Aqueous Phase Organometallic Catalysis Using $(MeCp)_2Mo(OH)(H_2O)^+$. Intramolecular Attack of Hydroxide on Organic Substrates

Kerry L. Breno, Michael D. Pluth, Christopher W. Landorf, and David R. Tyler*

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

Received October 22, 2003

The hydrolysis of esters and difunctional ethers catalyzed by $Cp'_2Mo(OH)(H_2O)^+$ (**1**) ($Cp' = \eta^5$-$C_5H_4CH_3$) and the stoichiometric oxidation of CO to CO_2 in the presence of **1** are described. These reactions, combined with the previously reported nitrile hydrations and phosphate esters hydrolyses catalyzed by **1**, demonstrate that **1** is an effective homogeneous catalyst for hydration, hydrolysis, and oxidation reactions in aqueous solution under mild conditions (pH ∼7, ∼80 °C). Each reaction is proposed to proceed by intramolecular attack of the hydroxide ligand on a bound substrate. The intramolecular nature of the reaction is supported by the ester hydrolysis activation parameters ($\Delta H^{\ddagger} = 5.9 \pm 0.7$ kcal/mol and $\Delta S^{\ddagger} = -48 \pm 9$ eu), the lack of H/D exchange, and the significant increase (10^6-10^8) in the rate of hydrolysis over uncatalyzed hydrolysis.

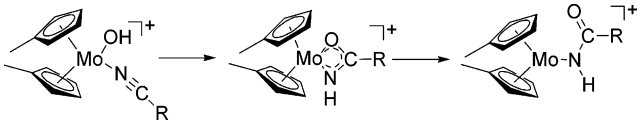
Introduction

Aqueous phase homogeneous catalysis is a burgeoning field, and the investigation of new, water-soluble catalysts is an active area of research.[1] As part of our development of new, water-soluble catalysts, we are exploring the aqueous chemistry of the $Cp'_2Mo(OH)(H_2O)^+$ (**1**) ($Cp' = \eta^5$-$C_5H_4CH_3$) complex.[2−6] In a recent paper, we reported that this complex was a catalyst for nitrile hydration reactions in aqueous solution (eq 1).[3]

$$R{-}C{\equiv}N \xrightarrow[0.1\text{-}5\%\ \mathbf{1}]{H_2O} R{-}\overset{\overset{O}{\|}}{C}{-}NH_2 \qquad (1)$$

A key step in the proposed mechanism was the intramolecular attack of a coordinated hydroxy ligand on a bound nitrile substrate (Scheme 1). This step has a precedent in the hydration of acetonitrile to acetamide catalyzed by $[Co(cyclen)(OH_2)_2]^{3+}$, which was shown to proceed by a route involving intramolecular hydroxide attack on a coordinated nitrile.[7] The intramolecular attack of hydroxide on bound substrates in Co(III) aquo/hydroxy complexes is not limited to the hydration of nitriles but extends to the hydrolysis of phosphate esters, amides, and amino acid esters, as well.[8−10] Similar intramolecular reactions with various substrates occur in other systems. For example, the intramolecular attack of hydroxide on a bound ester ligand is a key step in the *cis*-$Cu(H_2O)_2L_2^+$-catalyzed hydrolysis of carboxylic esters and phosphate diesters.[10−13] Likewise, intramolecular hydroxide attack is a proposed step in the hydrolysis of phosphate diesters with the Ni(tren)$(OH)(OH_2)^+$ catalyst.[12−14] These reports prompted our investigation into whether intramolecular attack of the hydroxide ligand in the $Cp'_2Mo(OH)(H_2O)^+$ complex on a bound substrate was a general reaction and, if so, if it could be exploited in other catalytic cycles. In this paper we report the results of our investigation.

Scheme 1. Intramolecular Attack of a Hydroxy Ligand on a Bound Nitrile to Form an Amidate Intermediate Leading to Hydration of the Nitrile



Experimental Section

General Procedures. All experiments were performed under a nitrogen atmosphere using standard glovebox techniques or a Schlenk line. All liquid substrates were degassed using three freeze−pump−thaw cycles, except for H_2O and D_2O, which were purged with nitrogen for at least 30 min prior to use. All NMR samples were prepared in an inert atmosphere and were sealed with septum caps or J-Young screwcaps. Reactions were brought to the required temperature

* Corresponding author. E-mail: dtyler@uoregon.edu.

(1) Cornils, B.; Hermann, W. A. *Aqueous-Phase Organometallic Catalysis: Concepts and Applications*; Wiley-VCH: Weinheim, 1998.
(2) Balzarek, C.; Weakley, T. J. R.; Kuo, L. Y.; Tyler, D. R. *Organometallics* **2000**, *19*, 2927−2931.
(3) Breno, K. L.; Pluth, M. D.; Tyler, D. R. *Organometallics* **2003**, *22*, 1203−1211.
(4) Breno, K. L.; Tyler, D. R. *Organometallics* **2001**, *20*, 3864−3868.
(5) Balzarek, C.; Tyler, D. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 2406−2408.
(6) Balzarek, C.; Weakley, T. J. R.; Tyler, D. R. *J. Am. Chem. Soc.* **2000**, *122*, 9427−9434.
(7) Kim, J. H.; Britten, J.; Chin, J. *J. Am. Chem. Soc.* **1993**, *115*, 3618−3622.
(8) Kim, J. H.; Chin, J. *J. Am. Chem. Soc.* **1992**, *114*, 9792−9795.
(9) Sutton, P. A.; Buckingham, D. A. *Acc. Chem. Res.* **1987**, *20*, 357−364.
(10) Chin, J. *Acc. Chem. Res.* **1991**, *24*, 145−152.
(11) Chin, J.; Jubian, V. *Chem. Commun.* **1989**, 839−841.
(12) Morrow, J. R.; Trogler, W. C. *Inorg. Chem.* **1988**, *27*, 3387−3394.
(13) Morrow, J. R.; Trogler, W. C. *Inorg. Chem.* **1989**, *28*, 2330−2333.
(14) De Rosch, M. A.; Trogler, W. C. *Inorg. Chem.* **1990**, *29*, 2409−2416.

10.1021/om0342558 CCC: $27.50
Publication on Web 03/19/2004

using an oil bath. ^1H, ^2H, and ^{13}C NMR spectra were measured on a Varian Inova 300 (299.95 MHz for ^1H, 46.04 MHz for ^2H, and 75.42 MHz for ^{13}C). IR spectra were measured on a Nicolet Magna IR 530 spectrometer. An Orion model 230 pH meter with a Corning NMR Micro Combo pH electrode was used to take pH readings, and all pD values reported herein are uncorrected. Mass spectra were recorded from an Agilent 1100 series LC/MS with an electrospray head. Gas chromatography data were recorded using a 100 μL sample loop (Alltech) on a model 1022 Perkin-Elmer autosystem gas chromotograph with a 6 ft Alltech Carbosphere 80/100 1/8 in. stainless steel column using helium as the carrier gas.

