately after mixing, identifying this species as $[Cp_2Mo(\mu\text{-}OH)_2MoCp_2]^{2+}$ (**D**) (see Supporting Information). This assignment can be made because hydrolysis of **2** is slow, as shown by a control experiment in which $^1$H NMR spectra of **2** in $D_2O$ were recorded over a period of 1h, with collection of spectra started immediately after mixing. The spectra do not change during this time period, showing that hydrolysis of **2** is slow. The remaining two species at 5.85 ppm and 5.75 ppm could not be identified.

The spectrum shown in Figure 3a shows that the dimer **D** is favored over any other hydrolysis product of **2**. Using $K'_{eq}$ the ratio of the resonances of **M'** and **D'** at

[**2'**] = 20 mM is calculated as 3:2, i.e. the monomer is favored in this case. One possible factor influencing this difference in the hydrolysis behavior is the different steric sizes of the Cp and the Cp' ligands, respectively.

The molecular structure of $[\mathrm{Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2}$ (Figure 4) shows only slight differences in the geometric parameters from that of the unsubstituted Cp analog[15] (Table 2). In fact, the two dimers **2** and **2'** are isostructural. The central Mo-O(1)-$\mathrm{Mo^i}$-$\mathrm{O(1^i)}$ tetragons have very similar geometric parameters, and no significant expansion of the metallocene core results from the methyl substituent.

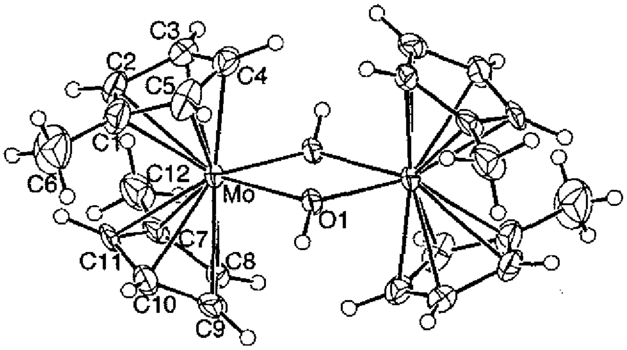
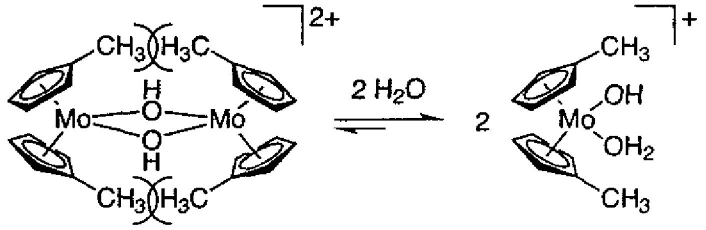


Figure 4. Molecular structure of **1'**. Only the dication is shown.

In solution, however, rotation of the cyclopentadienyl rings in **D'** can bring the methyl substituent into a position above the bridging OH groups, where it can interfere with a Cp-methyl group on the second molybdenum center (eq 2). These solution effects may arise despite the fact that in the solid state the two dimers **2** and **2'** show little or no differences in structure.



(2)

In addition to steric factors, electronic effects may influence the monomer-dimer equilibria. Ito and Yoden have shown that the methyl substituent on the Cp ring increases the electron density on the metal center in the molybdocene dihydride complex $Cp'_2MoH_2$.[30]

Table 2. Comparison of Selected Bond Lengths and Angles of **2** and **2'**

| $[(CpR)_2Mo(\mu\text{-}OH)_2Mo(CpR)_2](OTs)_2$ | **2** (R=H) | **2'** (R=Me) |
|---|---|---|
| Mo-O(1) | 2.092(2) Å | 2.106(3) Å |
| Mo-O($1^i$) | 2.100(2) Å | 2.095(3) Å |
| Mo-Cp(1) | 2.001(5) Å | 2.001(3) Å |
| Mo-Cp(2) | 1.996(5) Å | 1.997(3) Å |
| O(1)-Mo-O($1^i$) | 66.21(10)° | 67.0(1)° |
| Mo-O(1)-$Mo^I$ | 113.79(10)° | 113.0(1)° |
| Cp(1)-Mo-Cp(2) | 128.3° | 130.0(1)° |

Cp(1), Cp(2) are the centroids of rings C(1-5), C(7-11) respectively.

## Monomer-Dimer Equilibrium at Low pH

A 37 mM aqueous solution of $Cp_2MoCl_2$ (**1**) has a pD of 3.5, with two singlets of equal intensity at 5.85 and 6.05 ppm in its $^1H$ NMR spectrum. Upon dilution of this acidic solution with $D_2O$ (pD 3.5, adjusted by addition of HCl), the relative intensities of the two Cp-singlets changed (the pD remained at 3.5, Figure 5).[31]

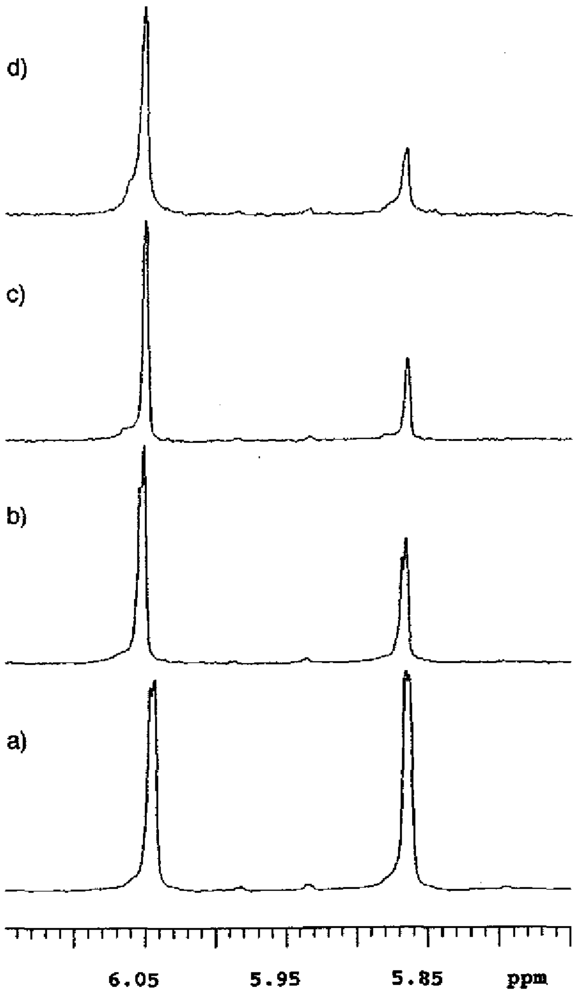


Figure 5. Dilution of $Cp_2MoCl_2$ (pD 3.5) with $D_2O$ (adjusted to pD 3.5).[31] Concentrations for $Cp_2MoCl_2$ are a) 37mM; b) 9.3 mM; c) 2.3 mM; and d) 0.58 mM. The pD remained at 3.5 over the course of the dilution experiment.

Similar to the cases described above, the concentrations of the two species were obtained from integration of the resonances at 6.05 ppm and 5.85 ppm, assigning the downfield resonance, which decreases upon dilution relative to the upfield resonance, to a dimeric complex. A monomer-dimer equilibrium at low pH is consistent with the half-order rate dependency for phosphate hydrolysis promoted by $Cp_2MoCl_2$.[7] From the plot of $[\text{Monomer}]^2$ vs. [Dimer] (Figure 2, ▲), the equilibrium constant $K_{eq} = 3.5\times10^{-2}$ M ± $1.3\times10^{-3}$ M is obtained.[32] Attempts to isolate these two forms of $Cp_2Mo(aq)$ under acidic conditions for more thorough analysis were unsuccessful.

## Conclusion

Molybdocenes exist in monomer-dimer equilibria in aqueous solution. The speciation of the molybdocene complexes depends only on the pH. The Cp' ligand renders formation of the monomer more facile than in complexes containing the Cp ligand. Both steric and electronic factors may influence the monomer-dimer equilibria. The results of this study are of fundamental importance for further investigations in the area of aqueous molybdocene chemistry and its application in C-H bond activation catalysis[11] and phosphate hydrolysis.[6,7]

## Experimental Section

All manipulations were carried out using standard Schlenk techniques under a nitrogen atmosphere and all aqueous solutions were thoroughly purged with prepurified nitrogen prior to use. Anhydrous manipulations were done in a Vacuum Atmosphere glovebox with less than 1 ppm $O_2$. The pH/pD measurements were carried out using a Shindengen pH BOY-P2 pH meter or a Beckman $\Phi 10$ pH meter with a 4 mm diameter probe (Beckman) inserted directly into the NMR tube, and the reported pD values are the uncorrected pH meter readings. The pD of $Cp_2MoCl_2(aq)$ was adjusted with concentrated deareated HCl or NaOH. Solutions at pH 7 were buffered using 4–morpholinepropanesulfonic acid, hemisodium salt (MOPS). $^1H$ NMR (299.95 MHz) spectra were recorded on a Varian Inova 300 spectrometer. Proton chemical shifts were referenced to residual solvent resonances. Molybdocene dichloride was purchased from Strem Chemical Co. (Newburyport, MA) and used as received. Deuterium oxide (99.9% D) was purchased from Cambridge Isotope Lab. (Andover MA), and all other necessary reagents were purchased from Aldrich Chemcal Co. (Milwaukee, WI) and used as received. Molybdocene dihydride[33] and $[(CpR_2)Mo(\mu\text{–}OH)]_2(OTs)_2$ (R=H, Me)[15,11] were prepared according to literature procedures.

## Molecular Structure of $[(CpMe)_2Mo(\mu\text{–}OH)]_2(OTs)_2$ (**2'**)

The dimeric complex was prepared as described previously.[11] Crystals were grown from methanol. A dark red tabular fragment of approximate dimensions 0.04 × 0.24 × 0.26 mm was attached to a fiber with silicon glue. The orientation parameters and cell dimensions were obtained from the setting angles of an Enraf-Nonius CAD-4 diffractometer for 25 centered reflections in the range $13^\circ<\theta<14^\circ$. Table 3 contains a summary of crystal data and the final residuals. A more extensive table including particulars of data collection and structure refinement can be found in the supplementary

Table 3. Crystallographic Data for **2'**

| | |
|---|---|
| Composition | $C_{38}H_{44}Mo_2O_8S_2$ |
| Formula wt | 884.76 |
| Crystal system | monoclinic |
| Space group | C2/c |
| a | 17.751(7) Å |
| b | 8.739(2) Å |
| c | 23.618(5) Å |
| $\beta$ | 99.32(3) ° |
| V, $Å^3$ | 3616(3) |
| Z | 4 |
| $d_{calc}$ | 1.625 g $cm^{-3}$ |
| T | 23 °C |
| Radiation, $\lambda$ | Mo K$\alpha$, 0.71073 Å |
| $\mu$ | 8.38 $cm^{-1}$ |
| Rel. trans. coeff. | 0.834-1.000 ($\varphi$) |
| No. obs. rflns | 2370 [$I \geq \sigma(I)$] |
| No. indep. rflns | 3166 |
| R(F), wR(F) | 0.047, 0.052 |
| $R(F^2)$, $wR(F^2)$ | 0.083, 0.103 |

$R(F) = \Sigma||F_0|-|F_c||/\Sigma|F_0|$; $wR(F^2) = [\Sigma w(|F_0|^2-|F_c|^2)^2/\Sigma w|F_0|^4]^{1/2}$

material. The systematic absences together with the centric distribution of intensities indicated space-group C2/c. Small absorption corrections based on azimuthal (ψ) scans were applied. A *SIR92 E*-map[34] showed the non-hydrogen atoms of the asymmetric unit. A difference synthesis showed minor alternative sites for the sulfonate oxygen atoms, resulting from a rotation about the S-C bond; these were refined isotropically [refined occupancy factor, 0.154(10)]. Other hydrogen atoms were refined anisotropically. Hydrogen atoms were included at the calculated positions and updated after each cycle of refinement, except for the H atom of the bridging OH group which was included at the position indicated by a difference synthesis. The final difference synthesis was featureless. The *teXsan* program suite,[35] incorporating complex atomic scattering factors, was used in all calculations.

## Bridge

*In the previous chapter considerable evidence was provided for the existence of* monomer-dimer equilibria in aqueous molybdocene chemistry. The information about the structure of the momoner and the dimer for the Cp'-substituted molybdocenes as well as the magnitude of the associated equilibrium constant was of significant importance in the investigation of the reaction mechanism of the catalytic H/D exchange. Chapter IV summarizes the results of a number of chemical and kinetic studies which support the mechanism for intermolecular C-H activation proposed in Chapter II. Chapter IV has been submitted for publication. It was co-authored by Timothy J. R. Weakley, who carried out the crystal structure determinations, and the author's advisor, David R. Tyler.

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(26) The solution species are labeled using capital letters, while the compounds isolated as solids are labeled using numerals.

(27) At a concentration of [**1'**] = 10.6 mM, the concentration of $OH^-$ changes by less than $10^{-3}$ mM (pH 6.2 → pH 6.7), less than 0.01% of the concentration of solute.

(28) A complex precipitated from an aqueous solution of $Cp_2MoCl_2$ by addition of $NaBPh_4$ gave an elemental analysis consistent with the formulation $[Cp_2Mo(OH)(OH_2)][BPh_4]\cdot 0.5\ H_2O$. See ref 1.

(29) Similar experiments were carried out in the absence of MOPS by adjusting the pD using NaOD in $D_2O$, resulting in identical $^1H$ NMR spectra. This indicates that the buffer does not coordinate to the metal center.

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(31) Difficulty in shimming the sample occasionally resulted in apparent 'splitting' of the resonances. The important information, however, i.e. the change in the relative ratios of the two molybdocene species upon dilution at pH 3.5, could be obtained from these spectra.

(32) This equilibrium constant is in agreement with $K_{eq} = 5.1\times10^{-2}$ M obtained from kinetic analysis of dimethylphosphate hydrolysis promoted by **1**;[6] Kuo, L. Y., unpublished results.

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# CHAPTER IV

# C-H BOND ACTIVATION IN AQUEOUS SOLUTION: KINETICS AND MECHANISM OF H/D EXCHANGE IN ALCOHOLS CATALYZED BY MOLYBDOCENES.

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## Abstract

The mechanism of the catalytic H/D exchange in alcohol substrates promoted by molybdocenes in $D_2O$ was shown to occur by C-H bond activation. Primary alcohols selectively exchanged α-hydrogens in aqueous solutions containing the catalyst precursor $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$, while some additional β-hydrogen exchange was observed in secondary alcohols. Tertiary alcohols did not undergo H/D exchange. Formation of chelate complexes such as the independently synthesized and crystallographically characterized glycolate complex $[Cp'_2MoOCH_2CH_2OH](OTs)$ inhibited the H/D exchange in multidentate alcohols. The exchange reaction was shown to proceed by formation of a ketone hydride molybdocene intermediate $[Cp'_2Mo(OCR^1R^2)H]^+$, which can reversibly dissociate the ketone ligand. The

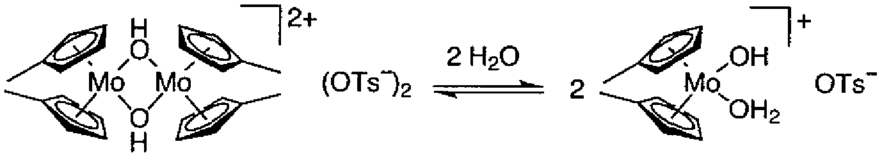
molybdocene hydride complex resulting from ketone dissociation was identified by independent synthesis and crystallographic characterization of the hydride complex $Cp'_2MoH(OTf)$. The H/D exchange reaction proceeds stepwise, with the active catalyst being derived from the monomeric complex $[Cp'_2Mo(OH)(OH_2)]^+$. At T = 90 °C, the exchange of the first methylene hydrogen of $PhCH_2OH$ occurs with a rate constant $k = 1.16\times10^{-4}$ $(\pm9.88\times10^{-7})$ $s^{-1}$. The activation parameters were determined as $\Delta H^{\neq} = 19.4$ (±0.2) kcal $mol^{-1}$ and $\Delta S^{\neq} = -22.7$ (±0.7) cal $mol^{-1}$ $K^{-1}$. A primary kinetic isotope of $k_{H,\ pD\ 6.4}/k_{D,\ pH\ 6.5} = 2.2$ was found.

## Introduction

Bent metallocenes of the type $Cp_2MX_2$ are soluble in aqueous solution, and over the past 15 years, the aqueous chemistry of metallocenes containing Ti,[1,2] Zr,[1] Hf,[3] V,[1] Nb,[4] Cr,[5] and Mo[6,7] has been explored. These studies have shown that molybdocenes are the most stable metallocenes in water with respect to hydrolysis of the cyclopentadienyl ligands.[6] If oxygen is excluded, no hydrolysis can be detected for aqueous solutions of molybdocenes over a period of several weeks. This remarkable stability allowed investigation of the molybdocenes' catalytic chemistry in water. Intending to gain an understanding of the origin of its anti-tumor activity, Kuo et al. found that aqueous solutions of $Cp_2MoCl_2$ are able to promote the hydrolysis of activated[8] and unactivated[9] phosphate esters.

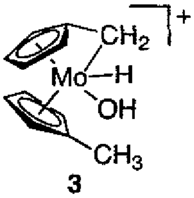
As part of our research program[10-16] on organometallic catalysis in water,[17] we investigated the aqueous chemistry of the dimeric molybdocene complex

$[Cp'_2Mo(\mu\text{–}OH)_2MoCp'_2](OTs)_2$ (**1**).[18,19] It was shown that the chemistry of this complex in water is related to that of the molybdocene dihalides. Aqueous solutions of either **1** or $Cp'_2MoCl_2$ consist of the same species, where the identity of the complexes in solution depends only on the pH. Under neutral conditions, aqueous solutions contain the dimeric complex **1** in equilibrium with the monomeric aquo hydroxy complex **2** (eq 1).



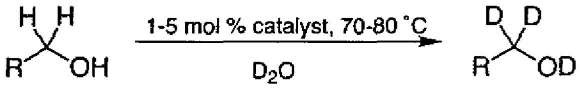
**1** **2** (1)

When a solution of **1** was heated in $D_2O$, the $CpCH_3$ protons of the cyclopentadienyl ligands of **1** and **2** were exchanged for deuterium.[19] This observation was explained in terms of an intramolecular C-H bond activation reaction proceeding through an intermediate hydride complex (3), analogous to the tucked–in tungstenocene complex $(\eta^5\text{-}Cp^*)(\eta^5,\eta^1\text{-}C_5Me_4CH_2)WH$ described previously.[16,20]



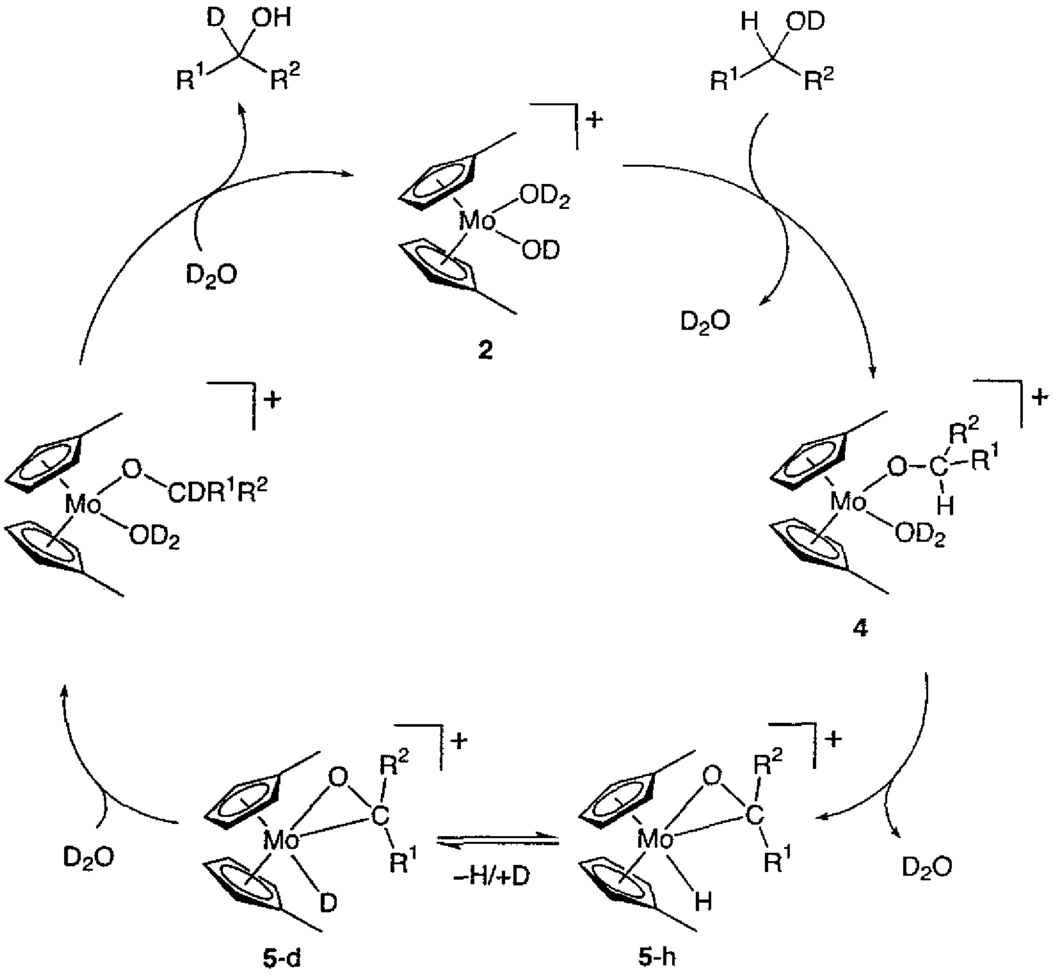
**3**

Of more interest, aqueous solutions of **1** also catalyze the intermolecular H/D exchange of α-protons in alcohols (eq 2). Similar to the intramolecular case, a mechanism was proposed that involves the activation of the C-H bond of the alcohol after coordination of the substrate to the metal center (Scheme 1).



(2)

The most notable step in this mechanism is the insertion of the metal center into the C-H bond of the alcohol (**4** to **5**-*h*). The activation of a C-H bond in aqueous medium is strongly sought after,[21] yet only a few examples of this reaction type are known that occur in water[22] and that are catalytic in the metal complex employed.[23,24]



$R^1$, $R^2$: H, alkyl, aryl

Scheme 1. Postulated mechanism for H/D exchange in alcohols.

In this paper we present experimental evidence in support of the proposed mechanism for H/D exchange in alcohols. This includes the isolation and characterization of important intermediates and analysis of the reaction kinetics. Additionally, the implications of this mechanism for the use of the molybdocene catalyst in other reactions is discussed.

## Results and Discussion

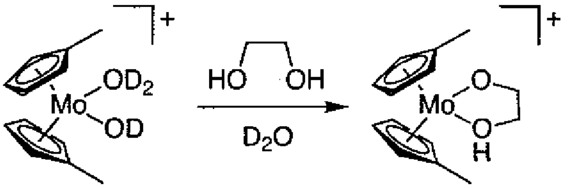
### Deuterium Exchange in Alcohols

After the initial observation of H/D exchange in methanol (eq 2, R=H),[19] a number of alcohols and other substrates were tested in this reaction. A solution of the substrate and catalyst **1** in $D_2O$ in a sealed NMR tube was heated for several hours and the disappearance of the α-H signals in the $^1$H NMR monitored periodically. In addition, $^2$H NMR spectra were recorded to confirm the presence of the deuterated product. The results of these experiments are shown in Table 1. Primary alcohols are selectively converted into the α,α-deuterated products, while secondary alcohols show incorporation of D on both α- and β-carbons. No H/D exchange is observed in *tert*-butanol. The lack of reactivity in the latter alcohol, which does not possess α-hydrogens, is readily explained by the proposed mechanism which proceeds by insertion of the metal center into the α-C-H bond (Scheme 1, **4** → **5**-*h*). With bidentate alcohols such as ethylene glycol, the reaction slows down significantly and a third major molybdocene species in addition to **1** and **2** is observed in the reaction solution by $^1$H NMR ($\delta = 5.38$ (m), 5.33 (m), 3.24 (s), 1.83 (s) ppm). The integral ratio and chemical shifts of the observed

Table 1. Intermolecular H/D Exchange with Alcoholic Substrates

| Substrate | c(ROH) (M) | mol% Cat(**1**) | T (°C) | t (h) | % H/D Exchange |
|---|---|---|---|---|---|
| MeOH | 1.02 | 0.9 | 102 | 39:00 | 67 |
| EtOH | 0.71 | 2.6 | 102 | 39:00 | 30 |
| $^n$PrOH | 0.55 | 3.2 | 85 | 68:40 | 48 |
| $^n$BuOH | 0.45 | 3.7 | 85 | 22:00 | 33 |
| benzyl alcohol | 0.28 | 4.8 | 80 | 21:30 | 90 |
|  | 0.19 | 7.8 | 80 | 46:00 | >99 |
| isopropanol | 0.36 | 4.3 | 86 | 20:40 | 23 |
| 2-butanol | 0.25 | 4.8 | 80 | 34:00 | 14 |
| *tert*-butanol | 0.29 | 5.0 | 80 | 5 days | 0 |
| ethylene glycol | 0.38 | 3.6 | 88 | 29:30 | 6 |
| 1,3-propanediol | 0.40 | 6.5 | 80 | 10 days | 39 |

resonance are consistent with a 1:1 molybdocene ethylene glycol adduct **6** (eq 3; this product is discussed further below).



