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Europium Ion Catalyzed Methanolysis of Esters at Neutral ${}_{s}^{s}$pH and Ambient Temperature. Catalytic Involvement of $Eu^{3+}(CH_3O^-)(CH_3OH)_x$

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The Eu^{3+}-promoted methanolysis of three esters, *p*-nitrophenyl acetate (**1**), phenyl acetate (**2**), and ethyl acetate (**3**) is reported, as well as the potentiometric titration of Eu^{3+} in MeOH at various $[Eu(SO_3CF_3)_3]$ (SO_3CF_3 = OTf). The titration data are analyzed in terms of two ionizations corresponding to macroscopic ${}_{s}^{s}pK_a^{\mathbf{1}}$ and ${}_{s}^{s}pK_a^{\mathbf{2}}$ values, which are respectively defined as the ${}_{s}^{s}$pH values at which the $[CH_3O^-]/[Eu^{3+}]$ = 0.5 and 1.5. As a function of increasing $[Eu(OTf)_3]$, ${}_{s}^{s}pK_a^{\mathbf{1}}$ increases slightly due to a proposed $Eu^{3+}/^{-}OTf$ ion pairing effect, which tends to reduce the acidity of the metal-coordinated CH_3OH, while ${}_{s}^{s}pK_a^{\mathbf{2}}$ decreases due to the formation of Eu^{3+} dimers and oligomers which stabilize the $(Eu^{3+}(CH_3O^-)_2)_n$ forms through bridging of the methoxides between two or more metal ions. For ester **1**, a detailed kinetic analysis of the reaction rates as a function of both $[Eu(OTf)_3]$ and ${}_{s}^{s}$pH in buffered methanol reveals that the ${}_{s}^{s}$pH/second-order rate constant (k_2) plot for the catalyzed reaction follows a bell-shaped profile, suggesting that the active form is a $Eu^{3+}(CH_3O^-)$ monomer with a kinetic ${}_{s}^{s}pK_a^{\mathbf{1}}$ of 6.33 ± 0.06 for formation and a ${}_{s}^{s}pK_a^{\mathbf{2}}$ of 8.02 ± 0.10 for its conversion into the inactive $(Eu^{3+}(CH_3O^-)_2)_n$ oligomeric form. At higher ${}_{s}^{s}$pH values, plots of k_{obs} vs $[Eu(OTf)_3]$ are linear at low metal concentration and plateau at higher metal concentration due to the formation of inactive higher order aggregates. The $Eu^{3+}(CH_3O^-)$ catalysis of the methanolysis of esters **1**, **2,** and **3** is substantial. Solutions of 10^{-2} M of the catalyst at ${}_{s}^{s}$pH 7.12 accelerate the reaction relative to the methoxide reaction at that ${}_{s}^{s}$pH by 8 530 000-, 195 000 000- and 7 813 000-fold, respectively.

Introduction

Transesterification reactions are important in organic and industrial chemistry, and many of these are known to be catalyzed by metal ions.[1] In previous studies we have demonstrated that La^{3+} ion shows a remarkable ability to promote the methanolysis of carboxylate esters,[2] activated amides,[3] and phosphate diesters.[4,5] Detailed study of the mechanisms of the first two of these reactions indicates that the active species is best described as a bis methoxy-bridged La^{3+} dimer with associated methanols of solvation, $(La^{3+})_2(CH_3O^-)_2(CH_3OH)_x$. This species, observable by electrospray mass spectrometry,[2] is conveniently formed in the neutral ${}_{s}^{s}$pH region[6] (${}_{s}^{s}pK_a$ 7.35) by simple treatment of $La(SO_3CF_3)_3$ solution in methanol with 1 equiv of $NaOCH_3$. As little as 5 mM of the dimeric catalyst can accelerate the transesterification reactions of a variety of esters (aryl, alkyl, aroyl, alkanoyl) relative to the background methoxide reaction by 40 000- to 18 000 000-fold at 25 °C.[2]

The remarkable acceleration of these reactions by La^{3+} suggests that other lanthanide ions might exhibit interesting catalytic properties. Herein we describe our studies of the

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[5] Brown, R. S.; Neverov, A. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1039−1049.