Materials. All substrates were used without purification except for acetone (Aldrich 99.5+%), which was dried and distilled with type 4A molecular sieves (Fischer), and acetonitrile (Fischer Scientific 99.9%), which was dried and distilled over CaH_2. H_2O and D_2O were degassed with scrubbed nitrogen for at least 30 min. D_2O (99.9% D) and $CD_3C(O)CD_3$ (99.9% D) were obtained from Cambridge Isotope Laboratory. Carbon monoxide (chemically pure) was obtained from Air Liquid. All remaining materials were obtained from Aldrich. The dimer $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs]_2$ was prepared as described previously.[5]

Carboxylic Ester Hydrolysis. The hydrolysis of ethyl acetate is used as a representative procedure for the hydrolysis of carboxylic esters. Experimental details for the hydrolysis of other carboxylic esters can be found in the Supporting Information. A minimum of three reproducible trials were collected for rate data. $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (0.0125 g, 14.1 μmol) and ethyl acetate (30 μL, 308 μmol) were added to 1.10 mL of D_2O. The resulting solution was bright green in color and was heated at 80 °C for 17 h. In the first NMR spectrum, taken before heating, traces of ethanol were detected in the sample and these resonances increased in intensity throughout the heating. ^1H NMR (300 MHz, D_2O, pD = 3.7): δ 4.13 (q, 2H, J = 7.2 Hz $CH_3CH_2(O)COCH_3$), 2.08 (s, 3H, $CH_3CH_2(O)COCH_3$), 1.23 (t, 3H, J = 7.2 Hz $CH_3CH_2(O)COCH_3$), 3.65 (q, 2H, J = 5.7 Hz CH_3CH_2OH), and 1.18 (t, 3H, J = 6.3 Hz CH_3CH_2OH). For the kinetic studies, the above procedure was repeated with and without buffer and monitored for over 800 h. For the buffered sample, $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (0.00217 g, 2.45 μmol), ethyl acetate (5 μL, 46.9 μmol), and hemi-sodium morpholinosulfonic acid (NaMOPS; 0.0217 g, 49.3 μmol) were added to 1.10 mL of D_2O.

Nitrile Hydration. The hydration of acetonitrile is presented here as a representative procedure for the hydration of nitriles. (See ref 3 for more complete experimental notes on nitrile hydration.) $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (0.0407 g, 45.9 μmol) was added to 5 mL of D_2O, and then a 750 μL aliquot of this solution (containing 12.78 μmol of total monomeric molybdenum complex) was added to 100 μL of acetonitrile (1.91 mmol). The resulting solution, which immediately turned pink, was flame sealed while frozen in liquid nitrogen. The sample was heated at 75 °C for 9 days in an oil bath. Before heating, the ^1H NMR (D_2O) resonance of the substrate was at δ 2.08 (s, 3H, CH_3CN); after heating for 9 days, a new resonance appeared at 1.98 (s, 3H, CH_3CONH_2). After heating for 9 days, the ^{13}C NMR (D_2O) showed four resonances at δ 177.3 (s, CH_3CONH_2), 119.2 (s, CH_3CN), 21.4 (s, CH_3CONH_2), and 1.0 (CH_3CN). After 30 days of heating, only the ^{13}C resonances at δ 177.3 and 21.4 remained.

Ether Hydrolysis. Ethyl vinyl ether (1.5 mL, 16 mmol) was reacted with 103 mg (116 μmol) of **1** in 10 mL of H_2O in a Schlenk flask. The flask was heated to 80 °C for 8 h. The resulting solution was then washed with $CDCl_3$ and extracted. The extract was examined by NMR. The products of the reaction extracted were ethanol and acetaldehyde. ^1H NMR (300 MHz, $CDCl_3$): δ 3.65 (q, 2H, J = 5.7 Hz CH_3CH_2OH), 1.18 (t, 3H, J = 6.3 Hz CH_3CH_2OH), and 2.20 (t, 3H, $CH_3C(O)H$). A minimum of three reproducible trials were collected for rate data.

A catalyst stock solution was prepared by adding $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (0.1128 g, 127 μmol) to 25 mL of D_2O. 2-Methoxyacetonitrile (100 μL,1.34 mmol) was then added to 500 μL (2.55 μmol) of the stock solution and sealed in a screw-cap NMR tube. The resulting solution turned a light pink color. The sample was heated at 85 °C for 7 days in an oil bath. The ^1H NMR resonances (D_2O) before heating were at δ 4.41 (s, 2H, CH_3OCH_2CN) and 3.50 (s, 3H, CH_3OCH_2CN). During heating, the following 1H NMR resonances (D_2O) for 2-methoxyacetamide appeared: δ 4.22 (s, 2H, $CH_3OCH_2CONH_2$) and 3.43 (s, 3H, $CH_3OCH_2CONH_2$). In addition, methanol (δ 3.35, s, 3H), glycolic acid (δ 3.99, s, 2H), and an unidentified peak at δ 3.86 (s) were detected. After heating, only a slight pink coloration remained in the sample. The kinetics of the reaction were modeled by GIT.[15] A minimum of three reproducible trials were collected for rate data.

Ethyl ether (100 μL, 963 μmol) was added to 1 mL (5.10 μmol of $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$) of the stock solution described above in an NMR tube. The sample was heated to 75 °C and monitored by NMR spectroscopy for a week. There were no detectable changes in the sample.

Oxidation of Carbon Monoxide. Distilled water (or alternatively D_2O) was added to 0.0450 g of $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (50.0 μmol) in a 5 mL volumetric flask in the glovebox. This solution was transferred to a Fisher-Porter bottle and subsequently removed from the inert atmosphere. The bottle was charged with 41 psi CO and heated in an oil bath at 81−85 °C for 21 h. During heating, the solution changed from a dark brown-green to a bright yellow. An aliquot of the solution was evaporated to yield a yellow-orange solid. IR (KBr): 3087, 2006, 1631, 1486, 1456, 1382, 1184, 1039, 1012, 814, 691, and 570 cm^{-1}. MS (m/z^+, relative intensity): 285.0 (100%) and 738.0 (8%), corresponding to $Cp'_2Mo(CO)H^+$ (**2**) and the cluster $2[Cp'_2Mo(CO)H]^+[OTs]^-$. The isotope patterns of the two ions seen in mass spectroscopy are consistent with the structures proposed above. ^1H NMR(300 MHz, d_6-acetone): δ 7.68 (d, 2H, J = 4.05 Hz, *o*-Ar $S_3OC_6H_4CH_3$), 7.36 (d, 2H, J = 3.90 Hz, *m*-Ar $S_3OC_6H_4CH_3$), 5.54 (m, 4H, J = 5.6 Hz, Cp′), 5.44 (m, 4H, J = 5.6 Hz, Cp′), 2.39 (s, 3H, $-CH_3$, $S_3OC_6H_4CH_3$), −8.09 (s, 1H, Mo−H, $Cp'_2Mo(CO)H$). Two hours after the completion of heating, the pH of the solution was 3.90; after 125 h, the pH of the solution had risen to 5.56.