**6**

(3)

The reactions of ketones under H/D exchange conditions result in β-deuteration. This is assumed to occur by simple protonation/deprotonation facilitated by coordination of the substrate to the molybdocene, which results in a decreased p$K_a$ for the ketone. Other non-alcoholic substrates such as ethers (THF, $Et_2O$) or amines ($HNEt_2$, $NEt_3$; buffered in neutral aqueous solution) did not undergo H/D exchange.

## Preparation and Structure of the Molybdocene Glycolate (6)

Glycolate complex **6** was prepared independently in order to confirm the identity of the unknown molybdocene species formed from ethylene glycol under H/D exchange conditions. The glycolate could be isolated from an alcohol solution of **1** and ethylene glycol. The $^1$H NMR spectrum of **6** showed resonances identical to those found in the H/D exchange reaction solution ($\delta$ = 5.38 (m), 5.33 (m), 3.24 (s), 1.83 (s) ppm).

Orange crystals of **6** suitable for X-ray diffraction were grown from methanol. The asymmetric unit contains two cations of very similar structure and two tosylate anions. The 1:1 stoichiometry implies that the glycolate ligand is monoprotonated. The quality of the data set did not allow the direct location of the protonation sites. However, in each cation there is one short and one longer Mo-O bond, 2.013(4) Å and 2.151(4) Å, respectively, for the fragment shown in Figure 1. Each of the oxygens that forms the longer bonds also makes a short contact with a sulfonate oxygen of a tosylate anion (see Supporting Information), implying that it is a proton donor.

A few neutral molybdocene alkoxide complexes from chelating diols have previously been prepared and characterized spectroscopically,[25,26] but only one complex, $Cp_2Mo(OCH(CF_3)_2)_2$, has been characterized crystallographically.[27] In this latter compound, the Mo-O bond lengths were determined as 2.065(5) Å and 2.101(5) Å, comparable to the bond lengths found in **6**.

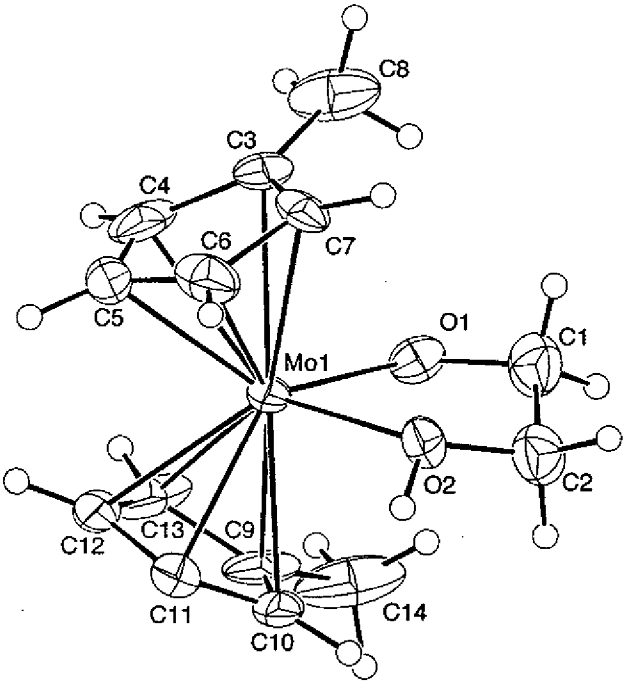
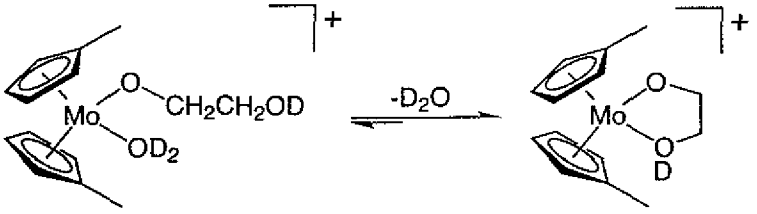


Figure 1. Molecular structure of $[Cp'_2Mo(OCH_2CH_2OH)]^+$(**6**). Only one cation is shown. Selected bond lengths (Å): Mo(1)-O(1), 2.013(4); Mo(1)-O(2), 2.151(4).

## Mechanistic Implications of Glycolate Formation

Two significant arguments for the proposed mechanism can be made based on the reactivity of ethylene glycol under H/D exchange conditions. First, because the exchange reaction is significantly slower than for monodentate alcohols, this argues against a simple protonation/deprotonation mechanism, facilitated by the molybdenum complex. If coordination of the alcohol resulted in a decreased p$K_a$ of the alcohol α-hydrogens, thereby making simple proton exchange more facile, the rate of the exchange reaction in aliphatic monodentate alcohols and ethylene glycol should not show any significant difference. Second, inhibition by a chelating alcohol shows that not only is coordination of the substrate required in the reaction sequence, but an additional vacant coordination site has to become available. The required coordination site is occupied in the complex formed in the reaction of the molybdocene fragment and ethylene glycol (eq 4).

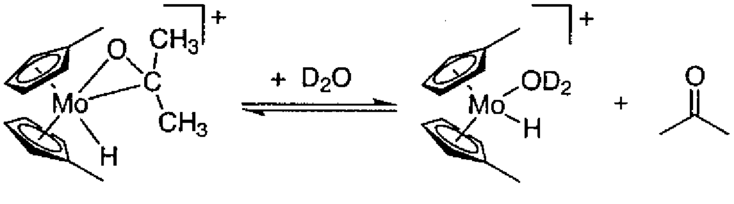


**4** ($R^1$=H, $R^2$=CH2OD) **6** (4)

It is the chelating ability of ethylene glycol that explains the sluggishness of the H/D exchange with this substrate. Also note that complex **6** is obtained as the monocation, with one glycol oxygen remaining protonated in the solid state. This is consistent with the proposed monocationic molybdocene intermediates along the reaction pathway.

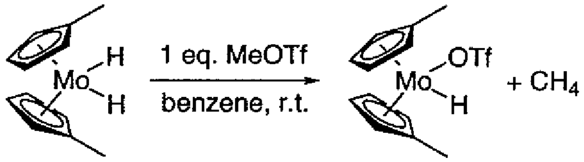
### Observation of Free Ketone and Preparation of the Hydride Intermediate

In the reaction solution of 2-propanol under standard H/D exchange conditions, a small amount of acetone, which is slowly deuterated, was detected by $^1$H NMR spectroscopy. In addition to free acetone, a set of four resonances with signals in the Cp region ($\delta$ = 4.87, 4.66, 4.08 and 3.57 ppm) of the $^1$H NMR spectrum were observed. These resonances are common for all H/D exchange reactions, independent of the nature of the alcohol substrate. Free acetone could conceivably arise from dissociation of the $\pi$-bonded ketone ligand from intermediate **5**. This would result in a molybdocene monohydride complex (**7**, eq 5).



**5-h** **7** (5)

In order to verify this assumption, the monohydride complex Cp'$_2$MoH(OTf) (**8**) was prepared. The synthesis of **8** (eq 6) was carried out similarly to the preparation of the cationic [Cp$_2$WH(C$_4$H$_4$O)][CF$_3$SO$_3$].[28] Thus, treatment of Cp'$_2$MoH$_2$ with 1 equivalent of MeOSO$_2$CF$_3$ in benzene at room temperature resulted in the formation of the solvent-free monohydride **8**.



**8** (6)

Orange-red crystals grown from hot benzene were analyzed by x-ray crystallography (Figure 2). Unlike the tungsten analog, which was prepared in coordinating solvents,[28] the molybdocene hydride was isolated as the neutral complex with the triflate anion occupying one of the equatorial coordination sites. The Mo-H bond length of 1.53(3) Å is short for a molybdocene hydride complex,[29] but not unusual, as the Mo-H bond distance in the fumaronitrile complex Cp$_2$Mo(H)(CHCNCH$_2$CN) was found to be 1.529 Å.[30]

Hydride complex **8** dissolved slowly in water to give a faint yellow solution (eq 7). In D$_2$O, four Cp resonances were observed at δ = 4.87, 4.66, 4.08 and 3.57 ppm,

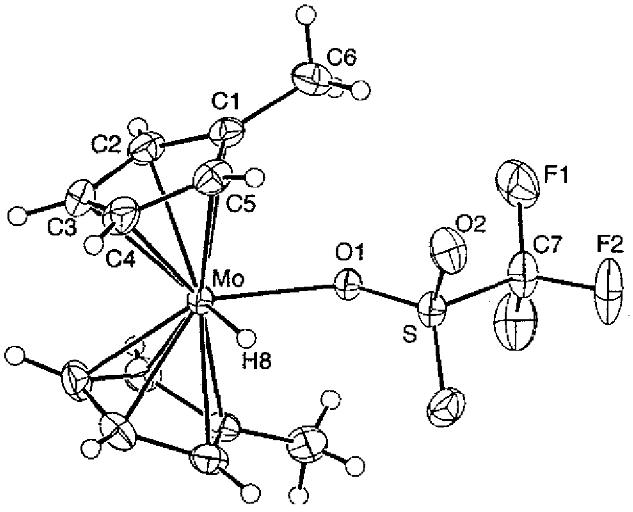
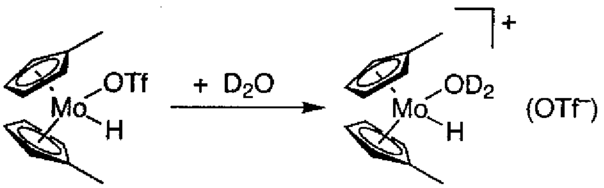


Figure 2. Molecular structure of $Cp'_2MoH(OTf)$ (7). Selected bond lengths (Å): Mo–H(8), 1.53(3); Mo-O(1), 2.186(2).

corresponding to those found in the H/D exchange reaction solution for the species suggested to be 7.



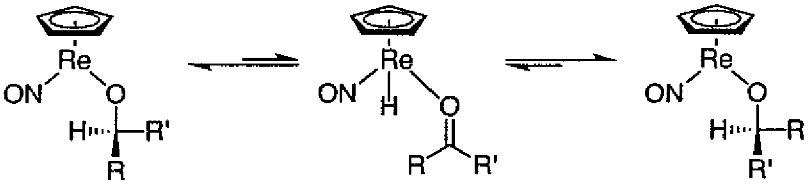
**8** **7** (7)

This reaction confirms the assignment of the common metallocene intermediate in the H/D exchange reactions as the molybdocene monohydride (eq 5). Characteristic of the metal-hydride is the resonance observed at $\delta = -8.41$ ppm. This resonance decreases over several days at room temperature in $D_2O$. For the Cp analog, the exchange of the hydride ligand by a deuteride was confirmed by $^2H$ NMR.[31]

## Comments on the Proposed Ketone Hydride Intermediate (5)

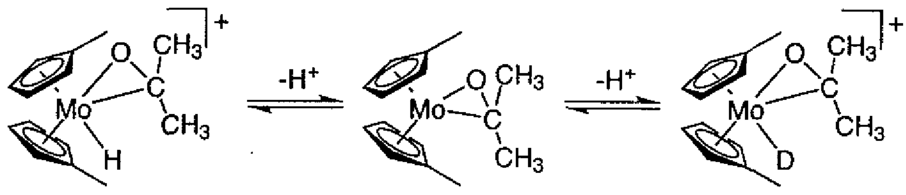
The formation of the π-ketone intermediate **5** (Scheme 1) is not unreasonable[32] because ketone complexes of molybdocenes have previously been prepared.[33-35] In addition, the structure of the formaldehyde complex $Cp_2Mo(\eta^2\text{-}OCH_2)$ was determined, showing side-on π-coordination of the carbonyl moiety.[33] This thermally robust complex readily underwent protonolysis with trifluoroacetic acid to yield $Cp_2Mo(O_2CCF_3)_2$ and MeOH.[36] This result is consistent with the mechanism in Scheme 1, whose main features are reversible π-ketone complex formation (**5**) and subsequent alcohol elimination.

The reversible β-H activation in alcohols has been described previously by Saura-Llamas and Gladysz.[37] They showed that chiral alcohols racemized rapidly in benzene solution in the presence of $CpRe(PPh_3)(NO)(OMe)$. This process was proposed to proceed through a ketone complex intermediate, in which the chiral alcohol replaced the OMe ligand (eq 8). No free ketone was observed, which was taken as an indicator that the racemization process proceeded intramolecularly.



(8)

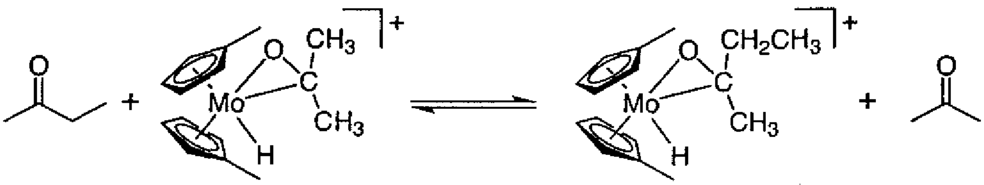
Precedents also exist for the reversible deprotonation/protonation of molybdocene complexes with π-coordinated ligands. Such reactions have been observed by Benfield and Green[38] who reported that the cationic complex $[Cp_2MoLH][PF_6]$ (L= ethylene, propylene) can be converted to the olefin complex $Cp_2MoL$ by treating it with dilute aqueous base. Addition of aqueous $NH_4PF_6$ to the neutral olefin complex converted it back to the parent molybdocene hydride olefin complex. These results suggest that the exchange of the hydride ligand by a deuteride likely occurs by a dissociative pathway (eq 9).[39]



**5-h** **5-d** (9)

## Transfer Hydrogenation

In order to elucidate whether the ketone dissociation is reversible, the H/D exchange reaction with 2-propanol as the substrate was carried out in the presence of an equal amount of 2-butanone. After 21 hours at 80 °C, the reaction mixture contained 2-butanol and acetone in addition to the starting materials, 2-propanol and 2-butanone. This indicates an equilibrium for ketone dissociation that can be described as shown in eq 10.



(10)

The overall result of this reaction is the conversion of a ketone into an alcohol, using a sacrificial alcohol as hydrogen donor, resembling the Meerwein-Pondorf-Verley reduction. Transfer hydrogenations of this type are well documented for late transition metals in *organic* solvents.[40-42] The molybdocene promoted reaction, however, is carried out in *water* with an early-transition-metal catalyst.

## Stepwise Exchange

The disappearance of the methylene resonance of benzyl alcohol at 80 °C in $D_2O$ was followed by $^1$H NMR (Figure 3). The integral over the methylene region of benzyl alcohol relative to the integral of the aromatic region for the benzyl alcohol was used to calculate the total concentration of methylene protons present in solution. This integral includes proton resonances from $PhCH_2OD$ (**A**), contributing two protons per **A** and from the monodeuterated product, PhCH*D*OD (**B**), contributing one proton per **B**. The total concentration of protons can therefore be expressed as [Protons] = 2[A] + [B] (Figure 4, squares). Because of a small isotope shift of the **B** methylene resonance (Figure 3), the concentrations of **A** and **B** can also be evaluated independently (Figure 4, diamonds and circles, respectively).[43]

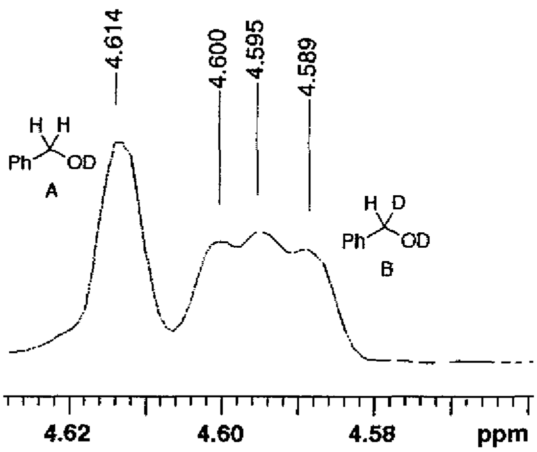


Figure 3. $^1$H NMR spectrum of $PhCH_2OD$ (**A**) and PhCHDOD (**B**) in $D_2O$.

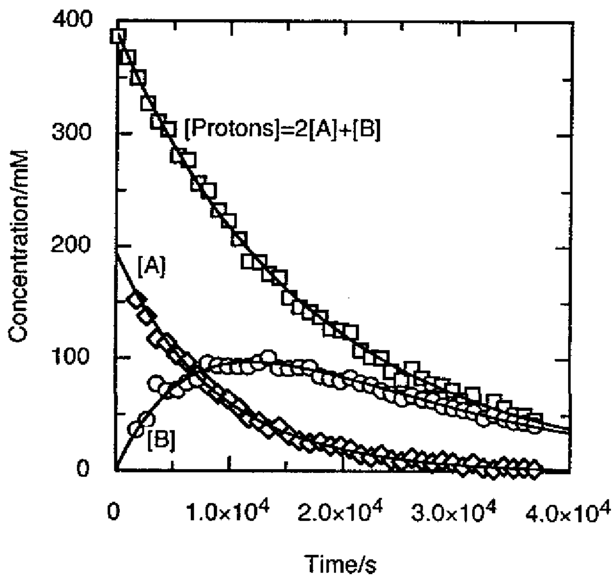
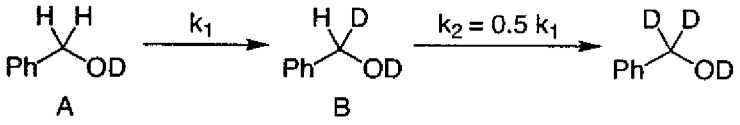


Figure 4. Plot of the concentrations vs. time for the deuteration of benzyl alcohol at T = 90 °C.

The concentration-time profile depicted in Figure 4 is consistent with a stepwise mechanism (eq 11).



(11)

H/D exchange of the first hydrogen is followed by release of the monodeuterated alcohol **B**. Substrate **B** then coordinates again to the metal center and the remaining hydrogen is exchanged. The latter step should occur with only half the frequency of the first exchange because the probability of exchanging the remaining H and thereby leading to a productive reaction (generating PhC$D_2$OD) is only 50 %. Since both steps are chemically identical, the rate constant $k_2$ for the second step should therefore be equal to 0.5 $k_1$.[44]

The integrated rate laws for this stepwise mechanism are shown in eqs 12-14.[45] $[A]_0$ represents the initial concentration of benzyl alcohol. The exchange of one hydrogen by deuterium proceeds with a rate constant $k_1$.

$$[\mathbf{A}] = [\mathbf{A}]_0 e^{-k_1 t} \tag{12}$$

$$[\mathbf{B}] = 2[\mathbf{A}]_0 e^{-0.5k_1 t} - 2[\mathbf{A}]_0 e^{-k_1 t} \tag{13}$$

$$[\mathbf{Protons}] = 2[\mathbf{A}]_0 e^{-0.5k_1 t} \tag{14}$$

Fitting the data[46] for the decrease in proton concentration, [Protons], with eq 14 affords a rate constant of $k_1 = 1.16\times10^{-4}$ ($\pm9.88\times10^{-7}$) $s^{-1}$ (Figure 4, solid line through [Protons] data). This rate constant was used to calculate concentration profiles for [A] and [B] (Figure 4, solid lines through [A] and [B] data), showing good agreement between the kinetic model and the experimental data.

The finding that the H/D exchange occurs stepwise has important mechanistic implications. It means that after incorporation of the first D, the substrate must dissociate from the metal center, and then the second D is incorporated in a second encounter with the catalyst. This implies that the reaction from the ketone hydride intermediate **5-*d*** (Scheme 1) back to the aquo hydroxy complex **2**, the reverse of the initial C-H bond activation pathway, is fast, which rules out that the rate determining step is in the second half of the cycle, from **5-*d*** to **2**.

## Evidence for a Monomeric Catalyst

Although all of the chemical evidence discussed thus far indicates that the catalytically active species is a monomeric compound (and hence the mechanism is formulated to involve a molybdocene monomer), additional information was sought to unequivocally establish this proposal. For this purpose, H/D exchange was carried out on benzyl alcohol with varying concentrations of catalyst at T = 90°C. The concentrations of dimer **1** and monomer **2** in the reaction solution were determined from the $^1$H NMR spectra. A plot of the observed rate constant, $k_{obs}$, against [**1**] and [**2**] is shown in Figure 5. Assuming that $k_{obs}$ is proportional to the concentration of monomer **2**, $k'$, the pseudo-first-order rate constant, is obtained from a linear fit to eq 15 (Figure 5). The dependence of $k_{obs}$ on the concentration of dimer **1** is then given by eq 16. The plot of $k_{obs}$ vs [**1**] with $K_{eq} = 7.90\times10^{-2}$ ($\pm1.0\times10^{-3}$) M[18] is shown in Figure 5.

$$k_{obs} = k'[\mathbf{2}] \qquad (15)$$

$$k_{obs} = k'\sqrt{K_{eq}[\mathbf{1}]};\ K_{eq} = \frac{[\mathbf{2}]^2}{[\mathbf{1}]} \qquad (16)$$

Alternatively, $k_{obs}$ could be proportional to the concentration of dimer **1** (eq 17). The corresponding dependence of $k_{obs}$ on monomer [**2**] is then described by eq 18. The results of linear regression of eq 17 and application of the obtained $k'$ in calculation of the theoretical curve for eq 18 is also shown in Figure 5 (dotted lines).

$$k_{obs} = k'[\mathbf{1}] \qquad (17)$$

$$k_{obs} = \frac{k'}{K_{eq}}[\mathbf{2}]^2 \qquad (18)$$

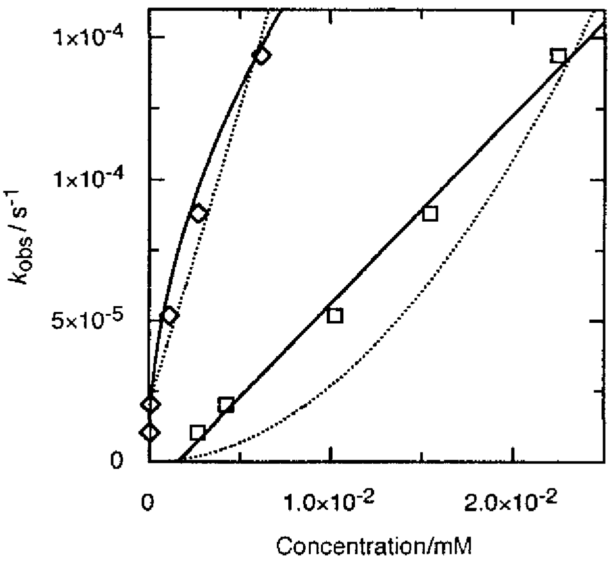


Figure 5. Concentration dependence of $k_{obs}$ at T = 90 °C. Open squares correspond to $k_{obs}$ vs. [Monomer **2**], open diamonds correspond to $k_{obs}$ vs. [Dimer **1**]. The solid line shows the fit to the model assuming that $k_{obs}$ is linearly dependend on [2], the dotted line shows the fit to the model considering $k_{obs} \propto$ [**1**].

From Figure 5 it is apparent that $k_{obs}$ in the H/D exchange reaction is not linearly dependent on [**1**]. The data, however, are in good agreement with a model assuming a linear dependence of $k_{obs}$ on monomer [**2**], from which it is concluded that the active catalyst is a monomeric molybdocene complex.

## Kinetic Isotope Effect

The reverse reaction of the H/D exchange, the incorporation of H into a deuterated substrate, was carried out with $d_7$-benzyl alcohol (193 mM) and catalyst **1** (15.2 mM) in $H_2O$. The disappearance of the methylene D resonance was monitored by $^2$H NMR at 80 °C, using the resonances of the aromatic deuterium nuclei as reference. The scatter for the NMR data is much larger than in the $^1$H NMR experiment, but nevertheless the resulting rates obtained from a fit to eq 14 were reproducible. The average rate constant of three kinetic runs at T = 80 °C was $k_{D, pH 6.5} = 2.18\times10^{-5}$ ($\pm2.75\times10^{-7}$) $s^{-1}$. The pH of the reaction solution changed during the course of the reaction, from pH 7.0 prior to heating to pH 6.5 after the kinetic run. The H/D exchange with $h_8$-benzyl alcohol (193 mM) in $D_2O$ (15.1 mM in **1**) proceeded with a rate constant of $k_{H, pD 7.1} = 8.13\times10^{-5}$ ($\pm1.07\times10^{-6}$) $s^{-1}$. After completion of the kinetic experiment, the solution had a pD of 7.1. In order to assess the effect of the slight change in pD on the reaction rate, an H/D exchange experiment was run with benzyl alcohol (193 mM) and **1** (15.2 mM) in $D_2O$ (80 °C), in which the pD was adjusted by adding toluenesulfonic acid, resulting in a reaction solution of pD 6.4.[47] The reaction rate under these conditions was $k_{H, pD 6.4} = 4.84\times10^{-5}$ ($\pm2.28\times10^{-7}$) $s^{-1}$,[48] smaller than $k_{H, pD 7.1}$, yet still considerably higher than $k_{D, pH 6.5}$.

