Intra- and Intermolecular H/D Exchange in Aqueous Solution Catalyzed by Molybdocenes[**]

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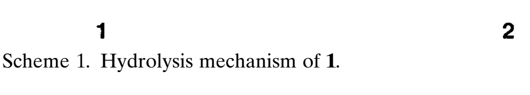
The promotion of organic transformations in aqueous solution by organometallic compounds is an area of intense investigation. Research in this field has led to exciting developments in homogeneous and aqueous biphasic catalysis.[1] As part of our studies in this area[2] we are investigating the catalytic behavior of molybdocenes in aqueous solution. Several detailed investigations of $[Cp_2MoCl_2]$ ($Cp = \eta^5$-C_5H_5) have been reported, chiefly because of its potential as an antitumor agent,[3] yet the identity of the molybdocene species present in aqueous solution remains somewhat ambiguous. The recent reports 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 $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2](OTs)_2$ (**1**, $Cp' = \eta^5$-$C_5H_4CH_3$) and studied its hydrolysis behavior. Surprisingly we found that H/D exchange occurred with the D_2O solvent for the hydrogen atoms on the Cp′ methyl 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 spectroscopy (see 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 ^1H NMR spectrum 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 an aqua-hydroxo complex analogous to **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 (see Supporting Information).



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 ^1H NMR spectroscopy (Figure 1). Over a period of three hours, the resonances for the Cp′ methyl 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 ^2H NMR spectrum[7] of this sample after cooling to room temperature revealed that the protons on the Cp′ methyl group had undergone H/D exchange with the D_2O solvent (Figure 1).[8]

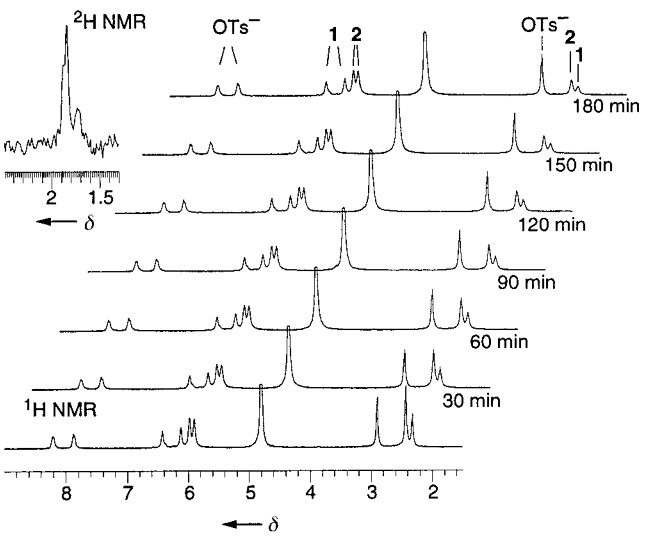
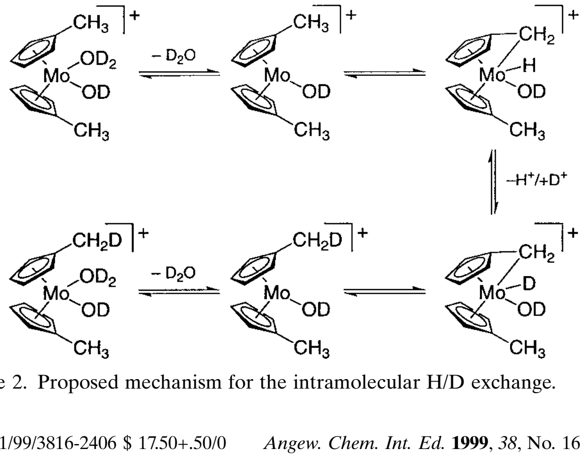


Figure 1. ^1H NMR spectra of a solution of **1** in D_2O at 75 °C recorded over a period of 3 h. The inset shows the ^2H NMR of the reaction solution after cooling to 25 °C.

A possible mechanism for the H/D exchange involves the intramolecular insertion of the molybdenum center into a C–H bond of the Cp′ methyl group (Scheme 2). This 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 $[Cp^*(\eta^5,\eta^1\text{-}C_5Me_4CH_2)WH]$ is formed.[9] The hydride ligand in the



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

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activated, tucked-in molybdenum complex can then exchange with the water molecules by a protonation/deprotonation reaction. Conversion of the deuteride complex back to the aqua-hydroxo complex results in a species now containing deuterium in the Cp′ methyl group.

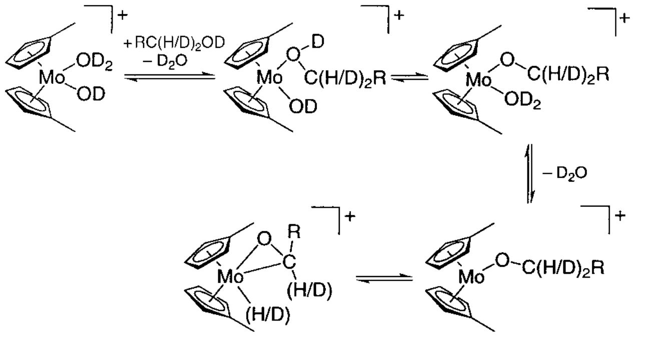
Alternatively, the H/D exchange could proceed by a simple proton exchange without participation of the metal center if the Cp′ methyl hydrogen atoms were sufficiently acidic. An experiment in which the aqueous molybdocene solution was adjusted to pD 12.8 and heated at 85 °C showed that the H/D exchange is slow, with only 17 % conversion after 3 h. This result is not consistent with a simple proton exchange. 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 ^1H and ^2H NMR spectroscopy. The results of these experiments are summarized in Table 1.