In a separate reaction, the headspace gas was analyzed to determine the gaseous products of the reaction of **1** with CO. $[Cp'_2Mo(\mu\text{-}OH)_2MoCp'_2][OTs^-]_2$ (0.1003 g, 113 μmol) was added to 5.0 mL of H_2O (0.28 mol) in the glovebox. This solution was transferred to a Fisher-Porter bottle and then removed from the glovebox. The bottle was charged with 40 psi CO and heated in an oil bath at 82 °C for 20 h. The reaction was allowed to equilibrate to room temperature for 30 min (while being stirred vigorously) before GC analysis of the gas in the headspace of the reaction vessel. The gases in the headspace were sampled six times at different pressures by GC and compared to the calibration curve determined for CO_2. The total amount of CO_2 calculated to be in the gas phase of the reaction was 198 ± 8 μmol or 87 ± 4% of the total CO_2 predicted by the proposed equation (eq 7, Results).

Inhibition and Competitive Reactions. A study of reaction rates as a function of metal complex concentration was not possible with the above reactions due to the presence of interfering inhibition or competition reactions. The hydration of nitriles is inhibited by the amide hydration product.[3] In addition, the ester (or ether) hydrolysis reaction is competitive with H/D exchange of the alcohol product and inhibited by acid coordination to the catalyst.[5] Thus, changing the

(15) (a) Stabler R. N.; Chesick, J. *Int. J. Kinet.* **1978**, *10*, 461. (b) McKinney, R. J.; Weigert F. J. Quantum Chemistry Program Exchange, Program # QCMPO22. (c) Weigert, F. J. *Comput. Chem.* **1987**, *11*, 273.

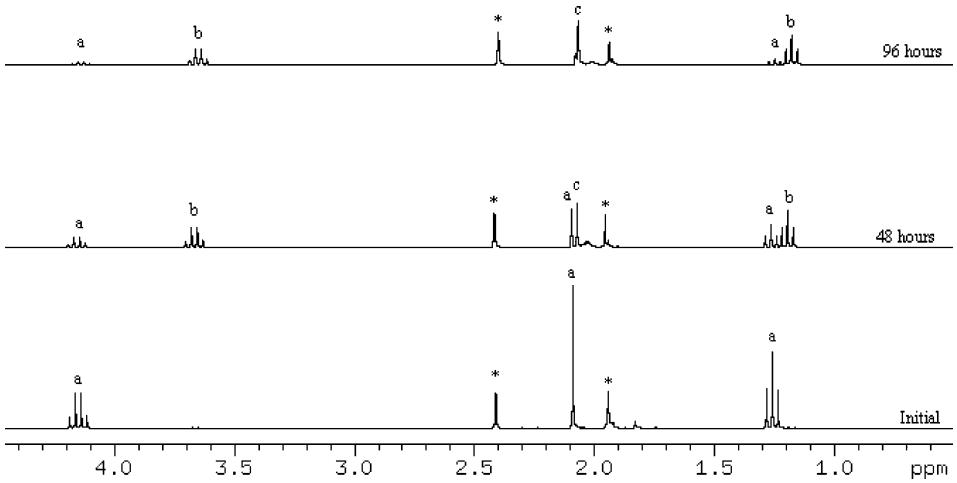
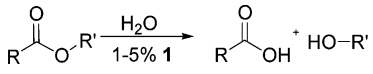


Figure 1. ^{1}H NMR spectra of ethyl acetate hydrolysis. The initial spectrum is shown at the bottom with increasing time shown vertically. Resonances of ethyl acetate are marked "a", ethanol "b", and acetic acid "c." The * resonances are attributed to the catalyst.

amount of catalyst in solution changed the rate of the inhibiting/competing reactions and complicated the catalyst dependence.

Results

Carboxylic Ester Hydrolysis. Simple unactivated carboxylic esters were hydrolyzed to their respective alcohols and carboxylic acids using catalyst **1** in aqueous solution (eq 2). As an example of this reactivity, the



(2)

hydrolysis of ethyl acetate to ethyl alcohol and acetic acid was monitored by NMR spectroscopy, and the results are shown in Figure 1. The figure shows the disappearance of the ethyl acetate resonances at 4.13, 2.08, and 1.23 ppm and the commensurate increase in the ethyl alcohol (3.65 and 1.18 ppm) and acetic acid (2.05 ppm) resonances. The product assignments were confirmed by comparison to NMR samples of authentic compounds in D_2O.

During the course of the reaction, the color of the solution changed from green-brown to bright green. In addition, the pD over the first 24 h of the reaction decreased to pD 3.7, consistent with the color change in the catalyst solution. (Solutions of the catalyst are brown at neutral pH but green when acidic.) The pseudo-first-order rate constant for hydrolysis was $(4.3 \pm 0.2) \times 10^{-6}$ s^{-1} at 65 °C. However, the reaction was inhibited by the drop in pH as the acetic acid formed. With the addition of the noncoordinating buffer Na-MOPS, the pH of the reaction mixture remained 7.1 over the course of the reaction. Under these conditions, the reaction was not inhibited, and the carboxylic ester hydrolysis pseudo-first-order rate constant was $(7.6 \pm 0.9) \times 10^{-6}$ s^{-1} (65 °C, pH 7.1), as obtained from an exponential decay fit of the data shown in Figure 2. This rate constant indicates a substantial increase ($\sim 10^6$) in the rate of hydrolysis compared to that for ethyl acetate in the absence of catalyst at neutral pH.[16]

(16) Schmeer, G.; Sturm, P. *Phys. Chem.* **1999**, *1*, 1025−1030.

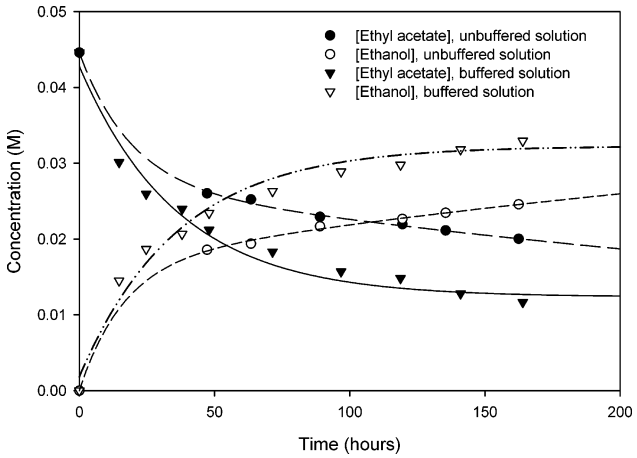


Figure 2. Disappearance of ethyl acetate and appearance of ethanol in the hydrolysis of ethyl acetate with catalyst **1** at 65 °C. The hydrolysis reaction (buffered to pH 7.1) is shown with triangles. The unbuffered hydrolysis reaction is shown with circles. The curves are exponential fits of the concentration vs time data.

Table 1. Rates of Ethyl Acetate Hydrolysis at Various Temperatures, pH 7.1

temp (°C)	k_{obs} (10^{-5} s^{-1})	k (10^{-3} M^{-1} s^{-1})	initial rate (10^{-3} M/h)
94	2.2 ± 0.2	4.8 ± 0.5	3.6 ± 0.4
74	1.0 ± 0.1	2.1 ± 0.2	1.6 ± 0.2
70	0.79 ± 0.09	1.7 ± 0.2	1.3 ± 0.1
66	0.76 ± 0.10	1.6 ± 0.2	1.2 ± 0.2
23	0.20 ± 0.07	0.43 ± 0.15	0.34 ± 0.1

The rates of ethyl acetate hydrolysis with catalyst **1** at neutral pD were evaluated at various temperatures between 23 and 95 °C. The results are shown in Table 1. In this table, k_{obs} is the pseudo-first-order rate constant for hydrolysis. The second-order rate constant is given by k.