The sensitivity of the H/D reaction to changes in pH does not allow the direct comparison of $k_H$ and $k_D$.[49] However, the ratio $k_{H, pD 6.4}/k_{D, pH 6.5} = 2.2$ is consistent with a primary isotope effect.[47]

In their study on alcohol epimerization (*vide supra*), Saura-Llamas and Gladysz[37] found $k_H/k_D = 2$ for the epimerization of the alcohol carbon. Similar isotope effects were reported for intramolecular β-hydride elimination reactions of alkyl complexes such as *n*-octyllithium[50] and other metal alkyl complexes,[51] with $k_H/k_D$ ranging from 1.5 to 4.7. These examples are all consistent with the isotope effect found in this study. The implications of the kinetic isotope effect are discussed below, in conjunction with the activation parameters for the H/D exchange.

## Activation Parameters

In order to obtain information about the activation parameters of the H/D exchange reaction, the deuteration of benzyl alcohol was carried out over the temperature range from 50 to 90 °C in 10 °C intervals. The rates at these temperatures were obtained by fitting the disappearance of the methylene proton resonances of benzyl alcohol to eq 14. An Eyring plot is shown in Figure 6. From a linear regression, the activation parameters were determined as $\Delta H^{\neq} = 19.4$ (±0.2) kcal mol$^{-1}$ and $\Delta S^{\neq} = -22.7$ (±0.7) cal mol$^{-1}$ K$^{-1}$.

These activation parameters, particularly the negative activation entropy, indicate that, in the rate determining step, the transition state acquires a considerable increase in order. This is generally interpreted in terms of an associative process.[52] In the first half of the mechanism (Scheme 1), this could apply to the addition of the alcohol to form the

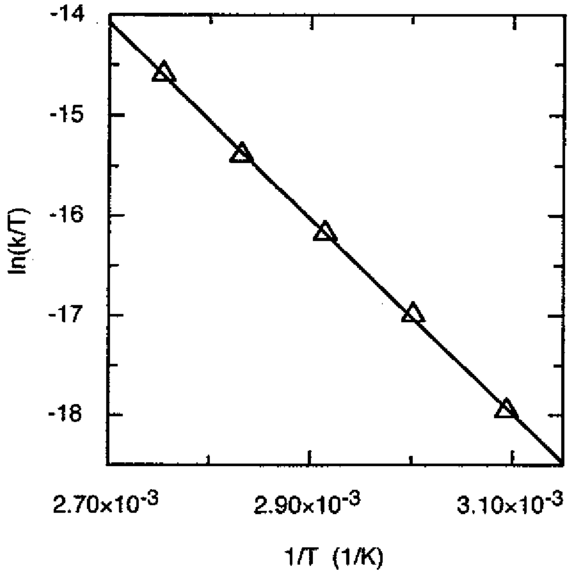


Figure 6. Eyring plot for the deuteration of benzyl alcohol (193 mM) catalyzed by **1** (15.1 mM) in $D_2O$.

alkoxide intermediate, **2** → **4**. The addition of alcohol to form **4**, however, does not involve breaking a C-H bond (or any other atom-H bond) and can therefore be ruled out as the rate determining step. Alternatively, addition of $D^+$ to the $\pi$-ketone intermediate in the course of the H/D exchange (eq 9) would be consistent with a negative activation entropy. This addition reaction, however, involves the breaking of an O-D bond and therefore should occur *more slowly* than the corresponding reaction with a deuterated substrate in $H_2O$, i.e. a kinetic isotope effect $< 1$ would be expected. It is therefore unlikely that this latter step in the H/D exchange pathway is rate-determining.

The dissociation of a proton from the ketone intermediate (eq 9) would be consistent with the observed kinetic isotope effect. While this step is dissociative, solvent reorganization could contribute significantly to the activation entropy, resulting in a negative $\Delta S^{\neq}$.

The C-H bond activation step in which the metal center inserts into the carbon hydrogen bond of the coordinated alkoxide, **4** → **5**-*h*, is also consistent with both the observed activation entropy and the kinetic isotope effect. In this insertion step, the degrees of freedom are reduced significantly in the formation of the ketone hydride complex, giving rise to a negative activation entropy. Furthermore, the $\alpha$-C-H bond is broken, which is in agreement with the observed isotope effect. Experiments to identify the rate-determining step unambiguously are currently underway.

## Summary

The molybdocene catalyzed H/D exchange reaction is one of the few examples of catalytic C-H bond activation reactions in *aqueous* solution. Substantial experimental evidence was provided that the mechanism of the catalytic H/D exchange in alcohols promoted by $[Cp'_2Mo(OH)(OH_2)]^+$ (**2**) occurs by the pathway in Scheme 1. Following the exchange of the aquo ligand and coordination of the alcoholic substrate, an alkoxide complex (**4**) is formed. Upon dissociation of the remaining aquo ligand, the coordinatively unsaturated molybdocene inserts into the α-C-H bond of the alkoxide, forming a ketone hydride intermediate (**5**-*h*). The ketone is labile toward dissociation, which opens up the possibility of using the molybdocene catalyst in hydrogen transfer reactions, whether it is in oxidations of alcohols using a sacrificial ketone as a reducing agent, or the reduction of a ketone employing a sacrificial alcohol. Ketone hydride complex **5** can undergo reversible protonation, which leads to the observed isotope exchange upon dissociation of the coordinated alcohol.

## Experimental Section

All manipulations were carried out in a nitrogen atmosphere using standard vaccum line techniques or a glovebox. Solvents were dried over and distilled from the appropriate drying agents.[53] All alcohols were dried over and distilled from $CaH_2$. $d_7$-Benzyl alcohol (97% D) was purchased from Aldrich and used as received. $D_2O$ (99.9% D) was purchased from Cambridge Isotope Laboratories and purged with $N_2$ for at least 30 min prior to use. $^1H$ and $^2H$ NMR spectra were recorded using a Varian Inova 300

(299.95 MHz for $^1$H, 46.04 MHz for $^2$H) or a GE 500 (500.13 MHz for $^1$H, 76.77 MHz for $^2$H) spectrometer. $[Cp'_2M(\mu\text{-}OH)_2MoCp'_2](OTs)_2$[19] and $Cp'_2MoH_2$[54] were prepared according to literature procedures. NMR samples were prepared in the glovebox. NMR experiments at higher temperatures were carried out in 5 mm NMR tubes which were flame sealed while frozen in $N_2$(l) prior to heating. pH measurements on NMR samples were carried out using a Corning NMR Micro Electrode, d = 3 mm, and a Hanna HI9023 pH meter with attached thermocouple. Prior to the measurement, the NMR tube was placed in a water bath together with the thermocouple to allow for thermal equilibration. All reported pD values were calculated according to pD = (pH meter reading + 0.4) to correct for the use of a glass electrode.[55,56] Elemental analyses were carried out by Robertson Microlit Laboratories, Inc., Madison, NJ.

### Synthesis of $[Cp'_2MoOCH_2CH_2OH][OTs]$ (6)

To a solution of 133 mg (0.15 mmol) of $[Cp'_2M(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ in 10 mL MeOH, 60μL ethylene glycol (67 mg, 1.08 mmol) was added and the reaction mixture was refluxed for 16 h. The solvent was removed in vacuo to give an orange oil. Trituration of the oil with THF afforded an orange solid. Orange crystals were grown by layering $Et_2O$ onto a solution of **3** in MeOH/THF (1:1) and cooling to –30 °C.

$^1$H NMR(300 MHz, $D_2O$) δ 7.48 (d, 6.5 Hz, OTs, 2H), 7.36 (d, 7.8 Hz, OTs, 2H), 5.38 (m, 4H), 5.33 (m, 4H), 3.24 (s, 4H), 2.37 (s, OTs–$CH_3$, 3H), 1.83 (s, 6H). Anal. Calc. for $C_{21}H_{26}MoO_5S$: C, 51.85; H, 5.39; Mo, 19.72; Found: C, 51.55; H 5.19; Mo, 19.04. The complex converts rapidly to **2** and free ethylene glycol when dissolved in $D_2O$.

## X-ray Structure Analysis of [Cp'$_2$MoOCH$_2$CH$_2$OH][OTs] (6)

A crystal of the dimensions 0.04 × 0.17 × 0.32 mm was mounted on a fiber with a coating of epoxy. The orientation parameters and cell dimensions were obtained from the setting angles of an Enraf-Nonius CAD-4 diffractometer for 25 centered reflections in the range $12.0° \leq \theta \leq 13.9°$. Table 2 contains a summary of crystal data and the final residuals. A more extensive table including particulars of data collection and structure refinement can be found in the supplementary material. The crystal decayed progressively and data collection was halted near the end of the shell $17° \leq \theta \leq 22°$, when the intensities of standard reflections had decreased 20%. The centric distribution of intensities indicated the space-group P(-1). A *SIR92 E*-map[57] showed all non-hydrogen atoms of the two independent formula units. Empirical absorption corrections based on the isotropically-refined structure (DIFABS[58]) resulted in no significant decrease in the residuals and standard deviations, and the results presented here are for uncorrected data. Hydrogen atoms bonded to carbon were included at positions recalculated after each cycle of refinement [$B(H) = 1.2B_{eq}(C)$; $d(C\text{-}H) = 0.95$ Å]. The final difference map confirmed that the compound was unsolvated. The *teXsan* program suite,[59] incorporating complex atomic scattering factors, was used in all calculations.

## Synthesis of Cp'$_2$MoH(OTf) (7)

In the glovebox, a solution of 100 mg (0.39 mmol) Cp'$_2$MoH$_2$ in 5 mL benzene was prepared. 45 mL (65mg, 0.40 mmol) MeOTf was added and the solution was stirred for 1 h. A reddish solid formed instantly and evolution of gas bubbles was observed.

Table 2. Crystallographic Data for **6**

| | |
|---|---|
| Composition | $C_{21}H_{26}MoO_5S$ |
| Formula wt | 486.43 |
| Crystal system | triclinic |
| Space group | P(-1) |
| a | 12.233(2) Å |
| b | 12.779(3) Å |
| c | 14.825(2) Å |
| $\alpha$ | 89.40(2)° |
| $\beta$ | 73.53(2)° |
| $\gamma$ | 68.79(2)° |
| V | 2061(1) $Å^3$ |
| Z | 4 |
| $d_{calc}$ | 1.568 g $cm^{-3}$ |
| T | 22 °C |
| Radiation, $\lambda$ | Mo K$\alpha$, 0.71073 Å |
| $\mu$ | 7.66 $cm^{-1}$ |
| No. obs. rflns | 3344 [$I \geq \sigma(I)$] |
| No. indep. rflns | 4472 |
| R(F), wR(F) (obs.) | 0.067, 0.087 |
| R($F^2$), wR($F^2$) (all) | 0.042, 0.043 |

$R(F) = \Sigma||F_0|-|F_c||/\Sigma|F_0|$; $wR(F^2) = [\Sigma w(|F_0|^2-|F_c|^2)^2/\Sigma w|F_0|^4]^{1/2}$

The solvent was decanted off and the precipitate was washed with hexanes. The solid was recrystallized from hot benzene. $^1$H NMR(300 MHz, $C_6D_6$): δ 4.87 (m, 2H), 4.66 (m, 2H), 4.08 (m, 2H), 3.57 (m, 2H), 1.59 (s, 6H, Me), -8.41 (s, 1H); $^1$H NMR(300MHz, $D_2O$): δ 5.60 (m, 2H), 5.47 (m, 2H), 4.62 (m, 2H), 4.56 (m, 2H), -9.26 (m, 1H). Anal. Calc. for $C_{13}H_{15}F_3MoO_3S$: C, 38.62; H, 3.74; Found: C, 38.77; H 3.52.

## X-ray Structure Analysis of Cp'$_2$MoH(OTf) (7)

A dark red block of the dimensions 0.29 × 0.36 × 0.49 mm was sealed in a special glass capillary in the dry-box. The orientation parameters and cell dimensions were obtained from the setting angles of an Enraf-Nonius CAD-4 diffractometer for 25 centered reflections in the range $13.8^\circ \leq \theta \leq 14.9^\circ$. Table 3 contains a summary of crystal data and the final residuals. A more extensive table including particulars of data collection and structure refinement can be found in the supplementary material. The systematic absences together with the centric distribution of intensities indicated the space-group Pcbm. A *SIR92* *E*-map[57] showed all non-hydrogen atoms of the half-molecule constituting the asymmetric unit. An *E*-map in the alternative space group Pbc$2_1$ gave the same molecule, with a clear mirror-plane normal to *c*. Absorption corrections based on azimuthal scans ('ψ scans') were applied. All hydrogen atoms were located and refined isotropically. The *teXsan* program suite,[59] incorporating complex atomic scattering factors, was used in all calculations.

Table 3. Crystallographic Data for 7

| | |
|---|---|
| Composition | $C_{13}H_{15}F_3MoO_3S$ |
| Formula wt | 404.25 |
| Crystal system | orthorhombic |
| Space group | Pbcm |
| a | 12.0180(14) Å |
| b | 8.6571(6) Å |
| c | 13.9728(22) Å |
| V | 1453.7(3) $Å^3$ |
| Z | 4 |
| $d_{calc}$ | 1.847 g $cm^{-3}$ |
| T | 22 °C |
| Radiation, λ | Mo Kα, 0.71073 Å |
| μ | 10.8 $cm^{-1}$ |
| Rel. trans. coeff. | 0.863-1.000 (φ) |
| No. obs. rflns | 2251 [$I \geq \sigma(I)$] |
| No. indep. rflns | 2983 (265 syst. abs.) |
| R(F), wR(F) | 0.029, 0.033 |

$R(F) = \Sigma||F_0|-|F_c||/\Sigma|F_0|$; $wR(F) = [\Sigma w(|F_0|-|F_c|)^2/\Sigma w|F_0|^2]^{1/2}$

## Deuteration of Alcoholic Substrates

In the glovebox, 7-15 mg (7.9-17.0 μmol) **1** was dissolved in 0.7-1.4 mL $D_2O$. To the green-brown solution 30-40 μL alcohol was added. The resulting solutions were transferred to NMR tubes which were subsequently sealed. Initial $^1H$ and $^2H$ NMR spectra were recorded and the samples were placed in a temperature controlled oil bath. The reaction progress was monitored regularly by $^1H$ and $^2H$ NMR.

## Transfer Hydrogenation

In the glovebox, 16 mg (18 μmol) **1**, 30 μL (355 μmol) 2-butanone, and 27 μL (352 μmol) 2-propanol were dissolved in 1 mL $D_2O$. The solution was transferred to two NMR tubes which were subsequently sealed. Initial $^1H$ and $^2H$ NMR spectra were recorded and the samples were placed in a temperature-controlled oil bath at 80 °C. The reaction progress was monitored regularly by $^1H$ and $^2H$ NMR.

## Stepwise Exchange

In the glovebox, a solution of 54.9 mg (62 μmol) **1**, 100 μL (996 μmol) benzyl alcohol, and $D_2O$ was prepared in a 5 mL volumetric flask. The solution was stirred until all of the solid had dissolved. The solution was transferred to NMR tubes which were subsequently sealed. One sample at a time was placed in the NMR magnet and the VT temperature was controlled at 60, 70, 80 and 90 °C, respectively. $^1H$ NMR spectra were recorded in 20 min intervals with 4 scans/spectrum. The entire methylene proton resonance, consisting of contributions from $C_6H_5CH_2OD$ (**A**) and $C_6H_5CHDOD$ (**B**) was integrated versus the resonance corresponding to the aromatic protons. In addition, the individual contributions of **A** and **B** were evaluated by integration of their respective resonances versus the resonance corresponding to the aromatic protons.

## Catalyst-Concentration Dependence

In the glovebox, a solution of 76.7 mg (86.7 μmol) **1**, 500 μL (4.83 mmol) benzyl alcohol, and $D_2O$ was prepared in a 25 mL volumetric flask. The solution was stirred until all solid had dissolved. This solution was successively diluted by a factor of 3/5, adding 2 mL of reaction solution and $D_2O$ to a 5 mL volumetric flask. Samples with catalyst concentrations of 17.3, 10.4, 6.24, 2.25 and 1.35 mM were transferred to NMR tubes which were subsequently sealed. Concentrations of **1** and **2** after hydrolysis were obtained by integrating the $CpCH_3$ resonances in the $^1H$ NMR spectrum at $\delta = 1.81$ and 1.93 ppm, respectively, versus the integral of the $^-O_3SC_6H_4CH_3$ resonance at $\delta = 2.40$ ppm. The VT temperature was controlled at 90 °C and $^1H$ NMR spectra were recorded in 20 min intervals with 4 scans/spectrum.

## Temperature Dependence

In the glovebox, a solution of 133.9 mg (151 μmol) **1**, 200 μL benzyl alcohol (1.93 mmol), and $D_2O$ was prepared in a 10 mL volumetric flask. The reaction solution was transferred to several NMR tubes which were subsequently sealed. For the kinetic measurements, the VT temperature of the NMR was controlled at 50, 60, 70, 80 and 90 °C, and spectra were collected at intervals of 60, 30 or 15 min, respectively. The concentration of methylene protons was evaluated by comparing their integral to the integral corresponding to the aromatic protons. Rate constants were obtained by fitting the [Protons] vs. time data to eq 14.

### D/H Exchange in $d_7$-Benzyl Alcohol

In the glovebox, a solution of 133.7 mg (151 μmol) **1**, 200 μL $d_7$-benzyl alcohol (1.93 mmol), and $H_2O$ was prepared in a 10 mL volumetric flask. The reaction solution was transferred to several NMR tubes which were subsequently sealed. For the kinetic measurements, the VT temperature of the NMR was controlled at 80 °C and spectra were collected in 30 min intervals, using the lock channel of a 5 mm broadband probe of a GE 500 spectrometer to detect the $^2H$ signal. The concentration of methylene protons was evaluated by comparing their integral to the integral corresponding to the aromatic protons. Rate constants were obtained by fitting the [Protons] vs. time data to eq 14. $^1H$ NMR spectra of the reaction solution before the kinetic runs were acquired on a Varian Inova 300 spectrometer using the *presat* water suppression pulse sequence supplied with the Varian VNMR 6.1 software.

### H/D Exchange at pD 6.4

To a solution of benzyl alcohol (193 mM) and **1** (15.2 mM) in $D_2O$, toluenesulfonic acid monohydrate was added to afford a solution of pD 6.4. Kinetic experiments were carried out as described above. As determined after the kinetic runs, the solution had maintained pD 6.4.

## Bridge

Detailed mechanistic studies of the molybdocene catalyzed H/D exchange were discussed in the previous chapter. The molybdocene catalyst was found to also promote a number of other reactions in water such as ester and nitrile hydrolysis, aldehyde disproportionation, ether cleavage and reduction of olefins. This is described in Chapter V.

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(43) Under some circumstances (unsatisfactory shimming, line broadening as an effect temperature beyond resolution of the two individual resonances) and at early reaction times (**A** resonances much bigger than and therefore overlapping with **B**), separation of the **A** and **B** resonances is not possible. Rate constants can be obtained, however, from evaluation of the integral over the entire methylene region.

(44) This assumption does not take into account a secondary kinetic isotope effect arising from the non-exchanging C-D bond.

(45) The integrated rate laws (12) – (14) are based on the following reaction sequence:

$$\mathbf{A} \xrightarrow{k_1} \mathbf{B}$$

$$\mathbf{B} \xrightarrow{k_2} \textit{products}$$

$$k_2 = \frac{1}{2}k_1$$

with the rate laws

$$\frac{d[\mathbf{A}]}{dt} = -k_1[\mathbf{A}]$$

$$\frac{d[\mathbf{B}]}{dt} = -\frac{k_1}{2}[\mathbf{B}] + k_1[\mathbf{A}]$$

Evaluating [**A**] as

$$[\mathbf{A}] = [\mathbf{A}]_0 e^{-k_1 t}$$

gives the expression

$$\frac{d[\mathbf{B}]}{dt} = -\frac{k_1}{2}[\mathbf{B}] + [\mathbf{A}]_0 e^{-k_1 t}$$

With the initial condition $[\mathbf{B}]_0 = 0$, the differential equation is solved to give

$$[\mathbf{B}] = 2[\mathbf{A}]_0 e^{-0.5k_1 t} - 2[\mathbf{A}]_0 e^{-k_1 t}$$

The total concentration of methylene protons is given by

$$[\mathbf{Protons}] = 2[\mathbf{A}] + [\mathbf{B}]$$

or

$$[\mathbf{Protons}] = 2[\mathbf{A}]_0 e^{-0.5k_1 t}$$

(46) Non-linear data fitting was carried out with the program *pro Fit* 5.1 using the Levenberg-Marquardt algorithm: QuantumSoft, Postfach 6613, CH-8023, Zürich, Switzerland.

(47) Addition of TsOH to the reaction solution resulted in pD 6.4, which is 0.1 unit lower than the pH of the corresponding $H_2O$ solution (it was difficult to adjust the pD to exactly 6.5). Because the H/D reaction slows down with decreasing pH/pD, the calculated primary kinetic isotope effect can be considered a lower limit.

(48) A decrease in pH or pD can contribute to a change in rate if $[H^+]$ and $[D^+]$ appear in the rate law. Note that upon decreasing the pD from 7.1 to 6.4, the $^1H$ NMR spectrum in the Cp' region of **1** and **2** changes significantly, indicating that structural changes occur. These changes in the structure of the active catalyst may also contribute to the decrease in rate.

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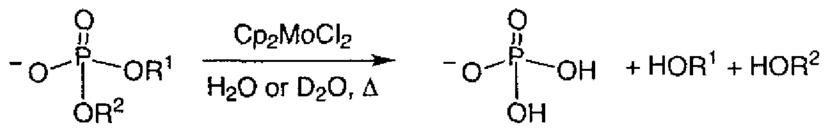
# CHAPTER V

# THE CHEMISTRY OF WATER-SOLUBLE MOLYBDOCENES TOWARD ALCOHOLIC AND NON-ALCOHOLIC SUBSTRATES

## Introduction

In this chapter, the reactivity of a number of different substrates in aqueous solution containing the monomeric and dimeric molybdocene complexes $[Cp'_2Mo(OH_2)(OH)]^+$ (**1**) and $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2]^{2+}$ (**2**) is described. The goal of these studies was to evaluate the reactivity of functional groups other than alcohols, such as ethers, amines, nitriles, alkenes and alkynes in the presence of molybdocenes.

Only very little is known about the aqueous reaction chemistry of molybdocenes.[1,2] Significant work in this area was carried out with the goal to understand the mechanism by which molybdocenes act as anti-cancer agents.[3-6] In this context, a number of nucleotide and nucleobase complexes coordinated to the $[Cp_2Mo]$ fragment have been prepared.[3,4] Additionally, the coordination of the molybdocene to oligonucleotides in aqueous solution has been investigated.[5] The early results pertaining to the anti-cancer activity of molybdocenes motivated the investigations of phosphoester hydrolysis reactions, which have been reported recently (eq 1).[7,8]



$R^1$ = p-nitrophenyl, Me
$R^2$ = H, p-nitrophenyl, Me

(1)

It is interesting to note that no methanol was detected by $^1$H NMR spectroscopy in the molybdocene promoted hydrolysis of dimethylphosphate (DMP).[8] This can now be explained by the H/D exchange that occurs with the hydrolysis product methanol which renders it invisible to $^1$H NMR spectroscopy.

The following sections describe the chemistry of a number of additional alcoholic substrates not discussed in the preceding chapters as well as the reactivity of amines, nitriles, aldehydes and unsaturated ethers in aqueous solutions containing $[Cp'_2Mo(\mu{-}OH)_2MoCp'_2](OTs)_2$ (**3**). The results of these studies are placed in the context of the respective substrate's reactivity with other metal catalysts. In addition, the preparation of the catalytically active molybdocene solutions from the molybdocene dichloride $Cp'_2MoCl_2$ (**4**) as the precursor is described.