Table 1. Intermolecular H/D exchange with alcoholic substrates.

RCH_2OH	$c(RCH_2OH)$ [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

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 alkoxo-aqua complex. Upon dissociation of the aqua ligand the metal center inserts into the α-C–H bond to form a hydrido species which can also be regarded as a π-carbonyl complex.[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. Proposed mechanism 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 (see Table 1). In addition, ^1H 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 isopropyl alcohol 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 acetone/water (100 mL/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, 4H; *p*-OTs), 7.10 (d, ^3J(H,H) = 8 Hz, 4H; *p*-OTs), 5.96 (t, ^3J(H,H) = 2 Hz, 8H; Cp′), 5.73 (t, ^3J(H,H) = 2 Hz, 8H; Cp′), 2.28 (s, 6H; *p*-OTs-*Me*), 1.75 (s, 12H; Cp′-*Me*), 1.27 (s, 2H, OH); elemental analysis 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 **1** (5–10 mg) and substrate (20–30 µL) in D_2O (0.7 mL) 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 monitored by ^1H and ^2H NMR spectroscopy.

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[8] The difference in chemical shifts of the CD_3 resonances at 25 °C and the CH_3 resonances at 75 °C is caused by the shifting of the water resonance reference signal with inrceased temperature. The ^{1}H and ^{2}H spectra show equivalent chemical shifts at 25 °C.

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Ionization of Ozone/Chlorofluorocarbon Mixtures in Atmospheric Gases: Formation and Dissociation of $[CHX_2O_3]^+$ Complexes (X = Cl, F)[**]

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The interest in chemical interactions between ozone and halocarbons, and their impact on the ozone layer depletion, has almost exclusively concerned neutral species. Yet, since the advent of rocket-born mass spectrometers, a rich ionic chemistry is known to occur in the atmosphere, and the lifetimes of certain pollutants have been shown to be limited by ionic reactions.[1] This has stimulated the study of ionized halocarbons in atmospheric gases,[2–4] as well as of the ionic chemistry of ozone, leading inter alia to the detection of elusive cations such as O_3H^+,[5] whose role in the chemistry of the upper atmosphere had long been postulated.[6, 7] So far, however, ozone and halocarbons have been studied separately, and no information is available on the ionic chemistry of gases containing both species, a serious limitation that contrasts with the approach successfully followed in the study of the corresponding homolytic reactions.

Here we report the highlights of the first study specifically aimed at examining ionic reactions occurring in atmospheric gases (O_2, N_2) containing both ozone and a halocarbon. Although several halomethanes—including $CHCl_2F$, $CHClF_2$, CHF_3, and CH_3F—were investigated, we shall concentrate on a typical example, that is, the ionization of $CHCl_2F/O_3$ mixtures diluted in O_2. The salient feature of the experiments performed in the chemical ionization (CI) ion source of the spectrometer (see Experimental Section) is the addition to ozone of the $CHClF^+$ ion [Eq. (1)], which is formed in turn by dissociative charge transfer from O_2^+ and O_3^+ to the halocarbon [Eq. (2)].

$$\mathrm{CHClF^+ + O_3 \rightarrow \underset{\mathbf{1}}{CHClFO_3^+}} \qquad (1)$$

$$\mathrm{CHCl_2F + O_n^+ \rightarrow CHClF^+ + O_n + Cl} \qquad (2)$$

Occurrence of process (2) was demonstrated by Fourier transform ion cyclotron resonance (FT-ICR) experiments involving the reaction of isolated O_3^+ ions with $CHCl_2F$ at 10^{-8} to 10^{-7} Torr. The inefficient collisional deactivation in this pressure range prevents detection of **1**, since any complex formed would undergo back dissociation. Collisional deactivation is considerably more effective at much higher pressures, up to 0.5 Torr, typical of O_2/CI experiments, which allows stabilization and hence detection of **1**. The collisionally activated dissociation (CAD) mass spectra of the stable population of **1** show only the $CHClF^+$ fragment—that is, back dissociation of the complex into its components—as expected for an electrostatic adduct. Ions **1** formed with excess internal energy undergo metastable dissociation, as shown by the mass-analyzed ion kinetic energy (MIKE) spectrum (Figure 1).

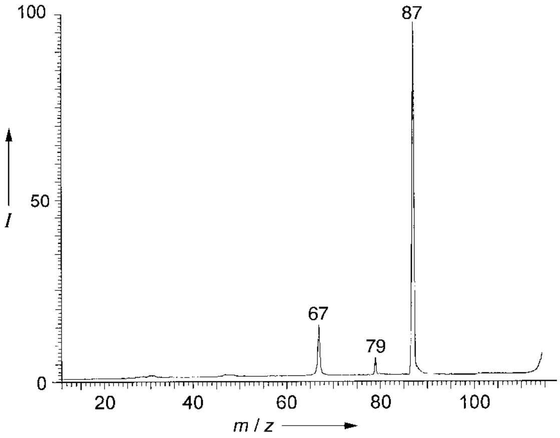

Figure 1. Typical MIKE spectrum of $CH^{35}ClFO_3^+$ ions, displaying the $HFClO_2^+$ fragment (*m*/*z* 87), the CFO_3^+ fragment (*m*/*z* 79), and the $CHClF^+$ fragment (*m*/*z* 67). *I* = intensity.

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