The Eyring plot for these data is shown in Figure 3, from which $\Delta H^{\ddagger} = 5.9 \pm 0.7$ kcal/mol and $\Delta S^{\ddagger} = -48 \pm 9$ eu were determined. (The large negative activation entropy is indicative of a constrained transition state and will be discussed in terms of the proposed mechanism of the reaction.) As mentioned, ethyl acetate is not the only carboxylic ester to be hydrolyzed with catalyst **1**. The hydrolyses of other esters such as butyl butyrate,

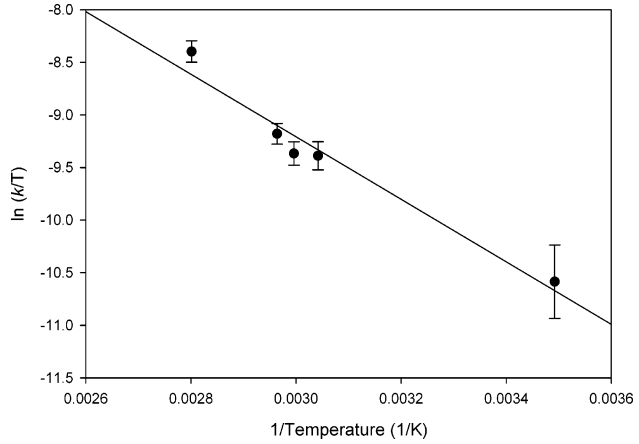
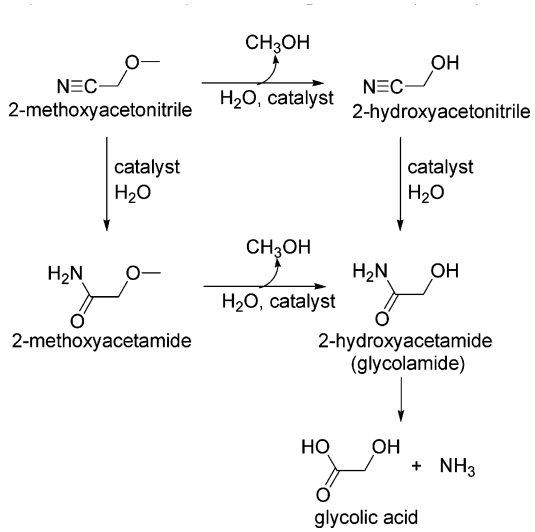
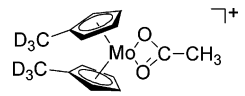


Figure 3. Eyring plot for the hydrolysis of ethyl acetate catalyzed by $Cp'_2MoOH(OH_2)^+$. Error bars represent one sigma.

Scheme 2. Hydrolysis of 2-Methoxyacetonitrile Promoted by Catalyst 1



norbornenyl acetate, vinyl acetate, and methyl cyanoacetate were followed by ^1H and/or ^{13}C NMR spectroscopy. In each case, the products of hydrolysis, the respective acids and alcohols, were observed and confirmed by the addition of authentic samples (see Supporting Information). The bidentate coordination of acetate to the Cp'_2Mo^{2+} unit was observed by ES-MS in the hydrolysis of norbornenyl acetate. The parent peak at 321 *m*/*z* is attributed to species **3**. This finding has mechanistic significance because the metal-coordinated acetate product is observed in both cobalt- and copper-catalyzed hydrolysis reactions.[11]



3, MW = 321

Ether Hydrolysis. The initial investigation of ethers began with unsaturated ethers. It was observed that, in aqueous solutions of **1**, vinyl ethyl ether hydrolyzed to form ethanol and acetaldehyde. The products were identified by extraction with $CDCl_3$ and subsequent comparison of their ^1H NMR spectra with authentic samples. The substituted ether 2-methoxyacetonitrile hydrolyzed at 75 °C using **1** as a catalyst according to the reactions shown in Scheme 2.[3] Methanol and glycolic acid were detected as products by NMR, as authenticated by additions of pure compound to the reaction mixture. Because glycolic acid and methanol are products of ether hydrolysis and nitrile hydration, it is evident that both reactions proceed with catalyst **1**. The kinetics of the reaction were modeled by GIT[4] using eqs 3−6. The rate constant of ether hydrolysis, k_{app}, was determined from the modeling to be 3.75×10^{-3} M^{-1} s^{-1}.

$$\text{catalyst} + \text{2-methoxyacetonitrile} \xrightarrow{k_{app}} \text{catalyst} + \text{methanol} + \text{2-hydroxyacetonitrile} \quad (3)$$

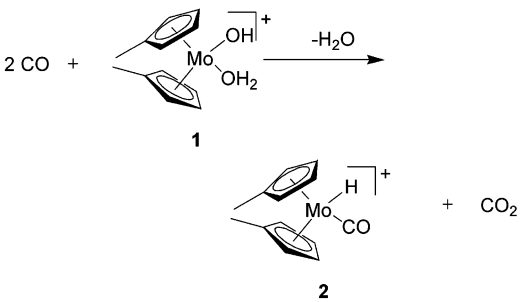
$$\text{catalyst} + \text{2-hydroxyacetonitrile} \xrightarrow{k_4} \text{catalyst} + \text{2-hydroxyacetamide} \quad (4)$$

$$\text{2-hydroxyacetamide} \xrightarrow{k_5} \text{glycolic acid} + NH_3 \quad (5)$$

$$\text{catalyst} + \text{2-hydroxyacetamide} \xrightarrow{k_2} \text{inhibition product} \quad (6)$$

Unactivated ethers did not reveal any reactivity detectable by NMR at 75 °C over the course of 7 days, and it is concluded that unactivated ethers such as diethyl ether do not hydrolyze under the mild conditions presented here. This observation is consistent with the fact that catalyst **1** and THF can be mixed in a solution without hydrolysis of the solvent or a change in the catalyst.

Nitrile Hydration. Our previous work[3] showed that **1** is a catalyst for the hydration of nitriles to their corresponding amides without subsequent hydrolysis to the carboxylic acids. For example, acetonitrile was hydrated to acetamide, but no acetic acid was detected.[3] To probe the generality of this result, a variety of monofunctional and bifunctional nitriles were hydrated with catalyst **1**. For convenience in discussing these results in the context of a generalized mechanism, selected results are presented again in Table 2.