## Additional Alcoholic Substrates

A summary of the alcohols tested in the H/D exchange reaction is given in Table 1. 1-Adamantanemethanol (entry 1) was chosen as a substrate to investigate the effect of steric bulk on the H/D exchange reaction. No H/D exchange was observed with this alcohol. In addition to steric influences the reaction may have also been inhibited by the low solubility of the substrate. Carrying out the exchange reaction in a 1:1 THF/$D_2O$ mixture with the intention to increase the solubility of the substrate did not result in

Table 1. Summary of Alcohol Reactivity

| | Alcohol | $c_{cat(3)}$ (mM) | $c_{alc}$ (mM) | Conditions | Comments |
|---|---|---|---|---|---|
| 1 | 1-adamantanemethanol | 12 | <50[a] | 80 °C, 2 d | no H/D exchange |
| | | 19 | 96 | 80 °C, 17.5 h 1:1 $D_2O$/THF | no H/D exchange |
| 2 | α-D-glucose | 7.3 | 66 | 80 °C, 13 h | complex reaction, observation of aldehyde resonance |
| 3 | choline chloride | 11 | 328 | 80 °C, 16 d | no H/D exchange |
| 4 | piperidine ethanol | 22 | 251 | 80 °C, 16 d | very little (<2%) H/D exchange, orange solution |
| 5 | $F_3CCH_2OH$ | 6.7 | 274 | 80 °C, 4 d | no H/D exchange |
| 6 | $HOCH_2(CF_2)_3CH_2OH$ | 8.0 | 99 | 85 °C, 44h | no H/D exchange |
| | | 9.6 | 62 | 80 °C, 3 d, MOPS | no H/D exchange |
| 7 | allyl alcohol | 20 | 588 | 85 °C, 4 d | see page 86 |
| 8 | 3-buten-1-ol | 12 | 232 | 80 °C, 3 d | pD 4.91 after reaction, formation of *n*-butanol |
| 9 | 4-penten-1-ol | 10 | 207 | 80 °C, 3 d | pD 5.25 after reaction, formation of *n*-pentanol |
| 10 | $HOCH_2CCCH_2OH$ | 9.8 | 193 | 85 °C, 2 d | orange-brown precipitate |
| | | 31 | 280 | 80 °C, 10 h | orange-brown precipitate |

[a] this alcohol is only slightly soluble in water

formation of the deuterated product. However, the effect that a cosolvent such as THF may have on the H/D reaction is unknown at this point. In the case of THF the solvent may have inhibited the exchange reaction by coordination to the metallocene.

The H/D reactions could conceivably be used to selectively deuterate (or tritiate, if $T_2O$ is used) biomolecules, which then can be used as tracer molecules in biochemical studies. Entries 2-4 (Table 1) represent alcohols of biological importance.

The reaction chemistry of α-D-glucose was very complex. H/D exchange at five different alcohol carbons can compete with formation of molybdocene chelates, similar to the formation of the molybdocene glycolate complex $[Cp'_2Mo(OCH_2CH_2OH)]^+$ (**5**, Chapter IV). The $^1H$ NMR spectrum did not allow for identification of the reaction products, and no attempts were made to isolate the reaction products.

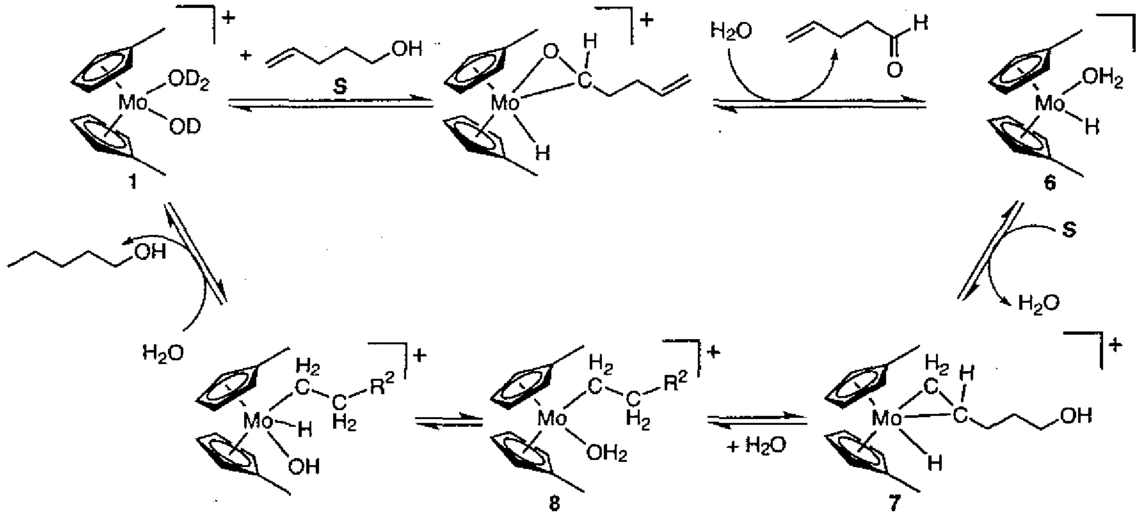
Choline chloride ($[HOCH_2CH_2N(CH_3)_3]Cl$, entry 3) did not undergo H/D exchange. This result is somewhat surprising because a complication arising from the non-coordinating ammonium headgroup would not be expected. It can, however, be rationalized considering the positive charges on both the catalyst and the substrate, which may inhibit formation of the molybdocene alkoxide intermediate.

The sluggishness of piperidine ethanol (entry 4) was expected. The reaction solution containing this amine substrate was basic, which has been shown to slow down H/D exchange (see Chapter II). The chemistry of amines will be discussed further below.

With fluorinated alcohols (entries 5 & 6) no H/D exchange occurs, which can be explained by their weak nucleophilicity. This prevents the nucleophilic substitution of a water ligand from the catalytically active molybdocene monomer $[Cp'_2Mo(OH_2)(OH)]^+$ (**1**).

## Reduction of Unsaturated Alcohols

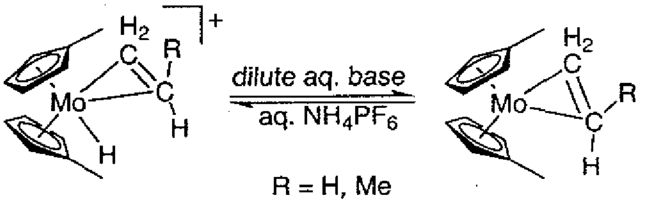
Very interesting results were obtained with unsaturated alcohols (Table 1, entries 7-9). For the longer chain unsaturated alcohols (entries 8 & 9) not only H/D exchange



Scheme 1. A possible mechanism for the reduction of ω-unsaturated alcohols. (The reduction of 4-pentenol (S) is shown.)

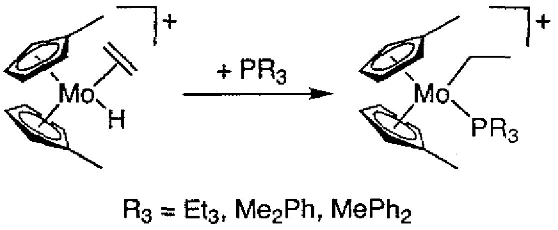
was observed, but additionally the corresponding saturated alcohols were formed.[9] During the course of this reaction the reaction solution became acidic.

The reduction of the olefin end of the unsaturated substrates requires hydrogen transfer to the carbons of the double bond. While there is no hydride ligand available on either the monomeric (**1**) or the dimeric (**2**) molybdocene complexes, some amount of hydride complex **6** is formed by dissociation of a π-carbonyl ligand from the hydride intermediate (Scheme 1, see also Chapter IV). Coordination of the olefin end of the unsaturated substrate to the molybdenum center then leads to the olefin hydride complex **7**. Such olefin hydride complexes of molybdocenes have been shown to undergo reversible protonation (eq 2).[10]



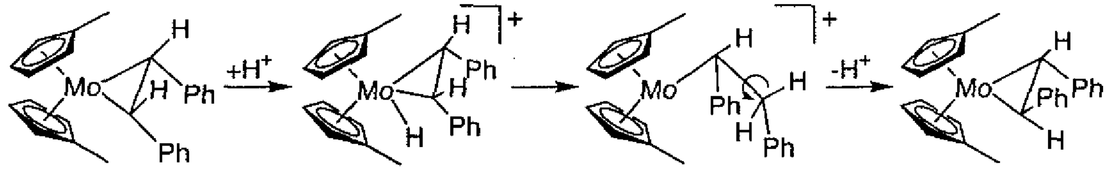
(2)

In addition, olefin hydride complexes underwent insertion reactions to the alkyl complex in the presence of nucleophiles, such as phosphines (eq 3).[10]



(3)

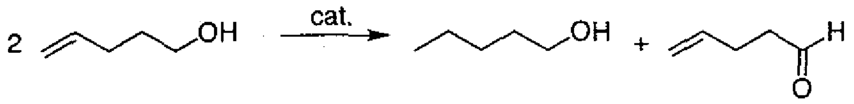
Olefin hydride complexes have also been inferred in the isomerization of molybdocene stilbene complexes (eq 4).[11]



(4)

The complete acidic hydrolysis of the $Cp_2Mo$(ethylene) complexes with HCl was reported to give ethane and molybdocene dichloride.[12]

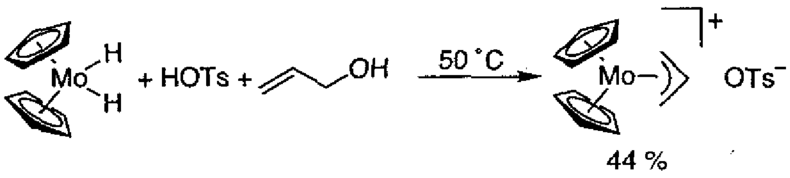
All these prior examples are in agreement with the mechanism shown in Scheme 1. $H_2O$ may act as a ligand to force formation of the alkyl aquo complex, which, after protonation, reductively eliminates the saturated product. Alternatively, the dangling alcohol end of the substrate could serve as a nucleophile. The overall reaction is stoichiometric, and it corresponds to a transfer hydrogenation (eq 5) similar to the MPV-like reaction between 2-butanone and isopropanol described in Chapter IV.



(5)

According to eq 5, one of the reaction products of the olefin reduction should be the corresponding aldehyde. The aldehyde, however, was not observed in the $^1$H NMR spectrum. This should not be construed as unusual, as aldehydes undergo disproportionation reactions themselves to afford carboxylic acid[13] and alcohol. The latter transformation will be discussed in the next section.

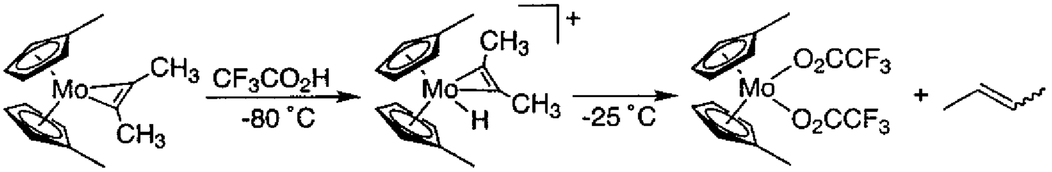
Reacting allyl alcohol under H/D exchange conditions did not only afford the deuterated allyl alcohol and the reduced *n*-propanol, but additional products were observed by $^1$H NMR. Ito at al. have recently described the reaction of molybdocene dihydride with allyl alcohol in EtOH in the presence of a protic acid in which the molybdocene $\eta^3$-allyl complex[14] is formed (eq 6).[15] Similarly, the additional products obtained from allyl alcohol and 3 in $H_2O$ may have arisen from formation of a molybdocene allyl complex. No attempts were made to further identify the products of this reaction.



(6)

The reaction of the alkyne substrate 2-butyne-1,4-diol (entry 10) under H/D conditions lead to rapid formation of an orange-red precipitate. No evidence was found for H/D exchange. The $^1$H NMR spectrum showed the formation of small amounts of products, including an aldehyde with its characteristic low field shift of $\delta = 9.3$ ppm. The reaction was also carried out the on a larger scale (198 mg **3**, 500 mg 2-butyne-1,4-diol). An orange precipitate, which was not soluble in organic solvents, was obtained, but no further attempts were made to characterize this solid material.

The formation of acetylene complexes of molybdocene is well known, and a number of complexes with various substituents on the acetylene ligand have been prepared.[12,16-19] Herberich et al. found that protonation of the 2-butyne complex afforded an alkenyl hydride molybdocene, which was only stable at low temperature (–80 °C, $d_6$–acetone).[19] The alkene was liberated at temperatures above –25 °C (eq 7), while the bis(trimethylsilyl)-derivative decayed at room temperature over a period of several hours.



(7)

It will require further experiments to establish if and how the aqueous alkyne chemistry of molybdocene is related to the chemistry observed in organic solvents.

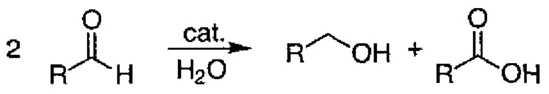
The reduction of unsaturated compounds described above is of interest to the synthetic (reduction of alkenes in water) and the mechanistic chemist. Further investigations are required to fully understand this area of aqueous molybdocene chemistry.

Table 2. Reactivity of Non-Alcoholic Substrates

| | Alcohol | $c_{\text{cat (3)}}$ (mM) | $c_{\text{substr.}}$ (mM) | Conditions | Comments |
|---|---|---|---|---|---|
| 1 | propionaldehyde | 7.3 | 385 | 89 °C, 16 d | disproportionation to propionic acid and propanol<br>pD drops to 3.1 |
| 2 | ethylacetate | 12.5 | 272 | 80 °C, 17 h | ethanol is formed,<br>pD drops to 3.7 |
| | | 12.5 | 272 | r.t., 17 h | ethanol is formed |
| 3 | acetonitrile | 15 | 768 | 80 °C, 16.5 h | 54% hydrolysis to acetamide,<br>precipitate is formed |
| 4 | allylmethylether (**9**) | 13.8 | 1 M | 80 °C, 3 d | precipitation,<br>substrate recovered |
| 5 | ethylvinylether (**10**) | 13.8 | 1 M | 80 °C, 3 d | ether cleaves, forms ethanol & acetaldehyde |
| 6 | $NEt_3$ | 12 | 295 | 80 °C, 5 h | no H/D exchange,<br>temperature dependent color change,<br>pD 12.3 |
| 7 | $HNEt_2$ | 17 | 268 | 85 °C, 5 d | no H/D exchange,<br>temperature dependent color change,<br>pD 12.8 |

## Aldehyde Disproportionation

As mentioned in the previous section, the reaction of aldehydes in water in the presence of molybdocenes lead to disproportionation (eq 8).

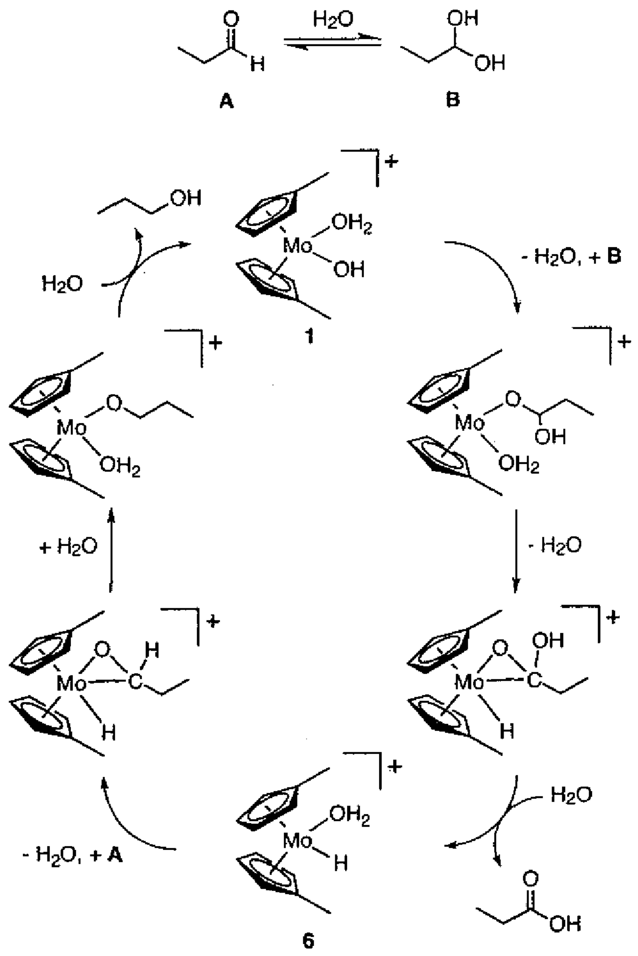


(8)

For the substrate propionaldehyde this reaction afforded propanol and propionic acid (Table 2, entry 1). The products were identified by their $^1$H NMR resonances: Addition of *n*-propanol and sodium propanate to samples of the reaction mixture resulted in an increase of the resonances at δ (ppm) 3.51(t), 1.50 (6), 0.85 (t) and 2.34 (q), 1.04 (t), respectively, confirming the assignment of the products. The formation of the carboxylic acid also explains the observed decrease in pD.

The metal-catalyzed disproportionation of aldehydes (Cannizzaro reaction)[20] has been reported for a number of pentamethylcyclopentadienyl (Cp*) aquo complexes of rhodium and iridium in water.[21,22] The transition metal catalyzed transformations in water give the free acid and the free alcohol, while in the aqueous, base-catalyzed reaction aldehydes with α-hydrogens typically undergo aldol condensations. In organic solvents, the disproportionation of aldehydes promoted by vanadocene,[23] rhodium allyl[24] and ruthenium[25] complexes leads to formation of the ester in the Tishchenko reaction.[26]

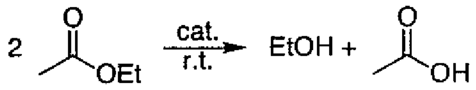
A possible mechanism for the molybdocene catalyzed disproportionation of aldehydes is shown in Scheme 2. This mechanism is based on a proposal by Cook et al. for Ir and Rh catalyzed aldehyde disproportionation. In water, propionaldehyde exists partially in its hydrated form (approximately 41%).[22] The diol coordinates to the molybdocene in a manner similar to the H/D exchange mechanism described in Chapter IV. Abstraction of the α-H affords a propionato hydride complex which subsequently dissociates the propionate. The resulting molybdocene hydride then reacts with a molecule of the free aldehyde. Reductive elimination liberates the reduced substrate, *n*-propanol, and catalyst **1** is regenerated.



Scheme 2. Possible mechanism for the disproportionation of propionaldehyde.

## Ester Hydrolysis

The carboxylic acid ester ethyl acetate was hydrolyzed rapidly (eq 9) by the molybdocene catalyst in aqueous solution (Table 2, entry 2). Even at room temperature this hydrolysis was facile. During the course of the reaction the pD of the reaction mixture decreased from neutral to pD 3.7 with concomitant change in color from green-brown to bright green.



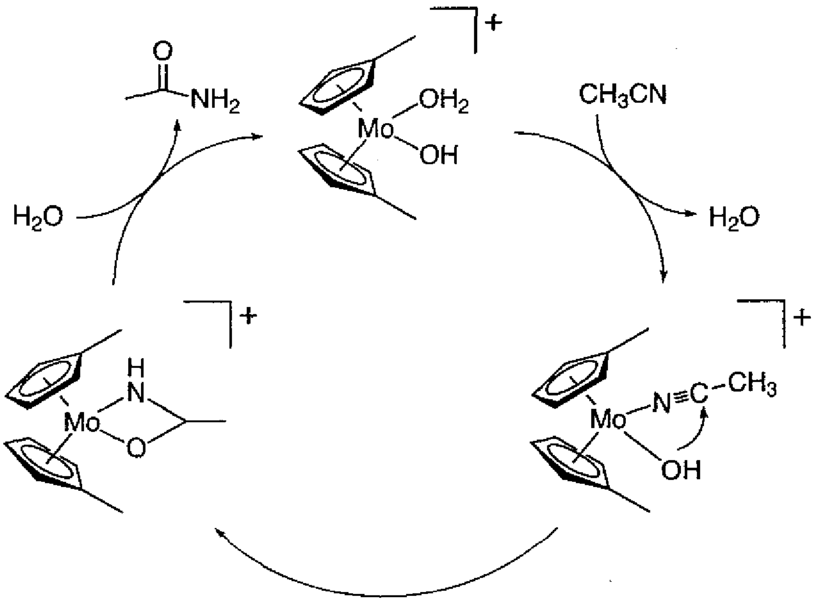
(9)

The molybdocene complex **3** adds to the extensive list of catalysts already available for transition metal promoted ester hydrolysis.[27] This list includes the Co complex (tris(3-aminopropyl)amine)Co(OH)($OH_2$) described by Chin and Banaszczyk.[28] The chemistry of this family of complexes closely parallels the chemistry of the molybdocenes, i.e. they do not only promote the hydrolysis of carboxylic acid esters, but also phosphate ester hydrolysis[29,30] and nitrile hydration[31,32] (see the following section).

## Hydration of Acetonitrile

A number of water-soluble transition metal complexes are known to catalyze the hydrolysis of nitriles to amides.[33,34,31,32,35-37] This is an industrially important transformation, which is evident from the large number of patents and papers published in this area.[38]

Aqueous solutions of **3** were found to catalyze nitrile hydration. At 80 °C, acetonitrile was converted catalytically into acetamide. A mechanism can be envisaged (Scheme 3) similar to that proposed by Kim et al. for Co complexes with tetradentate amines.[31,32,35] The pathway involving *intra*molecular nucleophilic attack rather than catalysis by a general base was found to occur with the Co-amine complexes. Mechanistic studies, of course, have to be carried out in order to elucidate if the same mechanism applies to the molybdocene system.



Scheme 3. Possible mechanism for the molybdocene-catalyzed hydration of acetonitrile to acetamide.

While reduction of molybdocene-coordinated nitriles with $HBF_4$ has been reported,[39] the ability of molybdocenes to hydrolyze nitriles to amide had previously been unknown. Of more interest than the hydrolysis of acetonitrile would be the hydrolysis of acrylonitrile to the industrially important acrylamide. This latter reaction as well as the mechanism of nitrile hydrolysis will most certainly be the subject of further investigations.

## Unsaturated Ethers

In order to investigate the reactivity of the molybdocenes in the presence of unsaturated compounds *without* an alcohol functionality, the unsaturated ethers allylmethylether (**9**) and ethylvinylether (**10**) were reacted under H/D exchange conditions (Table 2, entries 4 & 5). With **9**, precipitation of a gray solid occurred shortly after addition of the substrate to the reaction mixture. The $^1$H NMR of the reaction mixture showed only the starting material **9**. Extraction of the reaction mixture (46 μmol **3**, 11 mmol **9**, 5 mL $H_2O$, 80 °C, 3d) with $CDCl_3$ showed only unreacted starting material. No product from reduction of the double bond was observed. This is not surprising in light of the mechanism proposed for the reduction of unsaturated alcohols (Scheme 1). The active species in the reduction is the molybdocene hydride complex **6**, which is only formed upon reaction of **1** with an alcohol. Attempts to reduce the double bond in **9** with molybdocenes in water should therefore either be carried out with **3** in the presence of an alcohol or directly with a molybdocene hydride complex like $Cp'_2Mo(H)(OTf)$ (see Chapter IV).

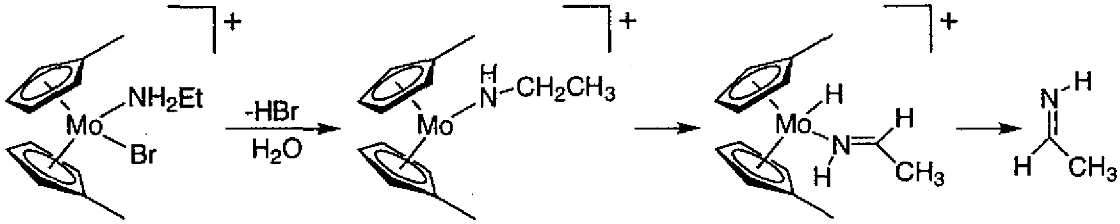
Unlike **9**, the vinyl ether **10** reacted rapidly in water in the presence of molybdocenes. Within 8 hours (0.1 mmol **3**, 16 mmol **10**, 80°C) was cleaved to give ethanol and acetaldehyde. These products were identified by extraction of the reaction solution with $CDCl_3$ and comparison of their $^1$H NMR spectra with authentic samples. Within the short reaction time, no disproportionation of the acetaldehyde (see above) was detected by $^1$H NMR.

## Reactivity of Amines

The chemistry of molybdocenes toward amines was investigated using $NEt_3$ and $HNEt_2$ (Table 2, entries 6 and 7). The secondary amine was chosen to allow the formation of an amido molybdocene complex by proton dissociation from the N-H bond

This is analogous to the formation of the molybdocene alkoxide in H/D exchange reactions with alcohols (see Chapter IV, Scheme 1). Both amine substrates, however, were inert toward H/D exchange under two different conditions. No H/D exchange occurred in solutions of pD > 12, resulting from simple addition of amine and catalyst **3** to $D_2O$, in agreement with the reduction of H/D exchange rates under basic conditions (Chapter II). In order to circumvent the problem of slower reaction rates at high pD, the deuteration of $HNEt_2$ (190 mM, 12 mM **3**) was also attempted in the presence of a buffer (0.44 M MOPS, 4-morpholinepropanesulfonic acid, hemisodium salt). Under these conditions, the molybdocenes existed as **1** and **2** (as evidenced by $^1H$ NMR), but no H/D exchange was observed. There was also no evidence for coordination of the amine to the molybdocene complex.