[6] For the designation of pH in nonaqueous solvents we use the forms described by Bosch and co-workers[8] based on the recommendations of the IUPAC: *Compendium of Analytical Nomenclature. Definitive Rules 1997*, 3rd ed.; Blackwell: Oxford, U.K., 1998. If one calibrates the measuring electrode with aqueous buffers and then measures the pH of an aqueous buffer solution, the term ${}_{w}^{w}$pH is used, if the electrode is calibrated in water and the "pH" of the neat buffered methanol solution then measured, the term ${}_{w}^{s}$pH is used, and if the electrode is calibrated in the same solvent and the "pH" reading is made, then the term ${}_{s}^{s}$pH is used.

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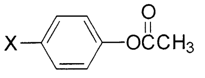
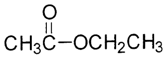
methanolysis of esters **1**−**3** with Eu^{3+}, introduced into $^{s}_{s}$pH-controlled buffered solutions as its commercially available trifluoromethanesulfonate (triflate) salt. This metal ion also has a remarkable catalytic effect on the rate of methanolysis of **1**−**3**, but it behaves quite differently from La^{3+} in terms of the catalytically active form and the overall speciation in solution.



1 X=NO2
2 X=H



$CH_3\overset{O}{\overset{\|}{C}}-OCH_2CH_3$

3

Experimental Section

Materials. $Eu(SO_3CF_3)_3$ (Aldrich) was used as received to prepare stock solutions in methanol. Methanol (anhydrous and HPLC grades) and $NaOCH_3$ were purchased from Aldrich and were used without further purification. *p*-Nitrophenyl acetate (**1**), phenyl acetate (**2**), and ethyl acetate (**3**) were commercial materials and were used as received.

Potentiometric Titration. Potentiometric titrations of the Eu^{3+}-containing methanol solutions were performed with a Radiometer Vit 90 Autotitrator under argon at 25 °C, as described in our recent publications with La^{3+}.[2−5] The concentrations of $Eu(OTf)_3$ in the range $(1.00-30.0) \times 10^{-4}$ M and sodium methoxide titrant (0.004−0.01 M solutions, prepared from stock 0.5 M sodium methoxide provided in a Sure Seal bottle) was calibrated by titrating standardized HCl (0.02 M in H_2O) with the endpoint taken to be pH 7.0. The values of the dissociation constants ($^{s}_{s}pK_a$) were calculated by using the computer program PKAS.[7] The $^{w}_{w}pK_w$ in the program was replaced by the autoprotolysis constant for methanol at 25 °C ($^{s}_{s}pK_{MeOH} = 16.77$).[8]

Kinetics. UV kinetics of methanolysis of **1** were monitored by observing the rate of the loss of $(2-10) \times 10^{-5}$ M starting material **1** at 265 nm and by the appearance of *p*-nitrophenol at 311 nm (for **1**) or phenol at 279 nm (for **2**) under pseudo-first-order conditions of excess metal ion ($(0.04-1.0) \times 10^{-3}$ M) at 25 °C using an OLIS-modified Cary 17 UV−vis spectrophotometer or SPECTRAmaxPLUS 384 microplate reader. For these runs the kinetics were determined under buffered conditions. The methods for determining and controlling the $^{s}_{s}$pH in methanol with buffers are reported in our earlier publications[2−4] and are based on procedures described by Bosch and co-workers.[8] The buffers, $(6.7-20) \times 10^{-3}$ M, used were *N*,*N*-dimethylaniline ($^{s}_{s}pK_a \sim 5.0$), 2,6-lutidine ($^{s}_{s}pK_a = 6.86$), *N*-methylimidazole ($^{s}_{s}pK_a = 7.60$), and *N*-ethylmorpholine ($^{s}_{s}pK_a = 8.28$). Because we have observed that added counterions can ion pair with Ln^{3+} ions[12] and affect their speciation in solution, the buffers were partially neutralized with $HClO_4$ in such a way to maintain the $[ClO_4^-]$ at a low but constant value of 5×10^{-3} M, which leads to a reasonably constant ionic strength in solution. Pseudo-first-order rate constants (k_{obs}) were evaluated by fitting the absorption vs time traces (followed for at least 3 half-times) to a standard exponential model.