(7)

Oxidation of Carbon Monoxide. Catalyst **1** undergoes a stoichiometric reaction with CO in aqueous solution to form CO_2, as detected and quantified by gas chromatography. The experimental CO_2 yield was calculated to be 87 ± 4% based on the stoichiometry in eq 7. (The remaining CO_2 is likely dissolved in solution and accounts for the increase in the pH over time after the solution is vented in a glovebox (see Experimental Section).) Initially, the solution of **1** was brownish-green, but during the reaction the solution became bright

Table 2. Hydration of Nitriles with the $[Cp'_2Mo(OH)(OH_2)]^+$ Catalyst

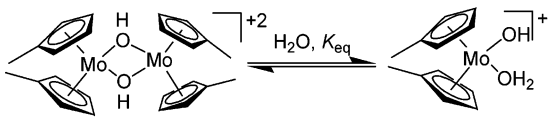
substrate	substrate (M)	[**1**] (M)	k_2 (10^{-6} M^{-1} s^{-1})	temp (°C)	initial rate (10^{-3} mol product/L·h)
acetonitrile	0.91	0.010	3.05	82	8.75
acrylonitrile	0.72	0.010	2.32	75	13.1
benzonitrile	0.89	0.009	0.20	85	33.6
3-bromopropionitrile	1.09	0.009	1.42	90	15.2
4-cyanopyridine	0.33	0.009	7.44	90	6.29
3-hydroxypropionitrile	2.43	0.009	14.2	90	329
isobutyronitrile	1.87	0.009	2.38	85	22.8
2-methoxyacetonitrile	2.23	0.009	3.67	85	256

yellow. The yellow solid was isolated, and spectroscopic analysis showed it to be $[Cp'_2Mo(CO)H][OTs]$ (**2**). The nonmethylated $[Cp_2Mo(CO)H]^+$ complex is well known, and the spectroscopic data are essentially identical.[17−20] The NMR showed that the molybdocene unit is intact with resonances at 5.54 and 5.44 for the bound cyclopentadienyl ligands. In addition the ^1H NMR showed a resonance at −8.09 ppm, consistent with the hydride resonance of $[Cp_2Mo(CO)H]^+$, −8.3 ppm.[19] The infrared spectrum showed a peak at 2006 cm^{-1} that is characteristic of a CO stretch in a molybdenum hydride/carbonyl.[18−20] Mass spectroscopy of the yellow solution showed *m*/*z* peaks at 285.0 (100%) with an isotope pattern consistent with a single Mo atom, as well as a second peak at 738.0 (8%) with an isotope pattern consistent with two Mo atoms (see Supporting Information). It is suggested that these peaks are due to the $Cp'_2Mo(CO)H^+$ species (predicted parent peak = 285) and the electrospray-induced cluster $[Cp'_2Mo(CO)H^+]_2[OTs]^-$ (predicted parent peak = 738). In summary, the spectroscopic evidence indicates that the yellow solid is $[Cp'_2Mo(CO)H][OTs]$ (**2**) and the reaction is as written in eq 7.

Discussion

To carry out homogeneous aqueous catalysis, water-solublizing groups such as sulfonated phosphines are often incorporated into the catalyst to impart water solubility. Although far less extensively studied, organometallic complexes with aquo or hydroxy ligands provide alternative means for water-solubilizing catalysts.[8,21−28] Among such complexes, the presence of early transition metals is rare.[2,27] The oxophilic nature of the earlier transition metals is thought to lead to limited water stability, reduced selectivity, and low reactivity in catalysis.[29] However, recent studies on **1** demonstrated the stability and utility of water-soluble molybdocene hydroxides in the catalytic hydration reactions of nitriles.[3] The results reported here extend these earlier studies to include the hydration, hydrolysis, and oxidation reactions of other substrates in aqueous solution. One of the most interesting features in these reactions is the role of the hydroxide ligand, which is shown below to be involved in intramolecular reactions with the bound substrates.

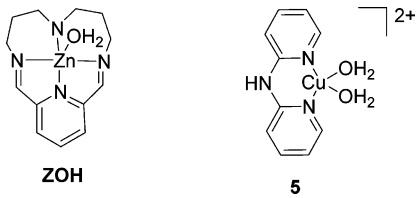
The Catalyst. Prior work demonstrated that, in aqueous solution, complex **4** is in equilibrium with catalyst **1** (eq 8; $K_{eq} = 7.9 \times 10^{-2}$ M at 23 °C, pD 7.8).[2,30] A prior study also determined that species **1** was the



4 **1** (8)

active catalyst by studying the reaction rates as a function of metal complex concentration.[5] Unfortunately, a similar direct method could not be used to determine the catalyst for the reactions in this study due to the presence of interfering inhibition or competition reactions (see Experimental Section). There is indirect evidence, however, that **1** is indeed the catalytically active species. Thus, in the case of nitrile hydration, when the amount of **1** in solution is decreased by the addition of $[N(n\text{-}Bu)_4^+][BF_4^-]$ to the solution (and the amount of **4** accordingly increased; eq 8), the rate of nitrile hydration is decreased, as monitored by NMR.[3]

Carboxylic Ester Hydrolysis. In the absence of catalysts, carboxylic esters do not readily hydrolyze at neutral pH. For example, in the absence of a catalyst, the rate constant for ethyl acetate hydrolysis in water is only 2.47×10^{-10} s^{-1}.[16] One of the catalysts previously used to hydrolyze carboxylic esters is a tetra-amino-coordinated zinc complex, ZOH.[28] This catalyst is only



ZOH **5**

efficient at catalyzing the hydrolysis of activated esters

(17) Igarashi, T.; Ito, T. *Chem. Lett.* **1985**, 1699−1702.
(18) Adams, M. A.; Folting, K.; Huffman, J. C.; Caulton, K. G. *Inorg. Chem.* **1979**, *18*, 3020−3023.
(19) Nakamura, T.; Minato, M.; Ito, T.; Tanaka, M.; Osakada, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 169−174.
(20) Ito, T.; Haji, K.; Suzuki, F.; Igarashi, T. *Organometallics* **1993**, *12*, 2325−2331.
(21) Abura, T.; Ogo, S.; Watanabe, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **2003**, *125*, 4149−4154.
(22) Ogo, S.; Abura, T.; Watanabe, Y. *Organometallics* **2002**, *21*, 2964−2969.
(23) Ogo, S.; Makihara, N.; Kaneko, Y.; Watanabe, Y. *Organometallics* **2001**, *20*, 4903−4910.
(24) Makihara, N.; Ogo, S.; Watanabe, Y. *Organometallics* **2001**, *20*, 497−500.
(25) Ogo, S.; Makihara, N.; Watanabe, Y. *Organometallics* **1999**, *18*, 5470−5474.
(26) Bernhard, P.; Helm, L.; Ludi, A.; Merbach, A. E. *J. Am. Chem. Soc.* **1985**, *107*, 312−317.
(27) Crane, T. W.; White, P. S.; Templeton, J. L. *Inorg. Chem.* **2000**, *39*, 1081−1091.
(28) Chin, J.; Zou, X. *J. Am. Chem. Soc.* **1984**, *106*, 3687−3688.
(29) Morales, D.; Elena Navarro Clemente, M.; Perez, J.; Riera, L.; Riera, V.; Miguel, D. *Organometallics* **2002**, *21*, 4934−4938.
(30) Compared to the η^5-C_5H_5 analogue, the methyl groups on the cyclopentadienyl ligands sterically hinder formation of the dimer and promote hydrolysis to the monomeric species ($K_{eq} = 3.5 \times 10^{-2}$ M at 23 °C, pD 3.5 for the η^5-C_5H_5-containing molecule).