These results are consistent with the observation that reduction of imines with $[Cp_2MoH_3]^+$ complexes is more facile than reduction of the corresponding ketones,[40,41] which indicates that an amine is more stable than an alcohol with respect to α-C-H bond activation. The activation of the α-C-H bond of primary amines, however, has been invoked as a step in the oxidation of amines to ketones with molybdocenes in water (eq 10).[1,2]



(10)

The oxidation product from the primary amines ($H_2NEt$ in eq 10) was obtained by hydrolysis of the dissociated imine ligand, which in the case of $H_2NEt$ was acetaldehyde. These results reported for the oxidation of primary amines[2] suggest that amines with only one alkyl substituent should be the more probable candidates for H/D exchange. This remains to be investigated before the claim can be made that amines in general do not undergo H/D exchange.

While no H/D exchange chemistry was observed with secondary and tertiary amines at pD > 12, a different interesting observation was made. Aqueous solutions prepared from **3** and amine ($HNEt_2$ or $NEt_3$) were orange at room temperature. Upon heating to 80 °C, the color changed to bright green. Multiple heating and cooling cycles showed that this process was reversible.

The color changes were reflected in the $^1H$ NMR spectra of the reaction solutions (Figure 1). At 30 °C, the solution contained a mixture of **A** ($\delta$ (ppm) = 5.23 (m, br); 5.10 (m, br)) and **B** ($\delta$ (ppm) = 6.08 (m, br); 5.14 (m, br)) with a small feature at $\delta$ (ppm) = 5.18 (m, br). Species **B** disappeared as the temperature was increased, identifying species **A** as the compound that gave rise to the green color. The identity of **A** and **B** in aqueous solution was independent of the amine ($NEt_3$, $HNEt_2$). The only resonances attributable to amines were those of the free substrates. There was no evidence for coordination of the amines to form appreciable amounts of amino molybdocene complexes. This suggests that the formation of **A** and **B** is only dependent on the pH. The observation that amine/molybdocene solutions buffered at neutral pH show only the resonances

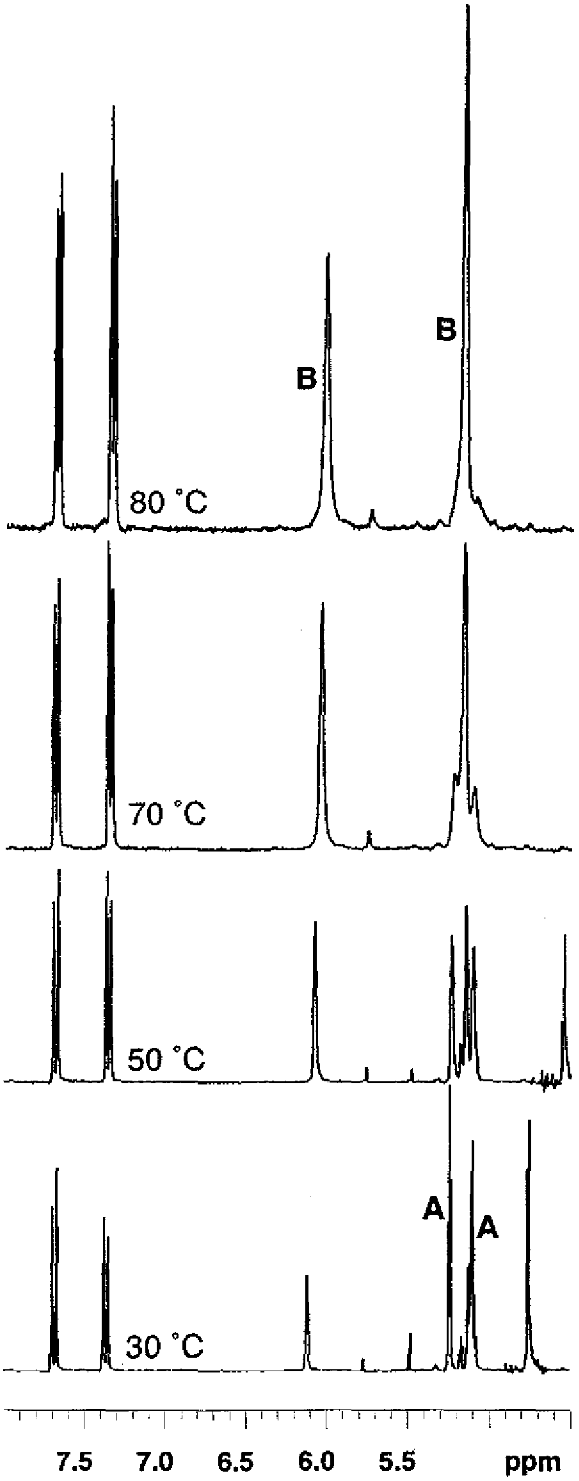


Figure 1. Variable temperature $^1$H NMR spectra of a solution of $NEt_3$ (295 mM) and **3** (12 mM) in $D_2O$.

for **1** and **2** (and no resonances for **A** or **B**) supports the supposition that it is not the presence of an amine which gives rise to the observed color changes. The identification of compounds **A** and **B** remains an interesting problem for future studies.

## Catalytic Activity of $Cp'_2MoCl_2$

Most experiments on the reactivity of molybdocenes were carried out with the dimeric complex **3** as the precursor. As described in Chapter III, however, aqueous solutions containing **1** and **2** can also be prepared from $Cp'_2MoCl_2$ (**4**) and adjustment of the pH to give a neutral solution. It was important to investigate if solutions prepared from **4** were also active for catalytic C-H bond activation. Heating a 16 mM solution of **4** in $D_2O$ (pD 3.3) to 85 °C for several hours resulted in only sluggish exchange of the Cp*Me* hydrogens (see Chapter II). However, adjusting the pD of a 32 mM solution of **4** in $D_2O$/MeOH with NaOH in $D_2O$ to pD 6.9 prior to heating resulted in rapid H/D exchange as it was observed for solutions of **3** (Chapters II and IV). Similarly, 50 mM solutions of **4** in 0.47 M MOPS buffer[42] and 0.7 M MeOH (80 °C) showed H/D exchange. From the $^1H$ NMR spectrum it was deduced that the buffer did not interact with the molybdocene (the chemical shift of **1** and **2** were identical in unbuffered solutions of **3** and buffered solutions of **4**) and therefore did not interfere with the H/D exchange reaction. This result is particularly interesting because it shows that catalytically active molybdocene solutions can easily be prepared from commercially available precursors, **4** (or possibly its non-methylated analog) and MOPS.

## Conclusions

The results described in this chapter demonstrate the versatility and utility of aqueous molybdocenes. The molybdocene catalyst was shown to promote ester and nitrile hydrolysis, aldehyde disproportionation, ether cleavage and reduction of olefins. These interesting reactions require more extensive investigation with respect to their mechanistic details and their general applicability. The work described in Chapters II-V, however, provides fundamental information which helps to better understand and appreciate the aqueous organometallic chemistry of molybdocenes.

## Experimental Section

All manipulations were carried out under a nitrogen atmosphere using standard vacuum line techniques or a glovebox. Solvents were dried over and distilled from the appropriate drying agents. All liquid alcohols and amines were dried over and distilled from $CaH_2$. $D_2O$ (99.9% D) was purchased from Cambridge Isotope Laboratories and purged with $N_2$ for at least 30 min prior to use. Solutions were buffered using 4–morpholinepropanesulfonic acid, hemisodium salt (MOPS, $pK_a$ 7.2). pH/pD measurements on NMR samples were carried out using a Corning NMR Micro Electrode, d = 3 mm, and a Hanna HI9023 pH meter with attached thermocouple. Prior to the measurement, the NMR tube was placed in a water bath together with the thermocouple to allow for thermal equilibration. All reported pD values were calculated according to pD = (pH meter reading + 0.4) to correct for the use of a glass electrode.[43,44] $^1H$ and $^2H$

NMR spectra were recorded using a Varian Inova 300 NMR spectrometer (299.95 MHz for $^1H$, 46.04 MHz for $^2H$).

In a typical experiment, 7-15 mg (7.9-17.0 μmol) **3** were dissolved in 0.7-1.4 mL $D_2O$ in the glovebox. Reactions in the presence of MOPS buffer were prepared using $D_2O$ stock solutions of 0.4-0.5 M MOPS, hemisodium salt. The substrate was then added to the green-brown molybdocene solution. The reaction mixture was transferred to NMR tubes which were subsequently sealed. Initial $^1H$ and $^2H$ NMR spectra were recorded and the samples were placed in a temperature-controlled oil bath. The reaction progress was monitored regularly by $^1H$ and $^2H$ NMR.

In the larger scale experiments, the appropriate reaction mixtures were heated in schlenk flasks sealed with PTFE stoppers. The reaction progress was monitored by $^1H$ NMR spectroscopy. When $H_2O$ was used, a sample of the reaction mixture was diluted with $D_2O$ and the $^1H$ NMR spectrum was recorded using the *presat* solvent suppression pulse sequence supplied with the VNMR software. After completion of the reaction, the reaction mixture was extracted with $CDCl_3$. After drying of the $CDCl_3$ solution over $MgSO_4$ the reaction products were analyzed by $^1H$ NMR.

## Bridge

In Chapter V, the reactivity of a number of different substrates was described. This provided both an overview of the versatility of the molybdocene catalyst as well as an outlook on questions which remain to be answered in future studies. Chapter V concludes the reports on the investigations of mechanisms and reactivity of molybdocenes in water. The following two chapters describe studies toward the elucidation of reaction mechanisms of organometallic radicals in aqueous media. In Chapter VI, the oxidation chemistry of $(CO)_3Fe(TPPTS)_2$ in water is discussed.

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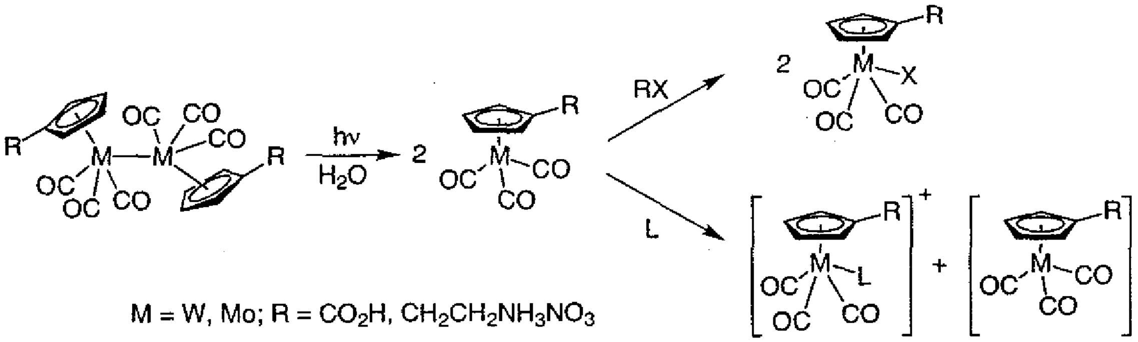
# CHAPTER VI

# GENERATION OF 17-ELECTRON ORGANOMETALLIC RADICALS IN AQUEOUS SOLUTION – CHEMICAL AND ELECTROCHEMICAL OXIDATION OF $(CO)_3Fe(TPPTS)_2$

## Introduction

The chemistry of 17-electron organometallic radical complexes has been studied in great detail.[1,2] The interest in 17-electron complexes arises because of their important role in a number of catalytic and stoichiometric transition metal promoted reactions. Organometallic radicals are often far more reactive than their 18-electron counterparts. Migratory insertion reactions[3] and ligand substitution reactions[4-9] are accelerated by several orders of magnitude. The substitution of $[(CO)_3Fe(PPh_3)_2]^+$ (**1**$^+$) by pyridine nucleophiles, for example, occurs $10^9$ times faster than in its 18-electron analog $(CO)_3Fe(PPh_3)_2$ (**1**).[6]

Most of the studies on organometallic radicals have been carried out in organic solvents. Research in this laboratory,[10-12] however, has recently focused on the investigation of 17-electron complexes in *water*.[13] By attaching ionic groups to the cyclopentadienyl ligands, the dimers $(CpCOO^-)_2W_2(CO)_6$,[10] $(CpCH_2CH_2NH_3^+)_2Mo_2(CO)_6$,[11] and $(CpCH_2CH_2NMe_3^+)_2Mo_2(CO)_6$[14] were rendered water-soluble. Photolysis of these dimers resulted in homolytic cleavage of the M-M bond and formation of 17-electron radicals. The chemistry of the water-soluble organometallic radicals was shown to be analogous to the chemistry in organic solvents: Atom abstraction from halide sources and nucleophilic attack on the metal center resulted in the formation of the corresponding halide complexes and the overall disproportionation of the dimers, respectively (Scheme 1).



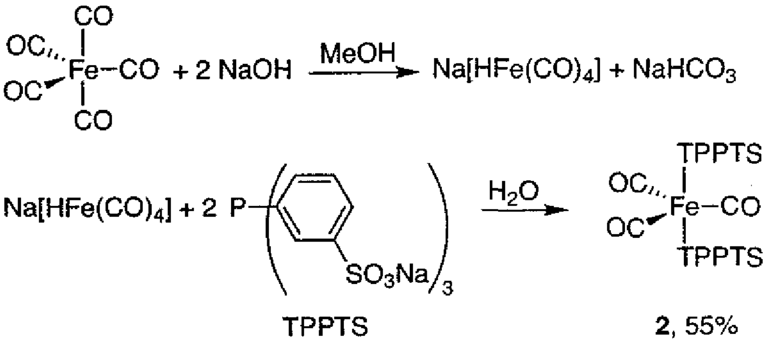
Scheme 1. Reactivity of organometallic radicals in water. Halide abstraction and ligand-induced disproportionation of photochemically generated water-soluble group VI 17-electron complexes.[10, 11]

With the goal of understanding the fundamental chemistry of organometallic radicals in aqueous solution, this study extends our previous work to a water-soluble iron carbonyl phosphine complex. Herein we report the facile synthesis, the molecular structure and the oxidation chemistry of the water-soluble complex $(CO)_3Fe(TPPTS)_2$ (**2**, TPPTS = triphenylphosphinetrisulfonate, sodium salt).[15,16] Its behavior upon chemical and electrochemical oxidation to the 17-electron complex $\mathbf{2}^+$ is compared to its analogs, **1** and $\mathbf{1}^+$, and other $(CO)_3Fe(PR_3)_2$ complexes (R = alkyl, aryl), which have been extensively studied in organic solvents.[17-22,6,23-32]

# Results and Discussion

## Synthesis of **2**

The synthesis of the complex $Fe(CO)_3(TPPTS)_2$ (**2**) has been described previously, starting from $Fe_2(CO)_9$ with low yields (20% after gel chromatography).[16] The isolated product still contained traces of the monosubstituted complex. An improved synthesis was therefore devised (Scheme 2) similar to the procedure described by Brunet et al. for **1**.[33] Complex **2** was prepared from $Fe(CO)_5$ and TPPTS via $[HFe(CO)_4]^-$.



Scheme 2. Synthesis of **2**.

After formation of $[HFe(CO)_4]^-$, the solvent was changed from MeOH to $H_2O$. This was necessary because the intermediate $[HFe(CO)_4]^-$ cannot be prepared directly from $Fe(CO)_5$ in water, yet water is required to dissolve TPPTS. The product was obtained in 55% yield, and it was easily recrystallized from $EtOH/H_2O$ to give spectroscopically pure crystals of **2** (IR ($D_2O$) 1896 (s), 1883 (sh) $cm^{-1}$; see Table 1), suitable for x-ray crystallographic analysis. The molecular structure of **2** is shown in Figure 1, and selected bond lengths and angles of **2** and **1**[29] are collected in Table 2.

Crystallographic data is given in Table 3. The molecular geometry of the trigonal bipyramidal complex **2** deviates from $C_3$ symmetry in that the P(1)-Fe-P(2) angle is 170°. Similar structural distortions have been reported for **1**[29,34] and other diphosphine tricarbonyl iron complexes.[35,31] The three CO ligands are coplanar, with one of the CO-Fe-CO angles considerably larger (C(1)-Fe-C(3): 125(1)°) than the remaining two angles, a common feature of diphosphine tricarbonyl iron complexes.[29,34,35,31]

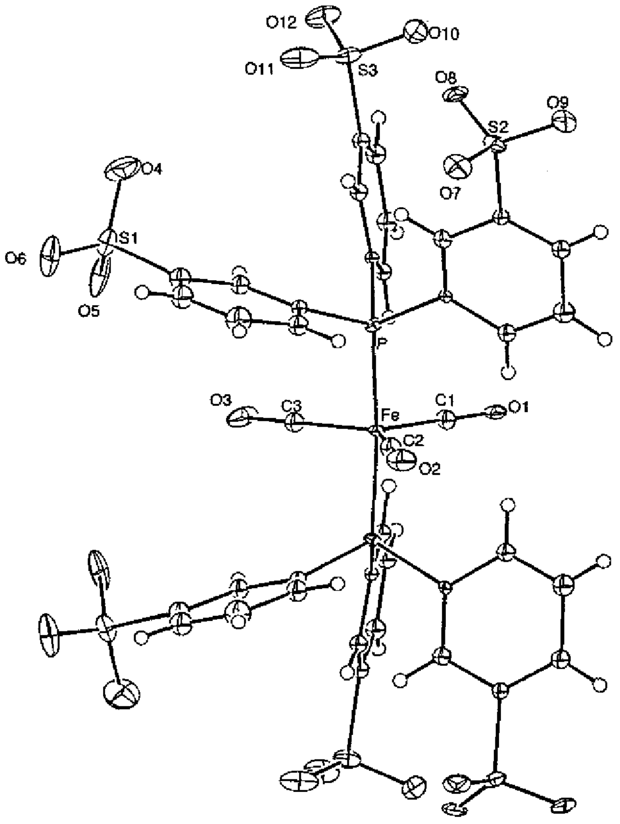


Figure 1. Molecular structure of **2**.

Table 1. Selected Infrared and $^{31}$P NMR Data

| complex | ν (cm$^{-1}$) | $^{31}$P NMR δ (ppm) |
|---|---|---|
| $(CO)_3Fe(PPh_3)_2$ | 1879$^{a, 20}$ | 82.6$^{b, 33}$ |
| $(CO)_3Fe(TPPTS)_2$ | 1885 (vs)$^{c, 16}$ | (74.76)$^{d, 16, 42}$ |
| $(CO)_3Fe(TPPTS)_2$ | 1896 (s), 1883 (sh)$^{d}$ | 84.2$^{d}$ |
| $(CO)_4Fe(PPh_3)$ | 2040, 1963, 1935$^{a, 20}$ | |
| $(CO)_4Fe(TPPTS)$ | 2050 (s), 1977 (s), 1944 (vs)$^{c, 16}$ | (84.95)$^{d, 16}$ |
| $(CO)_4Fe(TPPTS)$ | 2056 (m), 1984 (m), 1948 (s)$^{d}$ | |
| $[(CO)_3Fe(PPh_3)_2]_2Ag$ | 1925 (s), 1897 (vs)$^{a, 21}$ | |
| $[(CO)_3Fe(TPPTS)_2]_2Ag$ | 1990 (m), 1927 (s), 1903 (s)$^{d}$ | 73.1$^{d}$ |
| $[(CO)_3Fe(PPh_3)_2]^+$ | 1999$^{a, 21}$ | |

$^{a}CH_2Cl_2$; $^{b}CDCl_3$; $^{c}$KBr; $^{c}D_2O$

Table 2. Selected Bond Distances (Å)
and Angles (°) for **2** and **1**$^{35}$

| | $(CO)_3Fe(TPPTS)_2$ (**2**) | $(CO)_3Fe(PPh_3)_2$ (**1**)$^{35}$ |
|---|---|---|
| | Distances | |
| Fe-P(1) | 2.211(4) | 2.2201(9) |
| Fe-P(1') | 2.211(4) | 2.2144(9) |
| Fe-C(1) | 1.69(3) | 1.770(4) |
| Fe-C(2) | 1.72(2) | 1.765(4) |
| Fe-C(3) | 1.79(3) | 1.776(4) |
| C(1)-O(1) | 1.18(3) | 1.154(5) |
| C(2)-O(2) | 1.16(3) | 1.134(5) |
| C(3)-O(3) | 1.16(3) | 1.132(5) |
| | Angles | |
| P(1)-Fe-P(1') | 169.8(3) | 172.56(4) |
| C(1)-Fe-C(2) | 117(1) | 118.08(17) |
| C(1)-Fe-C(3) | 117(1) | 118.34(17) |
| C(2)-Fe-C(3) | 125(1) | 123.56(17) |
| Fe-C(1)-O(1) | 179(3) | 179.0(3) |
| Fe-C(2)-O(2) | 179(3) | 179.3(3) |
| Fe-C(3)-O(3) | 179(3) | 179.4(4) |

Table 3. Crystallographic Data for **2**

| | |
|---|---|
| Composition | $C_{39}H_{24}FeNa_6O_{21}P_2S_6 \cdot 6\ H_2O \cdot C_2H_6O$ |
| Formula wt | 1430.9 |
| Crystal system | tetragonal |
| Space group | P4/mnc |
| a | 18.257(4) Å |
| c | 33.939(4) Å |
| V | 11312(3) Å$^3$ |
| Z | 8 |
| $d_{calc}$ | 1.680 g cm$^{-3}$ |
| T | 22 °C |
| Radiation, $\lambda$ | Mo K$\alpha$, 0.71073 Å |
| $\mu$ | 6.79 cm$^{-1}$ |
| No. obs. rflns | 3021 [$I \geq 0.5\sigma(I)$] |
| Total rflns | 5675 |
| R(F), wR(F) | 0.163, 0.132 |

$R(F) = \Sigma||F_0|-|F_c||/\Sigma|F_0|$; $wR(F) = [\Sigma w(|F_0|-|F_c|)^2/\Sigma w|F_0|]^{1/2}$

## Chemical Oxidation of **2** with Ce(IV)

Stoichiometric amounts of $(NH_4)_2Ce(NO_3)_6$ were added to a solution of **2** in $D_2O$ and the reaction was monitored by IR. Upon addition of 1 eq of Ce(IV), gas bubbles evolved from the reaction solution and the absorbance of the characteristic band of **2** at 1896 $cm^{-1}$ decreased by 50% (Figure 2a). Addition of a second equivalent Ce(IV) resulted in complete loss of the $C\equiv O$ bands for **2**, and no other carbonyl-containing compound was observed in the IR spectrum(Figure 2b). This shows that two electron equivalents are required to completely oxidize the Fe(0) complex. The $^{31}P$ NMR recorded after completion of the reaction showed free TPPTS as the only phosphorous species in the reaction mixture.

The chemical oxidation of $(CO)_3Fe(PPh_3)_2$ (**1**) in organic solvents has been described previously.[19,20,22,25] In the non-coordinating solvent $CH_2Cl_2$, **1** is readily converted to the cation $\mathbf{1}^+$ using $[N(C_6H_4Br\text{-}p)]^+$.[19] This 17-electron cation was isolated as the $PF_6^-$ • 1/2 $CH_2Cl_2$ salt and its structure was confirmed to be distorted square-

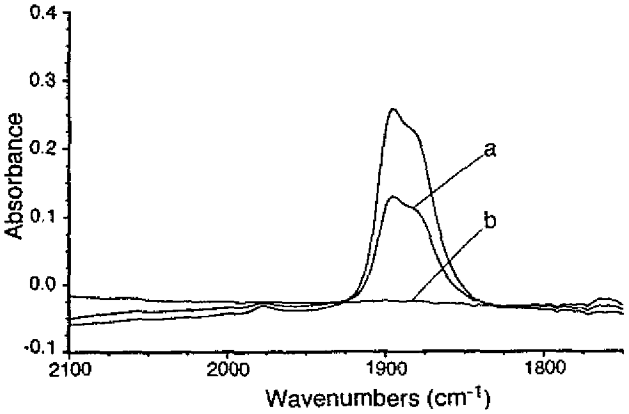


Figure 2. Oxidation of **2** (12 mM, $D_2O$) with (a) 1 eq Ce(IV), and (b) 2 eq Ce(IV).

$$2\,(CO)_3Fe(PR_3)_2 \xrightarrow{\quad} 2\,(CO)_3Fe(PR_3)_2^{+} + 2\,e^{-}$$

$$(CO)_3Fe(PR_3)_2^{+} + Nu \xrightarrow{\quad} (CO)_3Fe(Nu)(PR_3)_2^{+}$$

$$(CO)_3Fe(Nu)(PR_3)_2^{+} + (CO)_3Fe(PR_3)_2^{+} \xrightarrow{\quad} (CO)_3Fe(Nu)(PR_3)_2^{2+} + (CO)_3Fe(PR_3)_2$$

$$(CO)_3Fe(Nu)(PR_3)_2^{2+} \xrightarrow[fast]{Nu} Fe(Nu)_6^{2+} + 3\,CO + 2\,PR_3$$

Overall:

$$(CO)_3Fe(PR_3)_2 \xrightarrow{Nu} Fe(Nu)_6^{2+} + 3\,CO + 2\,PR_3 + 2\,e^{-}$$

a) $PR_3 = PPh_3$; Nu = pyridine b) $PR_3$ = TPPTS; Nu = $H_2O$

Scheme 3. Mechanism of the disproportionation of **1** and **2** upon oxidation in the presence of a nucleophile: a) see ref 6; b) this work.

pyramidal,[25] in agreement with ESR, IR and theoretical studies.[22,23,25] In the presence of coordinating solvents or added ligands, however, **1**+ decayed rapidly.[20,22,6] This is a consequence of a rapid associative ligand substitution/disproportionation sequence, which was shown by Therien et al. in an elegant study using double potential step chronocoulometry.[6] The general mechanism of this disproportionation of $\mathbf{1}^{+}$ by a nucleophilic ligand is shown in Scheme 3. The overall reaction starting from **1** requires two electrons and gives an Fe(II) complex as the reaction product (eq 1).

$$(CO)_3Fe(PPh_3)_2 + Nu \xrightarrow{\quad} Fe(Nu)_6 + 3\,CO + 2\,PPh_3 + 2\,e^{-} \qquad (1)$$

Considering the reactivity of **1** and $\mathbf{1}^{+}$ in coordinating solvents, the results of the oxidation of **2** by Ce(IV) can be rationalized as follows. IR and $^{31}P$ NMR spectroscopy showed that both the CO and the TPPTS ligands are substituted upon oxidation of **2**. Two electron equivalents are required to achieve complete substitution of **2**. Both these findings are consistent with a reaction analogous to eq 1. The reaction product is the hydrated Fe(II) complex (eq 2), as evidenced by formation of the red Fe(phen)$_3^{2+}$ complex upon addition of phenanthroline to the reaction solution.

$$(CO)_3Fe(TPPTS)_2 + 2\ Ce(IV) + 6\ H_2O \longrightarrow Fe(OH_2)_6^{2+} + 3\ CO + 2\ PPh_3 + 2\ Ce(III) \qquad (2)$$

The 2-electron oxidation of **2** is therefore proposed to proceed by a disproportionation mechanism as shown in Scheme 3b through formation of the 17-electron intermediate **2**$^+$.