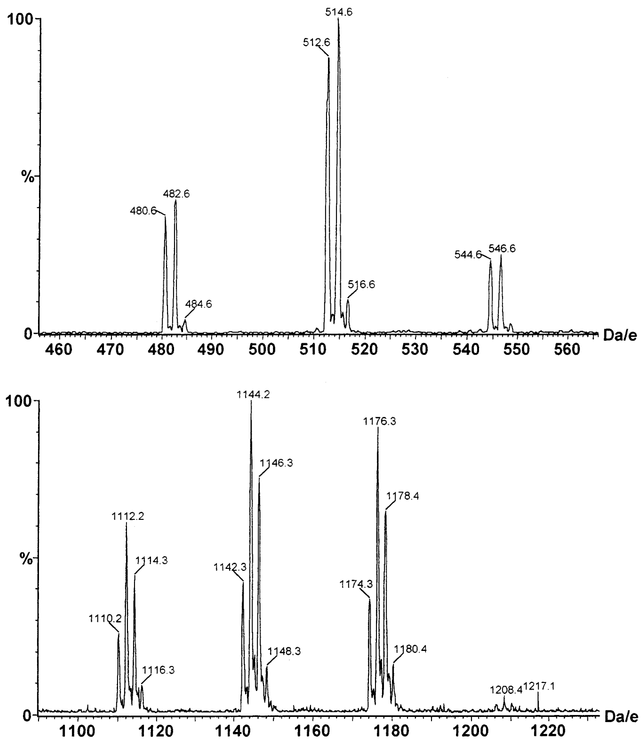


Figure 1. Two mass ranges of the ES-MS spectrum of a 0.001 M solution of $Eu(OTf)_3$ in methanol, cone voltage 31, showing the presence of monomeric and dimeric Eu^{3+} forms with associated counterions and methanols of solvation.

The kinetics of methanolysis of ethyl acetate (**3**) were determined by ^1H NMR at 25 °C using Bruker AC 200 and Avance 400 NMR machines. The active Eu^{3+} catalyst was generated in situ using 10^{-2} M $Eu(OTf)_3$ and known amounts of $NaOCH_3$ or $NaOCD_3$ in CD_3OD, after which **3** was added (1.0 M). The pseudo-first-order rate constant (k_{obs}) for the methanolysis was determined by fitting the CH_3CH_2O peak intensity vs time data to a standard exponential model.

Electrospray MS. Mass spectra of 10^{-3} M solutions of $Eu(OTf)_3$ in methanol were determined by using a VG Quattro mass spectrometer equipped with an electospray source operating at cone voltages between 15 and 90 V. Both monomeric and dimeric species peaks related to $[Eu(CF_3SO_3)_2]^+$ and $[Eu_2(CF_3SO_3)_5]^+$ can be observed (Figure 1), appearing as clusters having solvating methanol molecules, the number and intensity of which were found to be dependent on cone voltage. Higher order aggregates were not observed up to mass 3000. The electrospray MS of complexes of Eu^{3+} with added methoxide anions was undertaken by using methanol solutions containing 0.001 M of both $Eu(OTf)_3$ and Bu_4NOH (40% in water). Under those conditions a monomeric species containing a single methoxide anion $[Eu(CF_3SO_3)(CH_3O)]^+$ was observed as a cluster with 0−3 methanol molecules, depending on cone voltage being used. Peaks corresponding to $[Eu(CF_3SO_3)_2(CH_3OH)_n]^+$ with

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(8) (a) Bosch, E.; Rived, F.; Rosés, M.; Sales, J. *J. Chem. Soc., Perkin Trans.* **1999**, *2*, 1953. (b) Rived, F.; Rosés, M.; Bosch, E. *Anal. Chim. Acta* **1998**, *374*, 309. (c) Bosch, E.; Bou, P.; Allemann, H.; Rosés, M. *Anal. Chem.* **1996**, *68*, 3651.

(9) (a) Gómez-Tagle, P.; Yatsimirsky, A. K. *J. Chem. Soc., Dalton Trans.* **2001**, 2663. (b) He, H.; Martell, A. E.; Motekaitis, R. J.; Reibenspies, J. H. *Inorg. Chem.* **2000**, *39*, 1586.

(10) Hyperquad 2000 (Version 2.1 NT) available as referenced in: Gans, P.; Sabatini, A.; Vacca, A. *Talanta* **1996**, *43*, 1739.