such as methyl triflate; it does not hydrolyze methyl acetate, for example.[31] However, both activated and unactivated esters undergo hydrolysis with catalysts containing *cis*-diaquo ligands. For example, with Cu(II) catalysts, particularly **5**, methyl acetate and *p*-nitrophenyl acetate are readily hydrolyzed. Interestingly, the hydrolysis of the unactivated methyl acetate is at least 2 orders of magnitude faster than the hydrolysis of *p*-nitrophenyl acetate, indicating that the leaving group departure is not rate-determining.[11] Co(III) *cis*-diaqua complexes are similarly effective catalysts. Both *cis*-$[Co(trpn)(OH_2)_2]^{3+}$ and $[Co(trien)(OH_2)(OH)]^{2+}$ are hydrolysis catalysts for carboxylic esters and amino acid esters. The hydrolysis is promoted by direct coordination of the carbonyl group; without this coordination, little rate acceleration occurs. It is not surprising therefore that, because they bind carbonyl groups effectively, *cis*-diaquo Mo(IV) complexes are effective carboxylic ester hydrolysis catalysts. The ability of the *cis*-diaquo Mo(IV) unit to bond to carbonyl groups is demonstrated by the observation of **3** in the ES-MS spectrum of an aqueous mixture containing norbornenyl acetate and catalyst **1**. In summary of this section, the similarity between all of the effective hydrolysis catalysts is the presence of *cis*-diaquo ligands. This structural feature is important for two reasons. First, it provides a labile ligand that can be easily replaced by a carbonyl group of an entering ester. Second, with many catalysts, including catalyst **1**, the second "aquo ligand" is a hydroxy ligand at neutral pH. This hydroxy ligand can facilitate hydrolysis by acting as a general base or acting as an internal nucleophile (see the mechanism section below). Note that decreasing the pH of the solution will lead to the protonation of the hydroxy ligand, making a less effective base or nucleophile. The lower concentration of effective catalyst at acidic pH leads to a decrease in the rate of hydrolysis, as evident with the unbuffered (acidic) ester hydrolysis reactions ($k_{obs} = (7.6 \pm 1.0) \times 10^{-6}$ at pH 7.1 and $(4.3 \pm 0.2) \times 10^{-6}$ unbuffered).

Ether Hydrolysis. Activated, difunctional ethers hydrolyze in aqueous solution with catalyst **1**, but under similar conditions, monofunctional ethers do not hydrolyze. The likely reason is that the ether functionality is a weak ligand and is sterically hindered, which prevents coordination of the ether. Because only difunctional ethers hydrolyze, it is suggested that precoordination of the second functional group to the catalyst is required. For example, methoxyacetonitrile likely coordinates to the catalyst via the nitrogen of the nitrile functional group. It is suggested that hydrolysis of the ether functional group occurs after this coordination. It is noted that the ether hydrolysis reactivity parallels the coordination ability of the second functional group. For example, the hydrolysis of methoxyacetonitrile is faster than vinyl ethyl ether because the nitrile is a better ligand. Interestingly, a similar mechanism is employed to describe the hydrolysis of amino acid esters with Co(III) catalysts.[32] In this case, the other functional group (i.e., the amide group) binds to the catalyst and the amide or amino acid ester is then hydrolyzed.[32]

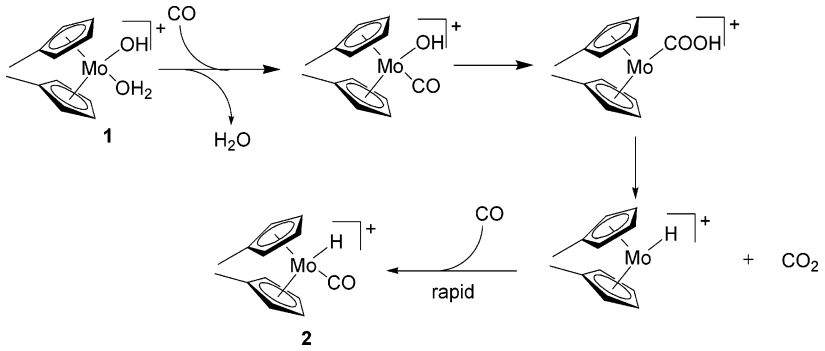
Phosphate Ester Hydrolysis. Catalysts for the aqueous phase hydrolysis of phosphate esters are used for endonuclease mimics, and they are used to decommission pesticides and chemical warfare agents.[14,33,34] Hydrolysis of phosphate esters is extremely slow due to the stability of the phosphate ester over that of carboxylic ester, ether, or amide linkages. The base-catalyzed hydrolysis of $NaOP(O)(OCH_3)_2$ is only 6.8×10^{-12} M^{-1} s^{-1} at 25 °C, and the water hydrolysis of dimethyl phosphate has been calculated to be a nearly stagnant 5.8×10^{-16} s^{-1} at pH 7, 70 °C. It has been reported that the *cis*-diaquo complexes of Co(III) are effective catalysts for the hydrolysis of dimethyl phosphate at 60 °C and pD 6.3 (6.2×10^{-7} M^{-1} s^{-1}, $[Co(cyclen)(OH_2)_2]^{3+}$). Note that two aquo ligands are required for efficient catalysis, as $[Co(tetren)(OH_2)]^{3+}$ does not catalyze the hydrolysis of phosphate esters.[8] Interestingly, the hydrolysis of bis(*p*-nitrophenyl)phosphate (BNPP) with $Cu(i\text{-}Pr_3[9]aneN_3)^{2+}$ at pH 7.2 proceeds with a similar rate constant (8.56×10^{-7} M^{-1} s^{-1}). Under similar conditions, Kuo et al. investigated the hydrolysis of phosphate diesters and triesters using Cp_2MoCl_2 as a precatalyst that forms $Cp_2MoOH(OH_2)^+$ at neutral pH. They reported a rate constant for hydrolysis of dimethyl phosphate of approximately 1.0×10^{-7} M^{-1} s^{-1} at pD 3−7. It is interesting to note that for each of these effective catalysts the rate enhancement is significant, a 10^8 enhancement over the hydrolytic process at neutral pH. As discussed in the mechanistic section below, the rate enhancement and coordinated hydrolysis products indicate that phosphate hydrolysis utilizes the *cis*-aquo ligand functionality to coordinate the phosphate and the second aquo (or hydroxy) ligand site to perform an intramolecular nucleophilic attack on the bound substrate.

Nitrile Hydration. The hydration of nitriles is an industrially important reaction, particularly in the context of acrylonitrile, where side products of olefin hydration often produce substantial impurities. While many catalysts have been used to hydrate nitriles[35−42] (also see Table 1 in ref 3), catalyst **1** is highly chemoselective for the nitrile hydration over olefin hydration. The hydration reaction is straightforward, and no subsequent hydrolysis of the amide occurs (except in the special case of 2-methoxyacetonitrile[3]). It is interesting to note that the most effective hydration catalysts have an open coordination site and an internal hydroxide that can participate in the hydrolysis.