## Oxidation of **2** with Ag(I)

The oxidation with Ce(IV) led to clean oxidation of **2** to give Fe(II) without detection of any intermediates or products containing CO. Upon addition of 1 eq AgNO$_3$ to an aqueous solution of **3**, a carbonyl containing intermediate **3** was observed (Figure 3a), with three new bands in the IR spectrum at 1990, 1927 and 1903 cm$^{-1}$. At the same time, the CO bands of **2** had disappeared. After one hour, the three bands of **3** had vanished again with the concurrent formation of metallic silver, evolution of gas and formation of **2**, as evidenced by its IR spectrum (Figure 3b). Following this reaction by

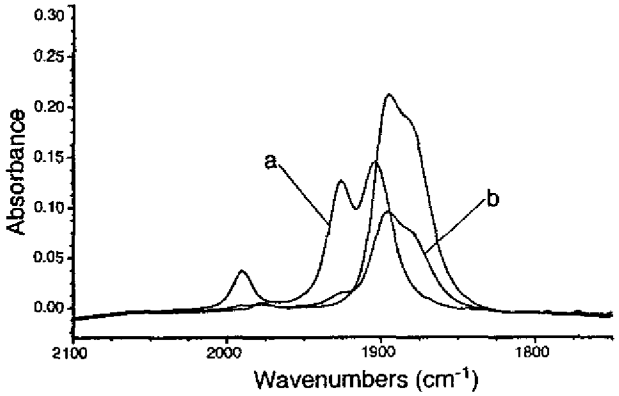


Figure 3. Oxidation of **2** (8.6 mM, D$_2$O) with 1 eq AgNO$_3$; a) 5 min after addition of Ag(I), formation of **3**; b) 1 h after addition of Ag(I).

$^{31}P$ NMR spectroscopy led to similar conclusions. Complex **2** was initially converted to the intermediate **3** ($^{31}P$ NMR: 73.1 ppm) which subsequently disappeared, and the resonance of the starting material grew in again. Similar observations were made by Baker et al. for the oxidation of $(CO)_3Fe(PPh_3)_2$ by $AgPF_6$ in $CH_2Cl_2$,[19] which were interpreted in terms of formation of an adduct between the iron complex and the silver cation to give a linear Fe-Ag-Fe complex. This intermediate was implied to subsequently decay to the disproportionation products as shown in eq 3.

$$\begin{gathered} 2\,(CO)_3Fe(PPh_3)_2 + 2\,Ag(I) \longrightarrow 2\,[((CO)_3(PPh_3)_2Fe)Ag(Fe(CO)_3(PPh_3)_2)]^+ \\ \longrightarrow Fe(II) + 3\,CO + 2\,PPh_3 + (CO)_3Fe(PPh_3)_2 + 2\,Ag \end{gathered} \tag{3}$$

Analogous intermediates have also been proposed in the electrochemical oxidation of **1** on mercury electrodes.[20,22] The longevity of the inferred Hg intermediate gave rise to chemically reversible cyclic voltammograms at Hg in $CH_3CN$, while cyclic voltammograms at Pt in $CH_3CN$ showed a chemically irreversible oxidation process. Eventually, the linear Hg and Ag intermediates decayed through formation of the radical cation $\mathbf{1}^+$ (which was detected by ESR, but not until some time after initial current flow, i.e. initial oxidation of **1**[22]).

## Cyclic Voltammetry of **2** in $H_2O$

Cyclic voltammetry (CV) experiments were carried out to obtain information about the oxidation potential of **2** in aqueous solutions. Initially, a Pt disk electrode was used as the working electrode. Oxidation of **2**, however, resulted in evolution of CO, which absorbed on the Pt electrode. The absorbed CO poisoned the electrode surface and altered the electrode reactions.[36,37] The absorption of CO was confirmed in a control experiment in which cyclic voltammograms were recorded with electrolyte solutions (0.1 M $NaClO_4$, 1 M $HClO_4$) purged with CO, in the absence of an analyte, showing sharp adsorption oxidation waves at potentials greater than 700mV. Similar effects have been observed for the oxidation of (benzylideneacetone)dicarbonyl(phosphine)iron(0) in DMF.[38] To circumvent this problem, the Pt electrode was replaced with a glassy carbon electrode. The cyclic voltammograms of **2** in 0.1 M $NaClO_4/D_2O$ obtained with the GC electrode are shown in Figure 4. The shift of the peak potential $E_p$ with increasing scan speeds indicates that the oxidation is electrochemically irreversible.[39,40] The oxidation is also chemically irreversible with no observable reduction wave even at 1000 mV/s. This chemically irreversible behavior was also observed in cyclic voltammetry of **1** in coordinating solvents[20] and in the presence of nucleophiles.[6] Rapid substitution of [$\mathbf{1}^+$] occurred faster than the timescale of the CV experiment, and thereby depleted the analyte solution of [$\mathbf{1}^+$] prior to the reverse reductive scan. The peak potential of the oxidation

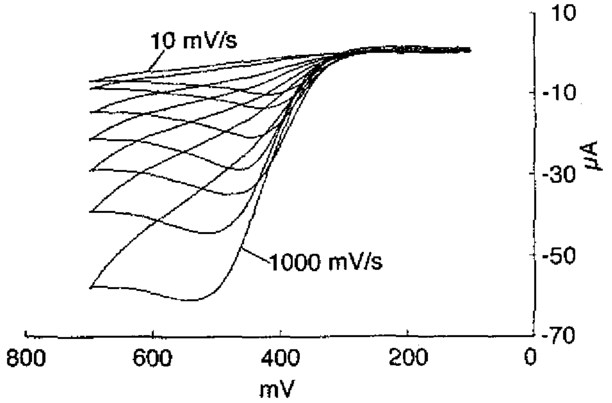


Figure 4. Cyclic voltammograms at different scan speeds. Experimental conditions: 0.4 mM **2** in 0.1 M $NaClO_4/H_2O$, glassy carbon working electrode, Ag/AgCl (3 M NaCl) reference electrode. Background voltammograms of the blank electrolyte solution are substracted. Scan speeds are 10, 20, 50, 100, 200, 400, and 1000 mV/s, respectively.

wave at 100 mV/s is $E_p = 466$ mV (vs. Ag/AgCl), which is comparable to the potentials reported for **1** (Table 4).

Table 4. Electrochemical Data for $(CO)_3Fe(PR_3)_2{}^{0/+}$-Couples:
(a) $PR_3 = PPh_3$, (b) $PR_3$ = TPPTS

| $PR_3$ | solvent | reference electrode (RE) | electrolyte | potential of RE vs. NHE (V)[39] | $E_{1/2}$ (V) | ref |
|---|---|---|---|---|---|---|
| (a) | $CH_2Cl_2$ | calomel/1M LiCl | 0.05M TEAP | 0.2801 | 0.33 [a] | 17 |
| (a) | $CH_2Cl_2$ | Ag/AgCl, sat'd LiCl | 0.1 M TBAP | 0.197 | 0.46 | 20 |
| (a) | $CH_2Cl_2$ | Ag/0.1 M $AgNO_3$ | 0.1 M TBAP | | 0.056 [b] | 6 |
| (a) | acetone | Ag/AgCl | 0.1 M TEAP | 0.197 | 0.54 [c] | 18 |
| (b) | $H_2O$ | Ag/AgCl (3 M NaCl) | 0.1 M $NaClO_4$ | 0.197 | 0.466 [d] | |

[a]*100 mV/s;* [b]*20 °C, 200mV/s;* [c]*20 °C, 500 mV/s;* [d]*100mV/s; only* $(E_p)_{ox}$*, no reduction* wave observed.

## Spectroelectrochemistry of 2

A 6.2 mM solution of **2** in 0.1 M $NaClO_4$ was oxidized on a gold mesh electrode inside the IR spectrometer and the reaction progress was monitored. At potentials greater than 850 mV (vs. Pt pseudo-reference) **2** was oxidized, resulting in a decrease of the bands for the starting material (Figure 5). As evident from the IR spectrum, no intermediate species were observed with this spectroelectrochemistry setup. The lifetime of the inferred oxidation product $\mathbf{2}^+$ is too short, and $\mathbf{2}^+$ will therefore be present in only smallest concentrations close to the gold mesh electrode surface. The use of an optically transparent thin layer electrode (OTTLE)[41] inside the IR cell would be a better choice for the detection of the radical intermediate, because with this method the reactive intermediate is generated across the entire IR window instead of just in localized areas

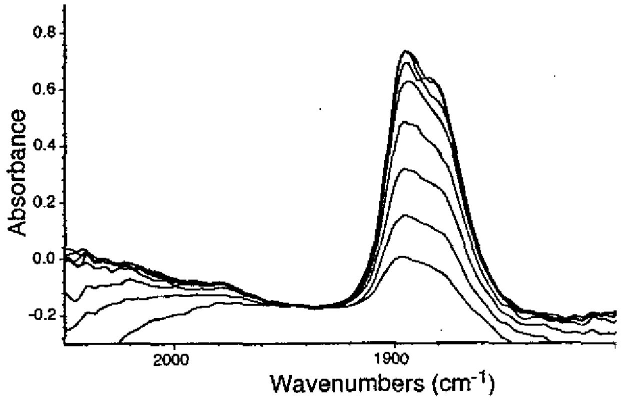


Figure 5. Spectroelectrochemical oxidation of **2** (6.2 mM, 0.1 M $NaClO_4/D_2O$) on a gold mesh working electrode. Oxidation monitored at 0.85 V vs. Pt pseudo reference electrode.

close to the gold grid. The spectroelectrochemistry experiment did, however, confirm that **2** can be oxidized electrochemically to lose its CO ligands, as it has been shown for the chemical oxidation (see above).

## Conclusions

The water-soluble iron complex $(CO)_3Fe(TPPTS)_2$ (**2**) was synthesized in good yields and was easily separated from the monosubstituted side product. X-ray crystallography confirmed the structure of **2**, which is closely related to its analog $(CO)_3Fe(PPh_3)_2$ (**1**). Chemical and electrochemical oxidation of **2** in water resulted in a 2-electron oxidation of the metal center to Fe(II), presumably by a disproportionation pathway, with concomitant loss of phosphine and carbonyl ligands. The electrochemical oxidation was both electrochemically and chemically irreversible, with an oxidative peak potential of $E_p = 466$ mV (vs. Ag/AgCl). These results for **2** in water parallel the behavior of **1** and **1**$^+$ in organic solvents. This confirms our earlier results which showed that the chemistry of organometallic radicals in water is equivalent to the chemistry of analogous radicals in organic solvents.

## Experimental Section

All manipulations were carried out in a nitrogen atmosphere, using vacuum line and dry box techniques. $D_2O$ (99.9%) was purchased from Cambridge Isotopes Labs and purged with $N_2$ for at least 30 min prior to use. $Fe(CO)_5$ was purchased from Strem Chemicals and used as received. TPPTS was a generous gift from I. Horváth. Solution IR spectra were recorded on a Nicolet Magna 550 FT-IR spectrometer, in a 0.1 mm pathlength $CaF_2$ cell. $^1H$ (299.95 MHz) and $^{31}P\{^1H\}$ (121.42 MHz, external 85% $H_3PO_4$) NMR spectra were recorded using a Varian Inova 300 spectrometer. Elemental analyses were carried out by Robertson Microlit Laboratories, Inc., Madison, NJ.

### Synthesis of $Fe(CO)_3(TPPTS)_2$

The preparation of **1** followed the method of Brunet et al. for the $PPh_3$ analog.[33] To a stirred solution of 116.2 mg NaOH (2.01 mmol) in 32 mL MeOH, 60 µL $Fe(CO)_5$ (89 mg, 0.46 mmol) was added via syringe. After 1 h, the color of the reaction mixture had changed from yellow to orange and an IR spectrum confirmed that $[HFe(CO)_4]^-$ had been formed. The solvent was reduced in vacuo to ~1 mL and 10 mL $H_2O$ was added. To this solution, 502 mg of TPPTS (0.88 mmol) was added and the mixture was refluxed for 17 h. The resulting solution was yellow-brown. Upon addition of 50 mL EtOH, a white precipitate formed which was filtered off, leaving behind a brown solution. The white precipitate was dissolved in 1 mL $H_2O$ and filtered. Removal of the $H_2O$ and recrystallization from $H_2O$/EtOH gave yellow plates, 370 mg (55%), suitable for x-ray analysis. IR ($D_2O$): 1896(s) 1883(sh) $cm^{-1}$; $^{31}P\{^1H\}$ NMR ($D_2O$): $\delta$ 84.2 ppm. The IR spectrum did not show any evidence for the presence of the monosubstituted complex $(CO)_4Fe(TPPTS)$. Anal. Calcd for $C_{39}H_{24}FeNa_6O_{21}P_2S_6$ C, 36.69; H, 1.89; Fe, 4.37; Na, 10.80; P, 4.85; Found: (crystalline material as used for x-ray analysis) C, 33.73; H, 3.07; Fe, 3.67; Na, 9.15; P 4.05. The elemental analysis confirms the 1:6:2 Fe:Na:P ratio. The disubstituted complex **2** was not obtained analytically pure, but it contained disordered solvent ($H_2O$ and EtOH). It can be formulated as **2** • 1 EtOH • 6 $H_2O$ (Calc. for $C_{41}H_{42}FeNa_6O_{28}P_2S_6$: C, 34.42; H, 2.96; Fe 3.90; Na, 9.64; P, 4.33). Herrmann et al. formulate the complex as the hexahydrate, **2** • 6 $H_2O$, and report: IR(KBr) 1885 $cm^{-1}$, $^{31}P$ NMR ($D_2O$) $\delta$ 74.76 ppm.[42]

The remaining brown solution is evaporated to dryness. The resulting residue is identified by IR as $(CO)_4Fe(TPPTS)$ (**2**): IR($D_2O$) $\nu(cm^{-1})$ 2056(m), 1984(w), 1948(s). Reported:[16] IR(KBr) $\nu(cm^{-1})$ 2050(s), 1977(s), 1944(vs).

### X ray Structure of 2

A yellow block of **2** of the dimensions 0.14 × 0.17 × 0.21 mm was mounted on a fiber. The orientation parameters and cell dimensions were obtained from the setting angles of an Enraf-Nonius CAD-4 diffractometer for 25 centered reflections in the range $9.6° \leq \theta \leq 10.8°$. Table 3 contains a summary of crystal data and the final residuals. A more extensive table including particulars of data collection and structure refinement is in the supplementary material. The crystal diffracted very weakly although with acceptably narrow peaks. The systematic absences together with the centric distribution of intensities indicated the space group P4/mnc. Absorption corrections based on azimuthal scans('$\psi$-scans') were not deemed necessary. A *SIR92 E*-map[43] showed all the non-hydrogen atoms of the half-complex constituting the asymmetric unit, with the Fe atom and CO ligands on a crystallographic mirror-plane. Because of the paucity of observed reflections [$I \geq 0.5\sigma(I)$] a full anisotropic refinement on $|F|$ could not be carried out. The Fe, S, P and Na atoms and the sulfonate O atoms were allowed anisotropic thermal parameters. Attempts to refine on $|F|^2$ using all data led to large residuals (R, wR ca. 0.30) and many non-positive-definite $U_{ij}$ values for carbon atoms. Aromatic hydrogen atoms were included at positions recalculated after each cycle of refinement [B(H) = $1.2B_{eq}$(C); d(C-H) = 0.95 Å]. The final difference synthesis showed a number of peaks up to 1.7 e Å$^3$, likely due to disordered Na and water O atoms on fractionally-occupied sites. The *teXsan* program suite,[44] incorporating complex atomic scattering factors, was used in all calculations.

### Oxidation of **2** with Ce(IV)

A solution of 26.2 mg (18 μmol) **2** in 1.5 mL $D_2O$ was prepared and an initial IR spectrum was recorded. Upon addition of 10.1 mg (19 μmol) $(NH_4)_2Ce(NO_3)_6$ the IR spectrum showed the decrease of the CO bands for **2** by approximately 50 %. Addition of another equivalent of Ce(IV) led to complete disappearance of the CO bands for **2**.

The $^{31}P\{^{1}H\}$ NMR after complete oxidation of **2** confirmed the presence of free TPPTS as the only phosphorous compound in the reaction mixture.

## Oxidation of **2** with $Ag(NO_3)$

A solution of 12.5 mg (8.6 μmol) **2** in 1 mL $D_2O$ was prepared and an initial IR spectrum was recorded. Subsequently, 1.5 mg (8.8 μmol) $AgNO_3$ was added and another IR spectrum was recorded, showing the formation of a new complex **3** (1990 (m), 1927 (s), 1903(s) $cm^{-1}$) with complete disappearance of the CO bands for **2**. After 1 h, a gray precipitate had separated from the solution. The IR spectrum then showed the disappearance of the intermediate **3**, while approximately 50% of the initial complex had reformed. Similarly, oxidation of **2** by $AgNO_3$ was followed by $^{31}P\{^{1}H\}$ NMR. After addition of $AgNO_3$ the resonance for **2** (84.2 ppm) disappeared completely and a resonance at 73.1 ppm was observed which was assigned to **3**. After 1 h, the resonance for **3** had vanished while the resonance for **2** had grown back in, initially being very broad.

## Electrochemical Studies

Aqueous electrolyte solutions were prepared with $H_2O$ purified to a resistivity of >17 mΩ with a Barnstead E-Pure water purification system. Cyclic voltammetry was carried out using a BAS-100B electrochemical workstation and a three electrode setup with a glassy carbon disk (d = 3 mm, BAS MF2012) or a Pt disk (d = 1.6 mm, BAS MF2013) working electrode, a Pt wire auxiliary electrode and a Ag/AgCl (3 M NaCl in

$H_2O$) reference electrode. In a typical CV experiment, 30-35 mg (21-24 μmol) of **2** was dissolved in 10 mL 0.1 M $NaClO_4$ stock solution. The yellow solution was added to an electrochemical cell and purged with argon for at least 15 min. Cyclic voltammograms were recorded at various scan speeds at 23 °C. It was necessary to clean the electrodes after every oxidation/reduction cycle, because a yellowish precipitate had settled on the electrode surface.

### Spectroelectrochemistry

For the spectroelectrochemistry experiments, an IR-electrochemistry cell was built similar to the cell described by Saravanamuthu et al.[45] A gold mesh working electrode was placed between two $CaF_2$ windows with two holes each through which the leads to the working electrode and two Pt wires for use as pseudo-reference and auxiliary electrode were inserted. The two $CaF_2$ windows were held apart by a 1 mm PTFE spacer. A solution of 9.1 mg **2** (6.2 μmol) in 1 mL $NaClO_4/D_2O$ was placed on the bottom window of the IR cell. Subsequently, the second $CaF_2$ window was placed on top of the electrode/sample solution assembly and the complete cell setup was placed in the IR spectrometer. This process of charging the cell with the analyte solution was necessary in order to fill the entire sample compartment, including the space within the gold mesh. Electrochemical oxidation was carried out using a BAS CV-27 Cyclic Voltammograph, operated in amperometry mode at a fixed potential. No current was observed at potentials <0.2 V. Complex **2** was readily oxidized at potentials greater than 0.85 V

(I > 200 μA). IR spectra were recorded throughout the oxidation process. As the oxidation progressed, gas bubbles evolved inside the cell.

## Bridge

The electrochemical studies discussed in Chapter VI provided valuable information about the oxidation chemistry of the water-soluble iron-carbonyl complex. Quantitative information with regard to the substitution rates in the iron complex in water, however, could not be obtained.

In the next chapter, the chemistry of a second water-soluble organometallic radical, $(CpCH_2CH_2NMe_3NO_3]Mo(CO)_3$, is described. The results of experiments designed to distinguish between an associatively and a dissociatively activated substitution mechanism are discussed.

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# CHAPTER VII

# STUDIES TOWARD THE SUBSTITUTION MECHANISM OF THE 17-ELECTRON ORGANOMETALLIC RADICAL $[(CpCH_2CH_2NMe_3)Mo(CO)_3]^+$ IN AQUEOUS SOLUTION

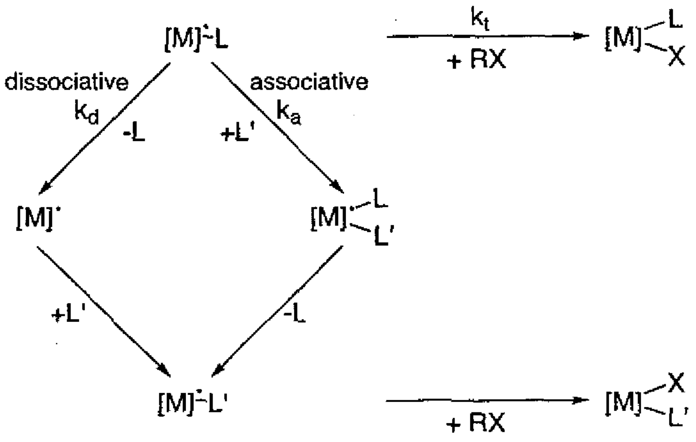
## Introduction

Organometallic radical complexes with an odd number of electrons, in particular 17- and 19-electron complexes, have been shown to be important intermediates in a number of transition metal promoted reactions.[1-4] This is largely due to their enhanced reactivity in fundamental organometallic reactions compared to their 18-electron counterparts. Substitution, insertion and electron-transfer reactions show rate increases of several orders of magnitude. The substitution of a CO ligand in the 17-electron complex $V(CO)_6$, for example, occurs at a rate which is $10^{10}$ faster than the rate of substitution in the 18-electron complex $Cr(CO)_6$.[5] Similarly, the substitution of a CO ligand in $[Fe(CO)_3(PPh_3)_2]^+$ proceeds more than $10^9$ times faster than in the parent 18-electron complex $Fe(CO)_3(PPh_3)_2$.[6]

Mechanistic studies have shown that most substitution reactions of 17-electron complexes are associatively activated.[2,7] One exception is the substitution of $V(\eta^5\text{–}C_5H_7)_2(CO)$ and similar vanadium pentadienyl complexes.[8] In those cases, the dissociative pathway competes successfully with the associative substitution, which is almost completely suppressed for electronic and steric reasons.

Among the most elegant studies showing the associative activation of substitution are the competition experiments by Fox, Malito and Poë ($Re(CO)_5$),[9] Herrinton and Brown ($Mn(CO)_5$),[10] and Turaki and Huggins ($CpW(CO)_3$).[11] Common to all three investigations was that the organometallic radical, once it had been generated, was allowed to undergo substitution as one reaction pathway. In competition with the substitution, the radical was also able to react with a halogen source in an atom abstraction reaction by virtue of its radical character (Scheme 1). Following ligand replacement, the resulting substituted species was trapped by halogen abstraction. Comparison of the ratios of the trapped products at varying concentrations of [L] identified the substitution reactions as associative processes. A more detailed explanation of the competition experiment is given later.