(11) In certain cases, particularly for the second dissociation step, titration curves were steeper than theoretical, indicating that there is some degree of cooperativity in this process. To describe it and obtain a better fit, we have used a four-proton model, where one dissociation step would be represented by two independent $^{s}_{s}pK_a$ values, each corresponding to dissociation of a half of an equivalent of protons. This approach is similar to one we used previously (ref 3) in the case of dimeric La^{3+} species.

(12) Neverov, A. A.; Gibson, G.; Brown, R. S., manuscript in preparation.

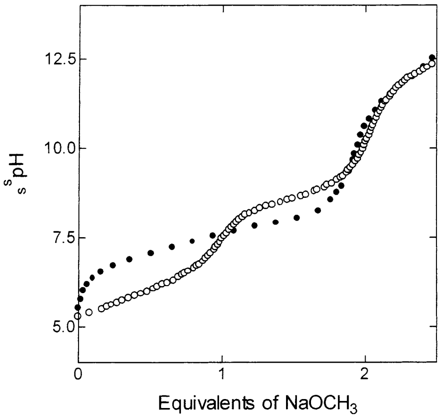


Figure 2. Potentiometric titration curves of Eu(OTf)$_3$ at 1 × 10^{-4} M (○) and 3 × 10^{-3} M (●) in CH$_3$OH at 25 °C.

1−4 methanol molecules were also observed, but higher order aggregates containing more than one Eu^{3+} could not be identified.

Luminescence Spectroscopy. Luminescence spectra of varying concentrations of Eu(OTf)$_3$ in methanol (HPLC grade, Aldrich) with or without added methoxide were recorded with a FeliX (Photon Technology) instrument at ambient temperature. The choice of HPLC grade methanol was dictated by the fact that the anhydrous solvent that was used for the kinetic experiments contained a small, but significant, amount of impurity that provided some background luminescence.

Results and Discussion

a. Potentiometric Titration of Eu^{3+} in Methanol. As expected based on the aqueous behavior of M^{3+} and what we have observed in our previous studies,[2−4] coordination of methanol to a lanthanide cation causes a drastic reduction in the CH$_3$O*H* ionization constants. Previously we noticed that, during the potentiometric titration of La^{3+} in methanol, there are two distinct titration steps. The first has an apparent $_s^s$p$K_a^{\mathbf{1}}$ of ∼7.3, consuming 1 equiv of CH$_3$O$^-$/ La^{3+}, and the second has an apparent $_s^s$p$K_a^{\mathbf{2}}$ around 10, which consumes about 1.5 equiv of CH$_3$O$^-$/La^{3+}.[3,4] We have analyzed the first in terms of formation of a dimeric La^{3+} species with two bridging methoxides and the second in terms of formation of (La^{3+})$_2$(CH$_3$O$^-$)$_5$. Our preliminary results in the present study immediately brought to light that at millimolar concentrations, Eu^{3+} displays a different behavior since only a single titration step consuming 2.0 equiv of OCH$_3$$^-$/Eu^{3+} was observed.

A more detailed study revealed a significant [Eu(OTf)$_3$] dependence of both the shape of the titration curve and the values of the ionization constants. Shown in Figure 2 are two titration curves obtained at Eu(OTf)$_3$ concentrations of 3 × 10^{-3} and 1 × 10^{-4} M. As indicated above, at the higher [Eu(OTf)$_3$] only one titration step can be observed, accounting for the release of two protons. However, at the lower concentration of 10^{-4} M there are two distinct steps, each corresponding to the release of one proton. Notably, the appearance of the second part of the latter titration curve is steeper than required for a single ionization event and suggests a more complex situation which is minimally presented in Scheme 1. Additional evidence for the kinetic role of these species is presented in part b.