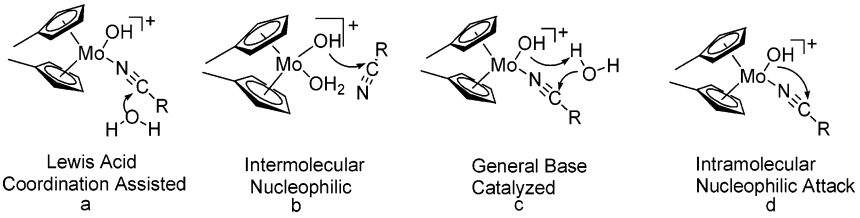
Oxidation of Carbon Monoxide. As part of another investigation into using **1** as a catalyst for Reppe

(31) Menger, F. M.; Ladika, M. *J. Am. Chem. Soc.* **1987**, *109*, 3145−3146.
(32) Angelici, R. J.; Hopgood, D. *J. Am. Chem. Soc.* **1968**, *90*, 2514−2517.
(33) Kuo, L. Y. *Abstr. Pap.−Am. Chem. Soc.* **2000**, *220th*, INOR-489.
(34) Kuo, L. Y.; Perera, N. M. *Inorg. Chem.* **2000**, *39*, 2103−2106.
(35) Ghaffar, T.; Parkins, A. W. *J. Mol. Catal. A: Chem.* **2000**, *160*, 249−261.
(36) Jensen, C. M.; Trogler, W. C. *J. Am. Chem. Soc.* **1986**, *108*, 723−729.
(37) Villain, G.; Constant, G.; Gaset, A.; Kalck, P. *J. Mol. Catal.* **1980**, *7*, 355−364.
(38) Villain, G.; Gaset, A.; Kalck, P. *J. Mol. Catal.* **1981**, *12*, 103−111.
(39) Yoshida, T.; Matsuda, T.; Okano, T.; Kitani, T.; Otsuka, S. *J. Am. Chem. Soc.* **1979**, *101*, 2027−2038.
(40) Djoman, M. C. K. B.; Ajjou, A. N. *Tetrahedron Lett.* **2000**, *41*, 4845−4849.
(41) Bennett, M. A.; Yoshida, T. *J. Am. Chem. Soc.* **1973**, *95*, 3030−3031.
(42) Murahashi, S.; Sasao, S.; Saito, E.; Naota, T. *J. Org. Chem.* **1992**, *57*, 2521−2523.

Scheme 3. Reaction of Catalyst 1 and Carbon Monoxide with Proposed Carboxylic Acid Intermediate



Scheme 4. Catalytic Hydration Pathways

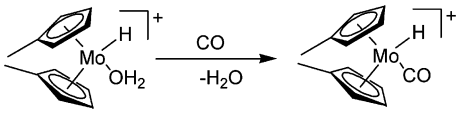


carbonylation, it was observed that **1** reacted with CO to form an inactive species. Analysis showed that the products were CO_2 and $Cp'_2MoH(CO)^+$ (**2**). This reaction is interesting because the catalyst mimics catalysts for the water-gas shift reaction (WGSR) (eq 9).[43]

$$CO + H_2O \rightarrow CO_2 + H_2 \qquad (9)$$

The typical WGSR catalytic cycle is comprised of four steps (illustrated in Scheme 3 for the case of **1**): (a) CO is coordinated to the metal center, (b) nucleophilic attack of hydroxide (or water) occurs on the coordinated CO, (c) decarboxylation of the newly formed carboxylic acid group yields a metal hydride, and (d) the metal hydride reductively eliminates H_2.[44] The reaction of CO with **1** is apparently similar, but the fourth step, elimination of H_2, does not occur. With complex **1**, the monohydride, Cp'_2MoH^+, does not react with the acidic solution to form H_2. Rather, a second carbon monoxide molecule binds irreversibly to the open coordination site, trapping the intermediate and forming an unreactive species, **2**. An incomplete cycle is not unprecedented, as $[Ru(dppe)(CO)(H_2O)_3]_2^+$ reacts with CO to form the cationic hydride $[Ru(dppe)(CO)_3H]^+$ and CO_2.[45]

The reaction of **1** with CO is relatively facile, with 30% conversion to **2** in 1 h at 80 °C under 1 atm of CO. Note that species **2** has been fully characterized by NMR, MS, and IR spectroscopy (see Experimental Section). In addition, **2** was independently synthesized by reacting $Cp'_2MoH(OTf)$ with CO (eq 10). Interestingly, **2** is completely unreactive under all anaerobic reaction conditions investigated. (Thus, it is stable in acidic and in basic solution below pH 9; it does not react with olefins, nitriles, alcohols, or esters at 80 °C.)



(10)

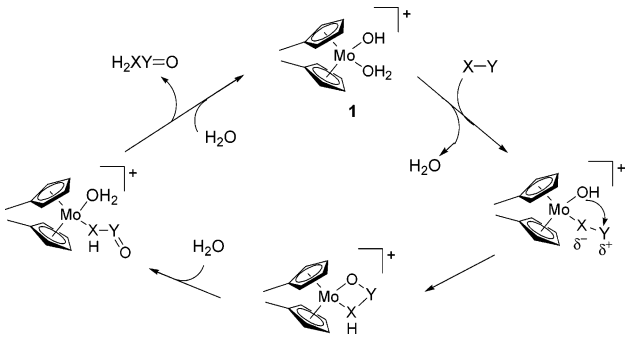
2

Proposed Mechanism. The major theme thoughout the reactions reported herein is that complexes with *cis*-diaquo ligands are often effective hydration catalysts. It is evident that the lability of the first aquo ligand and the hydrolysis assistance imparted by the second ligand increase the catalytic activity of such complexes. The intimate mechanism of the reactions can be explored by careful examination of each reaction. Catalyst **1** could catalyze the hydration/hydrolysis reactions in at least four different ways. First, catalyst **1** could simply act as a Lewis acid promoter for hydrolysis by coordinating the substrate (Scheme 4a). This is reasonable because, after ligand coordination, the electrophilic center on the ligand would be primed for attack by external water. Indeed, this has been shown to be an accurate description of the mechanism of rate enhancement of ester hydrolysis using monoaquo catalysts such as $[Co(tetren)(OH_2)]^{3+}$.[8] When Lewis acid activation is the mechanism of acceleration, the rate of hydrolysis is typically enhanced by 2−3 orders of magnitude.[46] Note, however, that $[Co(tetren)(OH_2)]^{3+}$ is an ineffective catalyst for the hydration of phosphate diesters, a reaction observed to be accelerated by catalyst **1**. Furthermore, Kuo et al. have observed that the rate of organophosphate ester hydrolysis catalyzed by $[Cp_2Mo(OH)(H_2O)]^+$ is 10^8 times greater than the hydrolysis in water alone.[34] Clearly, to account for the improved rate of hydrolysis, the metal must play a more active role than simple substrate coordination and activation.

A second possible mechanism involves the metal-bound hydroxide as a nucleophile in an intermolecular attack on an unactivated (noncoordinated) substrate (Scheme 4b). However, this possibility seems remote, as metal-bound hydroxides are not known as good nucleophiles. Sutton and Buckingham report that metal

(43) Ford, P. C. *Acc. Chem. Res.* **1981**, *14*, 31−37.
(44) Hutchings, G. J.; Gottschalk, F.; Hunter, R.; Orchard, S. W. *J. Chem. Soc., Faraday Trans. 1* **1989**, *85*, 363−371.
(45) Hargreaves, M. D.; Mahon, M. F.; Whittlesey, M. K. *Inorg. Chem.* **2002**, *41*, 3137−3145.
(46) Hendry, P.; Sargeson, A. M. *Aust. J. Chem.* **1986**, *39*, 1177−1186.