In addition to substitution, organometallic radicals can also undergo associatively activated electron transfer in the presence of a nucleophilic ligand. This reaction has



Scheme 1. General description of the competition experiment.

been shown to proceed through a 19-electron intermediate, which in turn has a sufficiently low reduction potential to reduce a variety of substrates S (eq 1).[3]

$$\underset{\substack{\text{17-electron}\\\text{complex}}}{L_nM^{\cdot}} \xrightarrow{L'} \underset{\substack{\text{19-electron}\\\text{complex}}}{L_nM^{\cdot}L'} \xrightarrow{S} \underset{\substack{\text{18-electron}\\\text{complex}}}{L_nML'} + \underset{\substack{\text{reduced}\\\text{substrate}}}{S^{\cdot-}} \qquad (1)$$

Significant work has been carried out in this laboratory on the photochemical disproportionation of metal-metal bonded dimers as a result of formation of 19-electron organometallic radical intermediates.[12-14] The disproportionation of metal-bonded dimers is exemplified by the photolysis of $Cp_2Mo_2(CO)_6$ in the presence of nucleophiles (Scheme 2). The reaction occurs by a chain mechanism. Homolysis of the metal-metal bond generates the organometallic radicals. The 17-electron radical $CpMo(CO)_3$ adds a ligand to form the 19-electron complex $CpMo(CO)_3L$ (2.2). This 19-electron radical in turn transfers an electron to an intact $Cp_2Mo_2(CO)_6$ dimer (2.3), which subsequently disproportionates to give $[CpMo(CO)_3]^-$ and another $CpMo(CO)_3$ radical in the chain propagation step (2.4).[15] In the case of small phosphines, i.e. phosphines with a small cone angle, the disubstituted cations are formed (2.8) instead of the monocations (2.3). Two pathways are possible for the formation of the disubstituted complex, one of which involves the substitution of the 18-electron substituted cation (2.5). Alternatively, substitution may occur on the intermediate 17-electron radical $CpMo(CO)_3$ to give the substituted radical $CpMo(CO)_2L$ occurs prior to formation of the 19-eletron adduct (2.6-2.7), whose fate is the electron-transfer process (2.8).

The chemistry outlined above was carried out exclusively in organic solvents, in agreement with the common notion that even traces of moisture may be detrimental to

$$Cp_2Mo_2(CO)_6 \xrightarrow{h\nu} 2\ CpMo(CO)_3 \qquad (2.1)$$

$$\underset{17\ e^-}{CpMo(CO)_3} + L \rightarrow \underset{19\ e^-}{CpMo(CO)_3L} \qquad (2.2)$$

$$CpMo(CO)_3L + Cp_2Mo_2(CO)_6 \rightarrow [CpMo(CO)_3L]^+ + [Cp_2Mo_2(CO)_6]^- \qquad (2.3)$$

$$[Cp_2Mo_2(CO)_6]^- \rightarrow [CpMo(CO)_3]^- + \underset{17\ e^-}{CpMo(CO)_3} \qquad (2.4)$$

$$\underline{Net}: Cp_2Mo_2(CO)_6 \xrightarrow{h\nu} [CpMo(CO)_3]^- + [CpMo(CO)_3L]$$

with L=small phosphine:

$$[CpMo(CO)_3L]^+ + L \rightarrow [CpMo(CO)_2L_2]^+ + CO \qquad (2.5)$$

or

$$CpMo(CO)_3 + L \rightarrow CpMo(CO)_2L + CO \qquad (2.6)$$

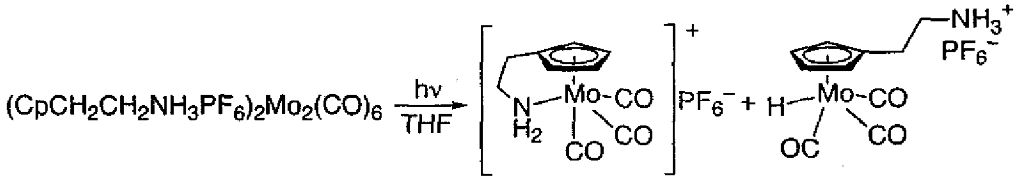
$$CpMo(CO)_2L + L \rightarrow CpMo(CO)_3L_2 \qquad (2.7)$$

$$CpMo(CO)_3L_2 + Cp_2Mo_2(CO)_6 \rightarrow [CpMo(CO)_2L_2]^+ + [Cp_2Mo_2(CO)_6]^- \qquad (2.8)$$

Scheme 2. Mechanism of the photochemical disproportionation of $Cp_2Mo_2(CO)_6$.

organometallic compounds. In recent years, however, *water* has received a lot of attention as a solvent in organometallic chemistry, finding application both in the research laboratory and in industry.[16] In this context, water-soluble precursors to organometallic radicals have been developed and their corresponding radicals' aqueous chemistry has been studied.[14] In one case, water-solubility was achieved by funtionalizing the Cp ligand of a tungsten carbonyl dimer with a carboxylic acid group to give the complex $(CpCOOH)_2W_2(CO)_6$.[17] At pH < 10, the solubility of this dimer is greater than 3 mM in $H_2O$. Its photochemistry qualitatively corresponds to that of its organic solvent soluble analog.[18] For example, photolytic cleavage of the W-W bond generated water soluble radicals, which disproportionated in the presence of the coordinating solvent water or other coordinating ligands. Suitable water-soluble substrates like methyl viologen and cytochrome $c^{III}$ were reduced by the 19-electron intermediate (eq 1). In addition, the photochemically generated radicals underwent atom abstraction reactions with water-soluble halogen sources such as trihaloacetates and trihaloalcohols to give $(CpCOO^-)W(CO)_3X$ (X = Cl,[17] Br,[7] I[7]) at high pH. The latter reaction has been studied quantitatively using laser flash photolysis by Zhu and Espenson.[7]

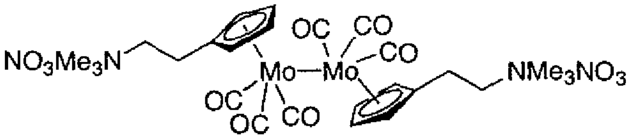
In a second case, a molybdenum carbonyl dimer was functionalized by using the aminoethylcyclopentadienyl ligand[19] to achieve solubility in water.[20] The complex $(CpCH_2CH_2NH_3^+)_2Mo_2(CO)_6$, which was only soluble up to 2.8 mM in water at pH 7, reacted identical to its organic soluble analog (see above, Scheme 2). Photolysis resulted in disproportionation, atom abstraction occurred in the presence of a halide source, and electron transfer was observed in the presence of a suitable substrate. In addition, intramolecular attack of the deprotonated aminoethyl tentacle ligand led to a tethered complex as shown in eq 2.[21]



(2)

In this study, the chemistry of a water-soluble organometallic radical was investigated with the goal to obtain a quantitative understanding of the reactivity of organometallic radicals in water. In analogy to the competition experiments described above (Scheme 1), the reaction of the water soluble organometallic radical with both a nucleophilic ligand and a halogen source was carried out in order to gain information about the associative or dissociative character of the substitution mechanism.

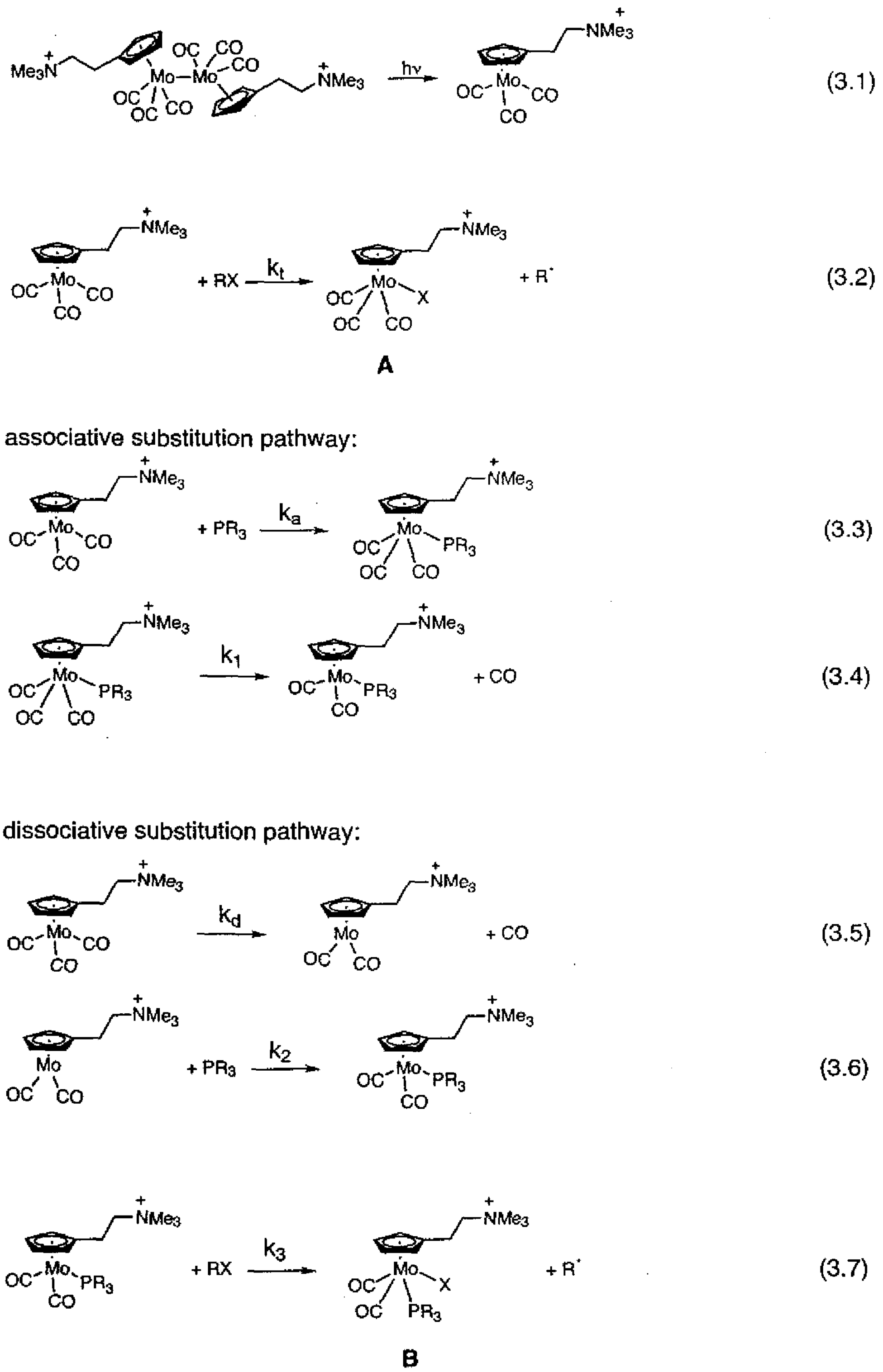
Rather than using one of the two water-soluble metal carbonyl dimers mentioned above, the trimethylammoniumethyl substituted molybdenum dimer **1** was prepared and studied.



**1**

This dimer was soluble over the entire pH range because its ionic character does not depend on the protonation state of its pendant ligand. It is also not prone to intramolecular attack from the amino ligand as is $(CpCH_2CH_2NH_2)_2Mo_2(CO)_6$. In addition, dimer **1** was highly soluble (> 15mM, nitrate counterion) in water.

The proposed competition experiment employing radicals generated photochemically from **1** is outlined in Scheme 3. The products of the reaction were expected to be the non-substituted halide complex **A** (3.2), and the halide complex trapped subsequent to substitution, **B** (3.7). The ratio of these products can be expressed in terms



Scheme 3. Detailed description of the proposed competition experiment employing **1**.

of the concentrations of nucleophilic ligand [L] and halide source [RX] (4.8), as derived from kinetic analysis of the reaction scheme (Scheme 4).

In the limiting case of a purely associative mechanism, eq 4.8 simplifies to a linear equation with the slope $k_a/(k_t[RX])$ and a zero intercept, while for the dissociative substitution a linear equation with the slope zero and the intercept $k_d/(k_t[RX])$ is obtained. A plot of the product ratio [Cp"Mo$(CO)_2$LX]/[Cp"Mo$(CO)_3$X] vs. [L] therefore enables one to easily distinguish between an associative and a dissociative substitution mechanism.

In the following section, the results of photochemical studies pertaining to the competition experiment are described. This is followed by a discussion of the results and an analysis of the encountered problems. In addition, general remarks about the photochemical generation of the water-soluble organometallic radicals from the Mo-Mo dimer **1** and their use in the proposed competition experiment are made.

## Results

### Synthesis and Water-Solubility of $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ (1)

The $[(CpCH_2CH_2NMe_2)_2Mo_2(CO)_6]$ (**2**) complex was synthesized as described previously by Kaul et al.,[22] with the slight modification that $K_2CO_3$ was used as a base to deprotonate the ammonium nitrate complex (Scheme 5). Initial attempts to introduce the third methyl group using $Me_3OBF_4$ in order to avoid possible radical side reactions with methyl iodide were unsuccessful. Methylation of the free base complex with $CH_3I$ in

$$\frac{d[\mathrm{Cp''Mo(CO)_3X}]}{dt} = k_t[\mathrm{Cp''Mo(CO)_3}][\mathrm{RX}] \qquad (4.1)$$

$$\frac{d[\mathrm{Cp''Mo(CO)_2L}]}{dt} = k_3[\mathrm{Cp''Mo(CO)_2L}][\mathrm{RX}] \qquad (4.2)$$

*steady state approximation:*

$$0 = \frac{d[\mathrm{Cp''Mo(CO)_2}]}{dt} = k_d[\mathrm{Cp''Mo(CO)_3}] - k_2[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]$$

$$\Leftrightarrow [\mathrm{Cp''Mo(CO)_3}] = \frac{k_2}{k_d}[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}] \qquad (4.3)$$

$$0 = \frac{d[\mathrm{Cp''Mo(CO)_3L}]}{dt} = k_a[Cp''Mo(CO)_3][L] - k_1[Cp''Mo(CO)_3L]$$

$$\Leftrightarrow k_1[\mathrm{Cp''Mo(CO)_3L}] = k_a[\mathrm{Cp''Mo(CO)_3}][\mathrm{L}]$$

with (4.3): $\Leftrightarrow k_1[\mathrm{Cp''Mo(CO)_3L}] = \frac{k_a k_2}{k_d}[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]^2$ (4.4)

$$0 = \frac{d[\mathrm{Cp''Mo(CO)_2L}]}{dt} = k_1[\mathrm{Cp''Mo(CO)_3L}] + k_2[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}] - \mathrm{k}_3[\mathrm{Cp''Mo(CO)_2L}][\mathrm{RX}]$$

$$\Leftrightarrow \mathrm{k}_3[\mathrm{Cp''Mo(CO)_2L}][\mathrm{RX}] = k_1[\mathrm{Cp''Mo(CO)_3L}] + k_2[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]$$

with (4.4): $\Leftrightarrow \mathrm{k}_3[\mathrm{Cp''Mo(CO)_2L}][\mathrm{RX}] = \frac{k_a k_2}{k_d}[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]^2 + k_2[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]$ (4.5)

*integrated rate laws,* with $[\mathrm{Cp''Mo(CO)_2}]$, [L] and [RX] constant:

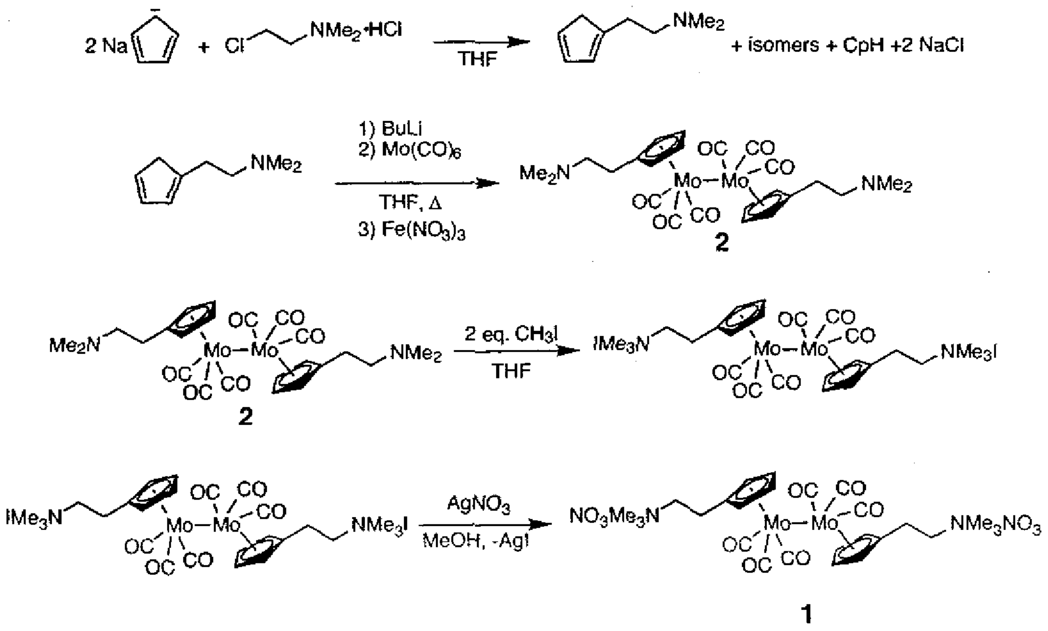
(4.3) in (4.1): $[\mathrm{Cp''Mo(CO)_3X}] = k_t[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}][\mathrm{RX}]\mathrm{t}$ (4.6)

(4.5) in (4.2): $[\mathrm{Cp''Mo(CO)_2LX}] = (\frac{k_a k_2}{k_d}[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}]^2 + k_2[\mathrm{Cp''Mo(CO)_2}][\mathrm{L}])\mathrm{t}$ (4.7)

with (4.7) and (4.6): $$\frac{[\mathrm{Cp''Mo(CO)_2LX}]}{[\mathrm{Cp''Mo(CO)_3X}]} = \frac{k_a[\mathrm{L}] + k_d}{k_t[\mathrm{RX}]} \qquad (4.8)$$

($\mathrm{Cp''} = (\mathrm{CpCH_2CH_2NMe_3}^+)$, L = phosphine)

Scheme 4. Derivation of the expression for the product ratio in the proposed competition experiment.



Scheme 5. Synthesis of $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ (**1**).

THF under rigorous exclusion of light, however, gave the dicationic complex $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6]I_2$, which was hardly soluble in water. The complex was rendered water-soluble by exchanging the counter ion with $AgNO_3$ in MeOH to give $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ (**1**). Its solubility was greater than 15 mM in $H_2O$ at 23 °C. The electronic spectrum of a solution of **1** (0.54 mM) in $H_2O$ showed $\lambda_{max}$ = 503 nm ($\varepsilon$ = 1590 $M^{-1}$ $cm^{-1}$), which was assigned to a $d\pi \rightarrow \sigma^*$ transition, based on comparison with similar cyclopentadienyl molybdenum tricarbonyl dimers.[20] The IR spectrum in $D_2O$[23] shows the typical bands for these dimers at 2011(w), 1957(s) and 1913(s) $cm^{-1}$ (Table 1).

Table 1. Selected Infrared Data

| complex | ν(CO), $cm^{-1}$ | ref. |
|---|---|---|
| $(CpMe)_2Mo_2(CO)_6$ [a] | 2012 (m), 1956 (s), 1912 (s) | 13 |
| $(CpCH_2CH_2NH_3NO_3)_2Mo_2(CO)_6$ [b] | 2009 (m), 1958 (s), 1908 (s) | 19 |
| $(CpCH_2CH_2NMe_3NO_3)_2Mo_2(CO)_6$ [c] | 2011 (m), 1957 (s), 1913 (s) | this work |
| $[CpMo(CO)_3(H_2O)]BF_4$ [d] | 2067, 1998, 1973 | 24 |
| $[(CpCH_2CH_2NH_3)Mo(CO)_3(H_2O)]^{2+}$ [b] | 2062 (s), 1996 (m), 1967 (s) | 19 |
| $[(CpCH_2CH_2NMe_3)Mo(CO)_3(D_2O)]^{2+}$ [c] | 2067 (s), 1979 (s) | this work |
| $Na[CpMo(CO)_3]$ [e] | 1899, 1796, 1743 | 28 |
| $[(CpCH_2CH_2NH_3)Mo(CO)_3]$ [b] | 1905 (s), 1783 (s), 1729(s) | 19 |
| $[(CpCH_2CH_2NMe_3)Mo(CO)_3]$ [c] | 1905 (s), 1772 (s, br) | this work |
| $CpMo(CO)_3Br$ [f] | 2050, 1980 | 25 |
| $[(CpCH_2CH_2NMe_3)Mo(CO)_3Br]^{+}$ [c] | 2056 (s), 1975 (s) | this work |
| $CpMo(CO)_3Et$ [g] | 2015, 1953 | 26 |
| $CpMo(CO)_3(CH_2CH_2CH_2Br)$ [f] | 2026 (s), 1945 (vs) | 27 |
| $[(CpCH_2CH_2NMe_3)Mo(CO)_3(CH_2CH_2OH)]^{+}$ [c] | 2023 | this work |
| $CpMo(CO)_3H$ [f] | 2025, 1945 | 26 |
| $[(CpCH_2CH_2NH_3)Mo(CO)_3H]^{+}$ [h] | 2024, 1943, 1929 | 19 |
| $[CpMo(CO)_2(PEt_3)_2]BF_4$ [i] | 1963 (s), 1884 (vs) | 30 |
| $[(CpCH_2CH_2NH_3)Mo(CO)_3PTA_2]^{+}$ [b] | 1957 (s), 1910 (s) | 19 |
| $[(CpCH_2CH_2NMe_3)Mo(CO)_2THBP_2]^{2+}$ [c] | 1962 (m), 1883 (s) | this work |
| $CpMo(CO)_2(PPh_3)Br$ [i] | 1980 (vs), 1890 (vs) | 33 |

[a] $CCl_4$; [b] $H_2O$ pH 7 buffer; [c] $D_2O$; [d] nujol; [e] THF; [f] cyclohexane; [g] pentane; [h] $H_2O$ pH 2 buffer; [i] $CH_2Cl_2$; PTA = phosphatriazaadamantane

## Photolysis of **1** in $D_2O$

A solution of **1** in $D_2O$ (12.5 mM) was irradiated ($\lambda > 524$ nm) and IR spectra were taken in intervals of 10 s (Figure 1). The bands for the dimer **1** (▲) decreased, while new bands at 2067, 1979, 1905 and 1772 cm$^{-1}$ grew in. By comparison to the photochemistry of $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ (Table 1), the new bands were assigned to $[(CpCH_2CH_2NMe_3)Mo^{II}(CO)_3(D_2O)]^{2+}$ (**4**; 2067, 1979 cm$^{-1}$; ■)[24] and $[(CpCH_2CH_2NMe_3)Mo^{0}(CO)_3]$ (**5**; 1905, 1772 cm$^{-1}$; ○). These are the products of disproportionation of **1**, resulting from homolysis of the Mo-Mo bond in the parent dimer complex (eq 3).

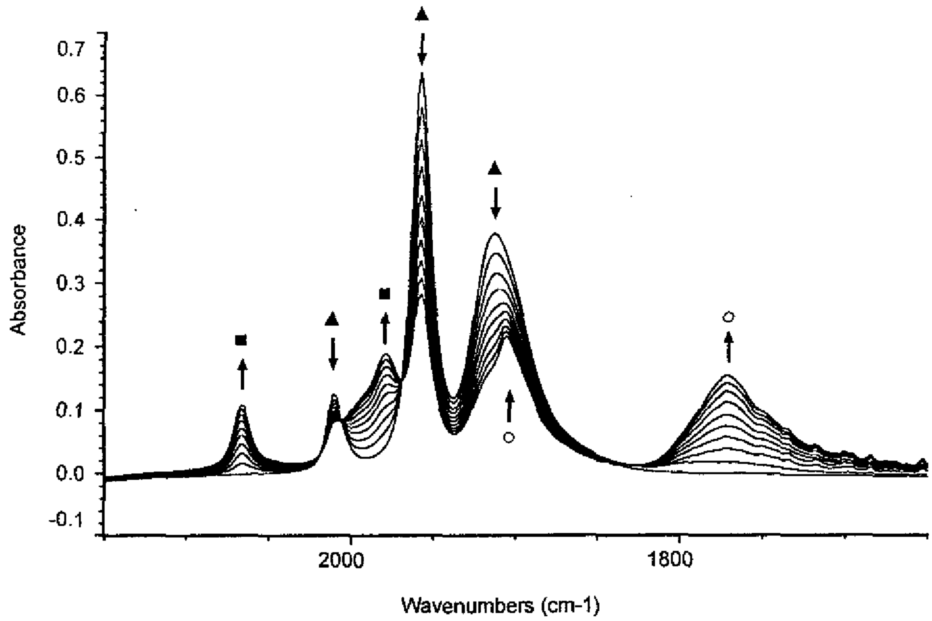
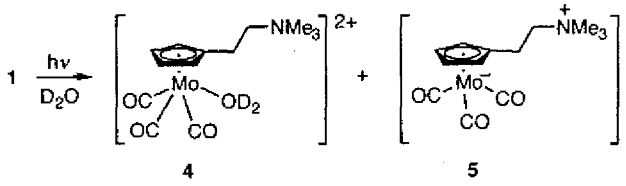


Figure 1. Photochemical disproportionation of **1** in $D_2O$.