Scheme 1. $n = 2, 3, ..., n$

$$Eu^{3+}(CH_3OH)_x \overset{K_a^{1}}{\rightleftharpoons} Eu^{3+}(CH_3O^-)(CH_3OH)_y + H^+$$

$$Eu^{3+}(CH_3O^-)(CH_3OH)_y \overset{K_a^{2}}{\rightleftharpoons} Eu^{3+}(CH_3O^-)_2(CH_3OH)_z + H^+$$

$$nEu^{3+}(CH_3O^-)_2(CH_3OH)_z \overset{K_{olig}}{\rightleftharpoons} (Eu^{3+}(CH_3O^-)_2(CH_3OH)_z)_n$$

Table 1. Macroscopic Apparent $_s^s$pK_a Values for the Dissociation of Eu^{3+}-Coordinated Methanol Molecules, T = 25 °C, CH$_3$OH Solvent

[Eu(OTf)$_3$], mM	$_s^s$p$K_a^{\mathbf{1}}$	$_s^s$p$K_a^{\mathbf{2}}$
0.1	6.07 ± 0.27	8.64 ± 0.007
0.2	6.04 ± 0.19	8.54 ± 0.14
1.0	6.62 ± 0.15	8.17 ± 0.14
2.0	6.76 ± 0.02	8.04 ± 0.07
3.0	7.17 ± 0.12	7.91 ± 0.15

To confirm the existence of the species suggested in Scheme 1, we obtained the electrospray MS of solutions of Eu(OTf)$_3$ in methanol at different concentrations of added base (see the Experimental Section). In the absence of base (see Figure 1), peaks attributable to the solvated metal ions with triflate counterions [Eu(CF$_3$SO$_3$)$_2$]$^+$ and [Eu$_2$(CF$_3$SO$_3$)$_5$]$^+$ were observed, while in the presence of 1 equiv of base (figure not shown), peaks attributable to the solvated Eu^{3+}-methoxide complex [Eu(CF$_3$SO$_3$)(CH$_3$O)]$^+$ were observed along with solvated [Eu(CF$_3$SO$_3$)$_2$]$^+$. In the presence of 2 equiv of added base, no definable peaks attributable to [Eu(CH$_3$O)$_2$]$^+$ were observed, which is consistent with the proposed oligomerization in Scheme 1.

Complex equilibria such as that shown in Scheme 1 have been successfully fit in studies of certain metal ions with ligands in aqueous solution.[9] In our case, we have little additional data about the identity of higher order (Eu^{3+})$_n$ species and our attempts at fitting the Eu^{3+} titration data to the simplified process shown in Scheme 1 using one of the more sophisticated commercially available programs[10] were unsuccessful when all metal ion concentrations were considered. To simplify the interpretation, we consider there are two conditional macroscopic $_s^s$pK_a values, $_s^s$p$K_a^{\mathbf{1}}$ and $_s^s$p$K_a^{\mathbf{2}}$, which are respectively defined as the $_s^s$pH values at which the CH$_3$O$^-$/Eu^{3+} ratios are 0.5 and 1.5. We calculate the apparent macroscopic $_s^s$pK_a values using the program PKAS,[7,11] using $_s^s$pK_{MeOH} = 16.77 as the autoprotolysis constant of the solvent. The computed macroscopic $_s^s$p$K_a^{\mathbf{1}}$ values refer to simple ionization of the first Eu^{3+}-bound CH$_3$OH, but the second macroscopic $_s^s$p$K_a^{\mathbf{2}}$ refers to a complex mixture of the microscopic $K_a^{\mathbf{2}}$ and K_{olig} processes in Scheme 1. Presentation of the data in terms of two conditional macroscopic $_s^s$pK_a values at each [Eu^{3+}] as in Table 1 aids in visualizing the trend of increasing $_s^s$p$K_a^{\mathbf{1}}$ and decreasing $_s^s$p$K_a^{\mathbf{2}}$ as the [Eu^{3+}($^-$OTf)$_3$] increases. The increase in $_s^s$p$K_a^{\mathbf{1}}$ can be explained by an ion pairing/salt effect (specific or nonspecific) that increases as the [Eu(OTf)$_3$] rises, leading to a reduction in the acidity of (TfO$^-$)$_x$Eu^{3+}-coordinated CH$_3$OH. Similar acidity weakening effects are observed for La^{3+}(CH$_3$OH)$_x$ in methanol containing other anions, particularly with more nucleophilic anions such as I$^-$, Br$^-$, Cl$^-$, or NO$_3$$^-$ in whose presence the first $_s^s$pK_a values can increase by as much as 3−4 units.[12]