Scheme 5. Proposed General Mechanism of Intramolecular Hydroxide Attack with Catalyst 1



hydroxides are only good (bimolecular) nucleophiles when the substrate is very electrophilic, as in the case of SO_2 or CO_2, or when the leaving group is particularly strong such as in activated esters, acid chlorides, or anhydrides.[9] Clearly, in the hydrolysis of ethyl acetate (as in nearly all of the reactions reported herein) there is neither a good leaving group nor a highly electrophilic substrate, and thus this mechanism cannot account for the catalytic activity.

A third mechanism can be postulated, based on the activity of the bound hydroxide ligand. If the substrate is coordinated to the metal center, the bound hydroxide ligand could act as a general base catalyst (Scheme 4c). If such were the case, an increased rate of hydrolysis via Lewis acid activation as well as general base catalysis would be expected. If general base catalysis were an important factor, the addition of buffer should increase the reaction rate due to the increased likelihood of general base catalysis by the buffer itself.[28] However, this was not observed experimentally. In fact, the addition of a noncoordinating buffer such as NaMOPS resulted in no net change in the reaction rate.[47] In addition, if this mechanism were operative, H/D exchange should occur at the α-position to the electrophilic atom due to formation of an enolate type species. However, no exchange was observed in the hydration of nitriles. (Unfortunately, the H/D exchange in the products (post-hydrolysis) of ester hydrolysis precludes using this analysis with the other substrates.)

The final and most likely mechanism of hydrolysis involves both Lewis acid activation of the substrate and intramolecular nucleophillic attack by the bound hydroxy ligand (Scheme 4d). The coordination of the substrate in place of a labile aquo ligand is the first step in the hydration (Scheme 5). The intramolecular attack of the hydroxide is facilitated by the juxtaposition of the ligands and the consequent high probability of orbital overlap.[9] Intramolecular hydroxide attack leads to the formation of a constrained cyclic intermediate. The molybdocene intermediate has not been isolated due to its reactivity, but it was observed in mass spectrometry analysis of the products of norborenyl acetate hydrolysis (see species **3**). It is noteworthy that the ability to stabilize the cyclic intermediate accounts for the increased reactivity of $[Co(trpn)(OH_2)_2]^{3+}$ over $[Co(tren)(OH_2)_2]^{3+}$ in phosphate ester hydrolysis.[10]

(47) At high concentrations of NaMOPS, it is possible that the concentration of monomeric catalyst **1** would decrease due to an equilibrium shift due to salt effects. However, this was not observed with the concentrations of buffer used in this experiment.

It is proposed that formation of the cyclic intermediate is the slow step in the catalytic pathway.[48] The activation parameters, $\Delta H^{\ddagger} = 5.9 \pm 0.7$ kcal/mol and $\Delta S^{\ddagger} = -48 \pm 9$ eu, measured for the hydrolysis of ethyl acetate with catalyst **1** are consistent with a geometrically constrained transition state. With $Cu(i\text{-}Pr[9]aneN_3)^{2+}$, the hydrolysis of phosphodiesters was reported to proceed via an intramolecular nucleophilic attack with activation parameters $\Delta H^{\ddagger} = 10.59$ kcal/mol and $\Delta S^{\ddagger} = -26.2$ eu.[49] (In this case, the bite angle of the tris(amino) ligand in the copper catalyst constrains the bound phosphate ester and hydroxide, in essence preorganizing the ligands and thereby making the activation entropy less negative.) Interestingly, Kuo measured the activation parameters for phosophate ester hydrolysis with Cp_2MoCl_2 and found $\Delta H^{\ddagger} = 9.8$ kcal/mol and $\Delta S^{\ddagger} = -49$ eu. He ascribed the catalytic activity to an intermolecular attack (4a) but could not rule out an intramolecular pathway with a constrained transition state.

The acceleration of hydrolysis by a factor of 10^8 as reported by Kuo for phosphate diesters using **1** and acceleration of carboxylic ester hydrolysis by a factor of 10^6 using **1** are both consistent with the dual activation mechanism in Scheme 5.[50] In systems that likely undergo the same intramolecular nucleophillic attack using other catalysts (such as $[Co(cyclen)(OH_2)_2]^{3+}$), the rate of dimethyl phosphate hydrolysis is on the order of 10^{10} times greater than that of water hydrolysis.[8] In summary, the high rate of acceleration shown by these catalyst systems is best explained by the dual activation pathway in Scheme 4d and Scheme 5.

Finally, it is noted that other researchers have used substitutionally inert complexes to confirm intramolecular hydroxide attack via isotope studies.[9,12] However, the lability of the aquo and hydroxy ligands in catalyst **1** prevented isotopic analysis because the coordinated ligands exchanged with the solvent on a shorter time scale than hydrolysis.

Conclusion

Complex **1** is a catalyst for the hydrolysis of carboxylic esters, ethers, and phosphate esters, the hydration of nitriles, and a stoichiometric reagent for the oxidation of carbon monoxide. In evaluating the structure/activity relationship of **1** and other hydration catalysts, it is apparent that *cis*-aquo/hydroxy ligands are ideally suited for catalyzing the hydrolysis/hydration/oxidation of organic substrates because the labile aquo ligand can be easily displaced to coordinate various functional groups and the second ligand (often a hydroxide) can promote hydration by way of an intramolecular attack

(48) In fact, the formation of the cyclic intermediate with amide substrates seems to be preventing amide hydrolysis. Interestingly, although catalyst **1** hydrolyzes difficult substrates such as phosphate esters and hydrates nitriles, the hydrolysis of amides was not observed under any reaction conditions used in this study. It does not seem plausible that hindrance of amide coordination to the catalyst is the problem because amide coordination is a noted inhibitor of nitrile hydrolysis (see ref 3). Therefore, the intramolecular hydroxide attack (to form the four-membered cyclic species) would seem to be problematic. The absence of amide hydrolysis by **1** counters the common belief that the hydrolysis behavior of carboxylic esters (particularly activated esters) can be used as models for amide hydrolysis by peptidases (see ref 10).

(49) Deck, K. M.; Tseng, T. A.; Burstyn, J. N. *Inorg. Chem.* **2002**, *41*, 669−677.

(50) Kuo, L. Y.; Barnes, L. A. *Inorg. Chem.* **1999**, *38*, 814−817.

on a bound substrate. Even early transition metals, typically dismissed as too oxophilic, can be used to form *cis*-diaqua type complexes, which are active catalysts. From the enhanced reactivity, activation parameters, and lack of H/D exchange, it is likely that the hydration, hydrolysis, and oxidation reactions proceed via an intramolecular hydroxide attack. The observations presented here promote the increased understanding of aqueous organometallic mechanisms and could be useful for the development of artificial hydrolytic enzymes and efficient catalysts for the destruction of chemical weapons.

Acknowledgment is made to the NSF for the support of this research and to Professor Louis Kuo for helpful discussions. K.L.B. acknowledges a DOE GAANN fellowship for partial support.

Supporting Information Available: Experimental details on the hydrolysis of other carboxylic esters and the mass spectrum of the products from the reaction of **1** with CO are available free of charge via the Internet at http://pubs.acs.org.

OM0342558