(3)

Photolysis of **1** in the Presence of a Halide Source

To verify the intermediacy of metal radicals in solution, photolysis of **1** in $D_2O$ ($\lambda > 524$ nm) was carried out in the presence of $Br_3CCH_2OH$ (Figure 2). The haloalcohol was used as the halide source instead of the haloacetate $X_3CCOOH$ (X=Cl, Br),[17,20,7] because precipitation occurred upon addition of either $X_3CCOONa$ or $X_3COOH$ to an aqueous solution of **1**. The metal halide product resulting from the reaction of a radical intermediate (e. g. [(CpCH$_2$CH$_2$NMe$_3$)Mo$^I$(CO)$_3$]$^+$ ,**6**) with a halide atom source has been taken as evidence for the cleavage of the metal-metal bond and generation of an

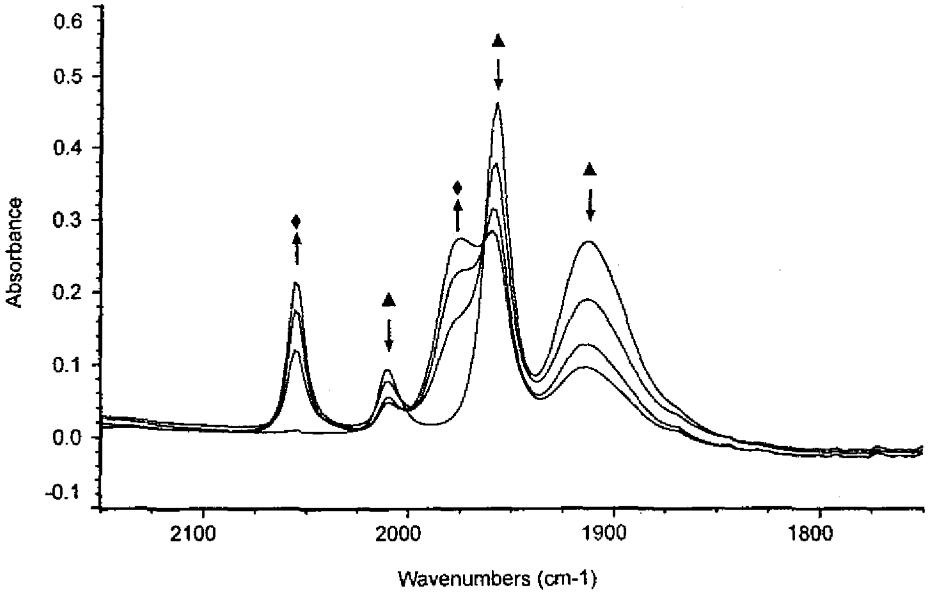


Figure 2. Photolysis of **1** in $D_2O$ in the presence of $Br_3CH_2OH$.

organometallic radical.[25] Indeed, photolysis of **1** (9.9 mM, $D_2O$) in the presence of $Br_3CH_2OH$ (82mM) resulted in exclusive formation of the halide trapped product $[(CpCH_2CH_2NMe_3)Mo^{II}(CO)_3Br]^+$ (**7**; 2056, 1975 cm$^{-1}$; ♦, Figure 2).[26] No product of disproportionation was observed. Similarly, $[(CpCH_2CH_2NMe_3)Mo^{II}(CO)_3Cl]^+$ was formed by photolysis of **1** in the presence of $Cl_3CCH_2OH$.

With the less efficient trapping reagent $BrCH_2CH_2OH$ (510 mM), disproportionation of **1** (12.5 mM) competed with halide formation. IR bands for the Mo$^{II}$ aquo adduct **4** (■) and the bromide **7** (♦) were observed (Figure 3), but hardly any Mo$^0$ complex **5** was detected. An additional IR band was observed (2023 cm$^{-1}$, ★), which can correspond to one of two molecules: a) the deuteride complex **8**[27,20] formed by 'Protonation' of the Mo$^0$ complex (**5**) or b) the alkyl complex **9**[28,27] obtained upon nucleophilic substitution[28,29] on the alcohol by complex **5** (Scheme 6).

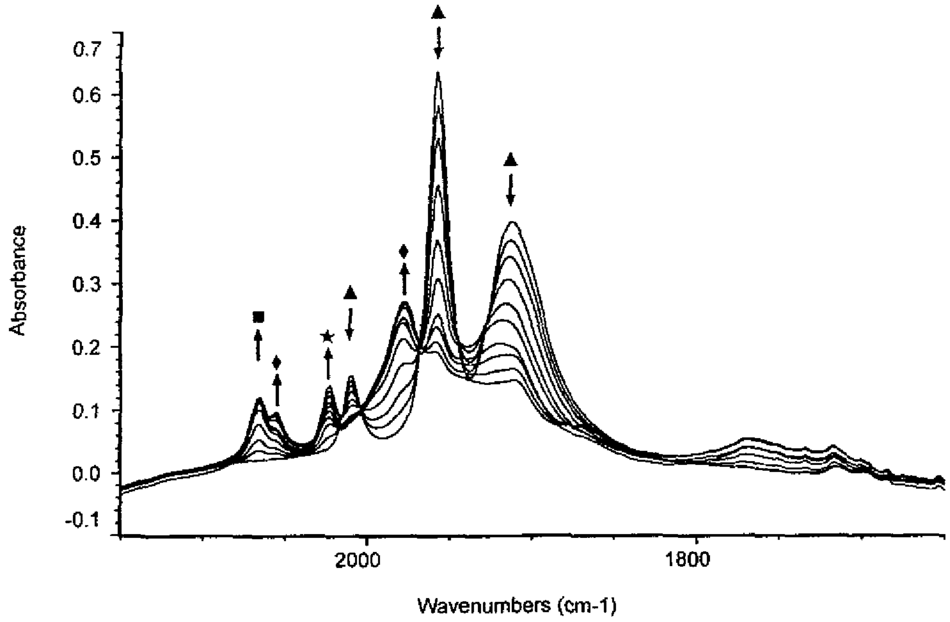
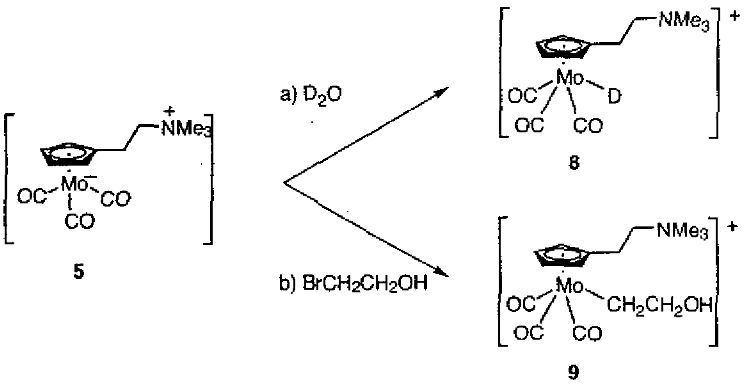


Figure 3. Photolysis of **1** in $D_2O$ in the presence of $BrCH_2CH_2OH$.



Scheme 6. Deuteration vs. nucleophilic substitution of **5**.

Previously reported hydride complexes show a diagnostic M-H stretch around 2023 $cm^{-1}$. In $D_2O$, however, the *deuteride* complex would be formed, whose M-D stretch should be shifted significantly to lower wavenumbers (~1435 $cm^{-1}$).[30] The additional band at 2023 $cm^{-1}$ (★), as shown in Figure 3, is therefore assigned to the alkyl complex **9**, in agreement with previously reported alkyl complexes of this type (Table 1). Monitoring the reaction mixture in the dark for 2h after photolysis showed that both the alkyl complex **9** as well as the aquo adduct **4** had disappeared to form exclusively bromide **7**.

## Disproportionation of **1** by Phosphines

The sulfonated water-soluble phosphine TPPTS (triphenylphosphinetrisulfonate, sodium salt) induced precipitation of the molybdenum dimer upon addition of TPPTS to an aqueous solution of **1**. The IR of the precipitate (KBr) showed that the Mo-Mo remained intact, i.e. no reaction involving the dimer had occurred. With TPPTS as the counterion, **1** is less soluble in water and therefore precipitates out.

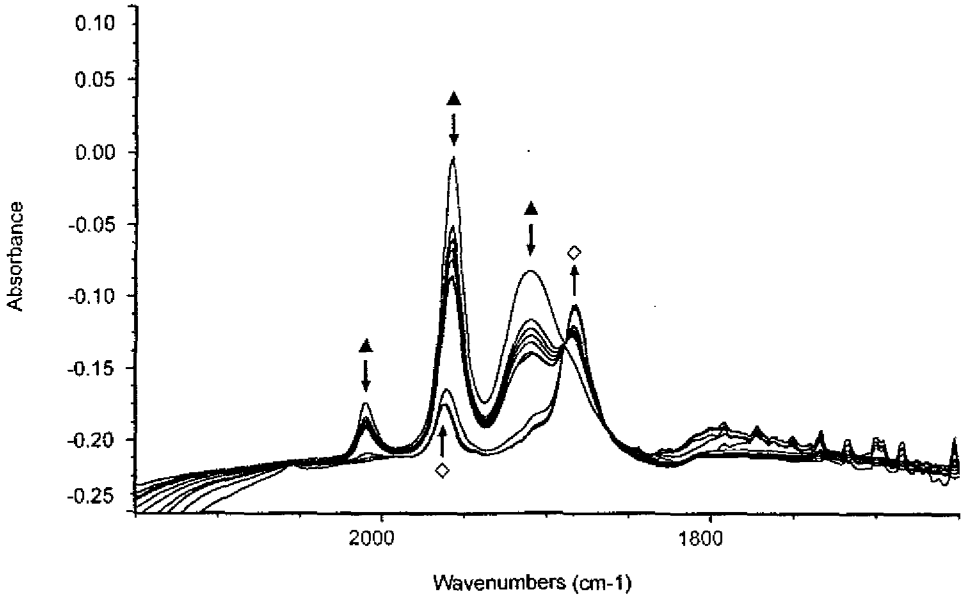


Figure 4. Photolysis of **1** in $D_2O$ in the presence of THBP.

With the water-soluble phosphine $P(CH_2CH_2CH_2CH_2OH)_3$ (THBP), however, **1** remained dissolved in $D_2O$. The molybdenum carbonyl dimer **1** was photolyzed ($\lambda > 524$ nm) in the presence of THBP. The IR spectrum of the reaction solution containing **1** (4.8 mM) and THBP (36 mM) showed the disappearance of **1** upon photolysis, with concurrent formation of the disubstituted complex $[(CpCH_2CH_2NMe_3)Mo^{II}(CO)_2(THBP)_2]^{2+}$ (**10**; 1962, 1883 $cm^{-1}$; ◇, Figure 4).[31] It is curious, however, that hardly any $Mo^0$ complex **5**, the second product of photochemical disproportionation of **1**, was detected.

## Studies Toward Competitive Photochemistry

After establishing the two fundamental reactions that are required for the proposed competition experiment (i.e. trapping of the photochemically generated $Mo^I$

radical **6** by bromide abstraction and its substitution chemistry in the presence of phosphines), photolysis experiments were carried out with **1** (14.1 mM, $D_2O$) in the presence of both $Br_3CCH_2OH$ and THBP. With a phosphine/halide ratio of 1.5:1 (110 mM:75 mM), only the halide trapped product, bromide complex **7**, was formed. Increasing this ratio to 2.1:1(152 mM:72 mM) resulted in exclusive formation of the phosphine substitution product **10**. This initially surprising result can be rationalized by considering the chemistry of THBP and tribromoethanol *with each other* in aqueous solution. Addition of 364 mmol tribromoethanol to 1 mL of a 0.42 mM solution of THBP in $D_2O$ efficiently converted all the phosphine to its corresponding oxide, as determined by the appearance of the oxide's $^{31}P$ NMR resonance at 60.3 ppm (THBP: $^{31}P$ NMR ($D_2O$): -32.1 ppm). The conversion of the phosphine to the phosphine oxide is thought to proceed through hydrolysis of a phosphonium salt intermediate, and hydrolysis of phosphonium salts derived from $\alpha$-polyhaloalkanes are known to give phosphine oxides.[32] Because of this reaction between phosphine and haloalcohol which occurs on the same or an even faster timescale than the competition experiment discussed above, this experiment could not be carried out under the desired conditions in aqueous solution.

## Discussion

### Comments on Aqueous Radical Chemistry

The experimental results presented in the previous section showed that the fundamental chemistry of the $(CpR)Mo(CO)_3$ radicals[33] is equivalent in aqueous and non-aqueous solvents, as it has been described before.[17,20,14] Radicals generated by photochemical homolysis from the water-soluble dimer $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$ (**1**) underwent atom abstraction reactions and disproportionation reactions analogous their non-water-soluble counterparts. As expected, no intramolecular chemistry with the trimethylammoniumethyl side chain was observed.

## Formation of Molybdenum Alkyl Complex in $D_2O$

As a new feature of aqueous $(CpR)Mo(CO)_3$ chemistry, this study provided evidence for the formation of molybdenum alkyl complex in $D_2O$. This type of reactivity was observed because bromine abstraction from bromoethanol by the initially formed radical $[(CpCH_2CH_2NMe_3)Mo^I(CO)_3]^+$ (**6**) occurred with a rate similar to that of disproportionation (which lead to the nucleophilic $[(CpCH_2CH_2NMe_3)Mo^0(CO)_3]$ (**5**)). Complex **5** then underwent facile nucleophilic substitution to give the alkyl complex **9**, as it has been observed previously for analogous $Mo^0$ complexes in organic solvents.[28,27] This reaction occurred despite the overall neutral charge of the zwitterionic complex **5**. Conversion of the alkyl complex to the bromide **7** may have occurred by nucleophilic displacement of the alkyl ligand by bromide ions.

## Comments on the Failure of the Proposed Competition Experiment

As it has been discussed above, the two reagents required for the competition experiment reacted with each other irreversibly and fast. The competition experiment could therefore not be carried out as proposed. Attempts to use pyridine instead of phosphine as the nucleophile and tribromoethanol as the halide source were unsuccessful as well with respect to trapping of any substituted radicals. Even in a 1:3 pyridine/$D_2O$ mixture with 74 mM bromoethanol, the irradiation of **1** gave exclusively the bromide **7** (note that the substitution by pyridines in this latter reaction would have produced the hydrophobic complexes $Mo(CO)_3(py)_3$ and $Mo(CO)_4(py)_2$, resulting from CpR loss subsequent to initial CO substitution[13]).

An additional intrinsic problem with the competition experiment should be noted. From all evidence presented so far on the aqueous chemistry of $CpRMo(CO)_3$ radicals, their chemistry can be considered identical in non-aqueous and aqueous solvents, in particular with respect to photochemical disproportionation of the parent dimer. The latter reaction with L = $PPh_3$ is thought to proceed through a 19-electron adduct, which transfers an electron to a parent dimer (see Scheme 2, 2.3). This, however, means that electron transfer occurs *prior* to dissociation of a CO ligand, and a substitution does not actually take place, but instead an 18-electron $Mo^{II}$ adduct is formed.

Disproportionation in the presence of a smaller alkyl phosphine, on the other hand, results in formation of the disubstituted $Mo^{II}$ complex (2.5-2.8). This process may proceed by rapid substitution of the $CpMo(CO)_3$ radical followed by adduct formation and electron-transfer to the parent dimer (2.6-2.8). The monosubstituted radical $CpMo(CO)_2L$ is formed as an intermediate and may be trapped as proposed. Alternatively, substitution by the second phosphine may occur from the monosubstituted 18-electron complex as a result of the electron-transfer reaction (2.5). In this case, a substituted 17-electron complex $CpMo(CO)_2L$ would never form and hence could not be trapped, which means that a competitive atom abstraction – ligand substitution experiment could not be carried out. It is questionable, however, whether ligand substitution can occur on the coordinatively saturated 18-electron cationic complex. It has been reported by several research groups that $[CpMo(CO)_3(PPh_3)]^+$ is inert toward substitution by a second $PPh_3$[34-36] if light is excluded,[37] yet note also that for this bulky ligand only the monosubstituted cation is formed in the photochemical disproportionation of the parent dimer (2.3). An example of a compound undergoing thermal disubstitution is the complex $CpMo(CO)_3Cl$, which is substituted by $PEt_3$ at room temperature in benzene to give the dicationic $[CpMo(CO)_2(PEt_3)_2]Cl$ only,[34] indicating that double substitution might occur with smaller and more basic phosphines.

The problem of electron-transfer reactions competing with substitution and trapping reactions may be circumvented if the $(CpR)Mo(CO)_3$ were generated in the absence of a reducible substrate, i.e. not from its parent dimer, for example by atom abstraction from a parent hydride complex.[11] This would require the preparation of both a water-soluble $(CpR)Mo(CO)_3H$ complex[38] as well as a water-soluble H-atom abstraction reagent.

## Experimental Section

All manipulations were carried out under $N_2$, using standard vacuum line and dry box techniques. Solution ($D_2O$) IR spectra were recorded on a Nicolet Magna 550 FT-IR spectrometer, in a 0.1 mm pathlength $CaF_2$ cell. $^1H$ (299.95 MHz) and $^{13}C$ (75.42 MHz)

NMR spectra were recorded using a Varian Inova 300 NMR spectrometer. All irradiations were carried out with an Oriel 200 W high pressure mercury lamp. A Corning cutoff filter CS 3-67 ($\lambda > 524$ nm, $< 0.5\%$ transmission for $\lambda < 524$nm) was used. THF was dried over K prior to use. $Br_3CCH_2OH$, $BrCH_2CH_2OH$, $Cl_3CCOOH$, $Cl_3CCO_2Na$, $Cl_3CCH_2OH$ were purchased from Aldrich Chemical Company and used as received. THBP was provided by Bend Research Inc., Bend, Oregon, and used as received. $[(CO)_3MoCpCH_2CH_2NMe_2]_2$ was prepared by a slightly modified literature procedure.[22] All other reagents were obtained from commercial sources and used as received.

### Preparation of $[(CpCH_2CH_2NMe_2)_2Mo_2(CO)_6]$

An aqueous solution of $K_2CO_3$ (25 mL, 1 g/mL) was added to a slurry of 6.81 g $[(CpCH_2CH_2NMe_2H)_2Mo_2(CO)_6](NO_3)_2$ (9.0 mmol) in 10 mL $H_2O$. The aqueous phase was extracted with $Et_2O$ (3x, 200 mL total). The combined, deep red organic phases were dried over $Na_2SO_4$. Evaporation of the solvent gave 3.48 g (5.5 mmol, 61 %) of a red crystalline solid. $^1H$ NMR ($CDCl_3$) $\delta$ 4.93 (s br, 4 H), 4.81 (s br, 4H), 2.31 (t, 7 Hz, 4H), 2.17 (t, 7 Hz, 4H), 2.00 (s, 12 H) ppm; $^{13}C$ NMR ($CDCl_3$) $\delta$ 112.39, 94.23, 91.83, 61.42, 45.61, 45.57, 27.50 ppm; IR (KBr) 1949, 1941, 1920, 1902, 1882 $cm^{-1}$.

### Preparation of $[(CO)_3MoCpCH_2CH_2NMe_3]_2I_2$

To a solution of 971 mg $[(CpCH_2CH_2NMe_2)_2Mo_2(CO)_6]$ (1.52 mmol) in 50 mL THF in an aluminum foil covered flask, 190 μL MeI (433 mg, 3.05 mmol) was added via syringe. The reaction mixture was stirred in the dark at ambient temperature for 7 h. A precipitate formed which was filtered in air. The complex $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6]I_2$ was obtained as a red powder which was dried in vacuo (1.24 g, 1.35 mmol, 89 %). Some of this material was recrystallized from methanol. $^1H$ NMR ($D_2O$) $\delta$ 5.62 (s br), 5.52 (s br), 5.36 (s br, 8 H total), 3.52 (m, 4H), 3.17 (s, 18 H), 2.98 (m, 4H) ppm; IR ($H_2O$) 2011(m), 1957(s), 1913(s) $cm^{-1}$.

### Preparation of $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6](NO_3)_2$

A solution of 455 mg $AgNO_3$ (2.68 mmol) in 50 mL MeOH was added to a stirred slurry of 1.24 g $[(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6]I_2$ (1.35 mmol) in 10 mL MeOH. The mixture was stirred for 10 min in the dark. A gray precipitate formed and the MeOH solution was deeply red colored. After filtration the filtrate was reduced to dryness. A fine red crystalline solid (768.6 mg, 0.98 mmol, 72 %) was obtained. $^1H$ NMR ($D_2O$) $\delta$ 5.62 (s br), 5.52 (s br), 5.36 (s br, 8 H total), 3.52 (m, 4H), 3.17 (s, 18 H), 2.98, m, 4H) ppm; IR ($H_2O$) 2011(w), 1958(s), 1911(s, br) $cm^{-1}$. Solubility in $H_2O > 15$ mM.

### Photochemistry Experiments

In a typical photochemistry experiment, solutions of the reagents (phosphine or halogen source) in $D_2O$ were added to a flask containing the water-soluble dimer **1**. Solutions of THBP in $D_2O$ had to be stirred for more than 15 min to assure complete dissolution. Samples of the reaction solution were withdrawn via syringe and added to a

$CaF_2$ IR cell. The cell was irradiated in 5 s or 10 s intervals and subsequently placed in the IR spectrometer to record the IR spectrum.

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# CHAPTER VIII

## CONCLUDING SUMMARY

In this dissertation the chemistry of three water-soluble organometallic compounds was described. The studies on the organometallic radical precursors, namely $(CO)_3Fe(TPPTS)_2$ and $(CpCH_2CH_2NMe_3)_2Mo_2(CO)_6$, confirmed that the chemistry of the radicals, for example rapid substitution reactions and facile atom abstraction reactions, is qualitatively identical in water and in organic solvents. The determination of mechanistic details and reaction rates, however, was found to be complicated by a number of problems.

Although the specific reasons for the inability to obtain quantitative data was different in each of the two systems that were studied, there was a common underlying feature to the encountered problems. In each case, the solvent water caused the complications in the kinetic studies, despite the fact that it did not interfere with the chemistry of the organometallic radicals themselves. In the electrochemistry of the iron complex the double potential step chronocoulometry experiment could not be carried out because some oxidation product passivated the electrode surface. The competition experiment involving the molybdenum carbonyl radicals was unsuccessful because the two crucial reagents reacted with each other in water before they could react with the organometallic radical.

Nevertheless, important information was obtained on the oxidation chemistry of $(CO)_3Fe(TPPTS)_2$ in water as well as on the photochemistry of the trimethylammonium functionalized molybdenum dimer, which will be of value to other researchers in this field. Perhaps most importantly, the description of the problems encountered will help to design more successful experiments for the determination of mechanisms in aqueous organometallic radical chemistry.

The most significant contribution that this dissertation makes to the field of aqueous organometallic chemistry comes from the investigation of molybdocenes in water. The finding that aqueous solutions of $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ catalyzed C-H bond activation reactions was both unexpected and exciting. Initially, the observation was made that the Cp*Me* groups of the cyclopentadienyl ligand exchanged their hydrogen atoms for deuterium in $D_2O$. Additional experiments revealed that with alcoholic substrates the C-H bond activation occurred even intermolecularly.

In order to understand the intimate mechanism of H/D exchange it was necessary to first gain knowledge of the hydrolysis chemistry of molybdocenes. Experiments with both unsubstituted and methylsubstituted molybdocenes showed that these complexes exist as monomers and dimers in an equilibrium in aqueous solution. Based on this information, further experiments involving chemical and kinetic studies provided evidence for the proposed mechanism. The crucial steps in the catalytic cycle were found to be the coordination of the alcohol to the metal center followed by formation of a ketone hydride intermediate, which subsequently undergoes H/D exchange with the solvent. Two important intermediates, a glycolate complex as well as a molybdocene monohydride, were independently synthesized and chararacterized. Analysis of the reaction kinetics revealed that the H/D exchange occurred stepwise, with a negative activation entropy. The large primary kinetic isotope effect as well as the previously mentioned chemical and kinetic evidence provided strong support for the proposed mechanism. One of the important results from the mechanistic studies was the realization that, under the appropriate conditions, molybdocenes may be used as oxidation or reduction catalysts in Meerwein-Pondorf-Verley-like hydrogen transfer reactions.

In additional studies, the molybdocene catalyst was found to catalyze nitrile hydrolysis, aldehyde disproportionation, ether cleavage and reduction of olefins. These reactions will require more detailed investigations with respect to their mechanisms and their general applicability. The results of the studies on aqueous molybdocenes that are discussed in this dissertation, however, may provide a starting point for future research in this area.

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