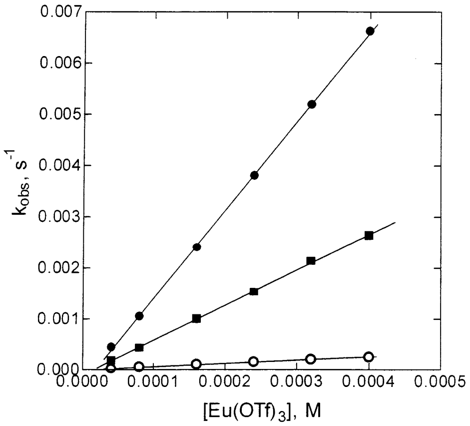


Figure 3. Plots of pseudo-first-order rate constants for the methanolysis of **1** vs [Eu(OTf)$_3$] at 25 °C; ${}_{s}^{s}$pH 4.52 (○), ${}_{s}^{s}$pH 5.52 (■), ${}_{s}^{s}$pH 6.2 (●).

Table 2. Second-Order Rate Constants for the Methanolysis of the Esters **1** and **2** Catalyzed by Eu(OTf)$_3$, T = 25 °C

ester	${}_{s}^{s}$pH	k_2, M^{-1} s^{-1}	ester	${}_{s}^{s}$pH	k_2, M^{-1} s^{-1}
1	4.52	0.65 ± 0.01	**1**	7.12	33.3 ± 1.3
1	5.00	2.2 ± 0.1	**1**	7.65	28.3 ± 1.5
1	5.52	6.89 ± 0.07	**2**	7.20	7.49 ± 0.16
1	6.20	17.2 ± 0.2	**2**	7.67	8.8 ± 0.4
1	6.70	27.7 ± 1.4	**2**	8.12	6.5 ± 0.25

In contrast to its effect on ${}_{s}^{s}$p$K_a^{\mathbf{1}}$, the second apparent dissociation constant (${}_{s}^{s}$p$K_a^{\mathbf{2}}$) drops with increasing [Eu(OTf)$_3$], consistent with a concentration-dependent dimerization or oligomerization. Taken together with the slightly steeper than normal appearance of the second titration curve, the oligomerization process shown in Scheme 1 (K_{olig}) apparently acidifies the metal-bound methanols, stabilizing the resulting Eu^{3+}(CH$_3$O$^-$)$_2$ by bridging methoxides between two metal ions and leading to a reduced ${}_{s}^{s}$p$K_a^{\mathbf{2}}$.

b. Kinetics. The rate of methanolysis of *p*-nitrophenyl acetate (**1**) increases markedly in the presence of Eu^{3+} at all ${}_{s}^{s}$pH values investigated; however, the overall kinetic behavior falls into two distinct ${}_{s}^{s}$pH regions. At ${}_{s}^{s}$pH values lower than 8.0, plots of k_{obs} vs [Eu(OTf)$_3$] were linear up to at least 5 × 10^{-4} M with a very small positive intercept (<10^{-5} M) (see Figure 3). In no case was there evidence for a significant upward curvature in the k_{obs} vs [Eu^{3+}] plots such as was observed for La(OTf)$_3$ catalysis of the methanolysis of esters and activated amides.[2,3] Therefore there is no evidence that dimers or higher order aggregates of Eu^{3+} are kinetically significant at these concentrations. In addition, this indicates that formation of higher order oligomers of reduced reactivity is not significant at these ${}_{s}^{s}$pH values and concentrations, otherwise the kinetic plots would show significant downward curvature. The slopes of the linear parts of the k_{obs} vs [Eu^{3+}] plots yield the second-order rate constants (k_2) for the metal-ion catalyzed methanolysis of **1** (Table 2). These, when plotted vs ${}_{s}^{s}$pH as in Figure 4, generate a bell-shaped profile maximizing around ${}_{s}^{s}$pH 7.1. The experimental second-order rate constants can only be obtained below ${}_{s}^{s}$pH 8−8.1 because the kinetic behavior drastically changes at higher ${}_{s}^{s}$pH values, as will be discussed later. The unit slope of the left-hand linear part of this graph indicates that there is only one CH$_3$O$^-$ involved in the catalytic transition state. This, coupled with the lack of any evidence for the kinetic involvement of species having more than one Eu^{3+} ion and the speciation of Eu^{3+} presented in Scheme 1, suggests the process shown in Scheme 2 in which a Eu^{3+}(CH$_3$O$^-$)(CH$_3$OH)$_y$ form is catalytically active.

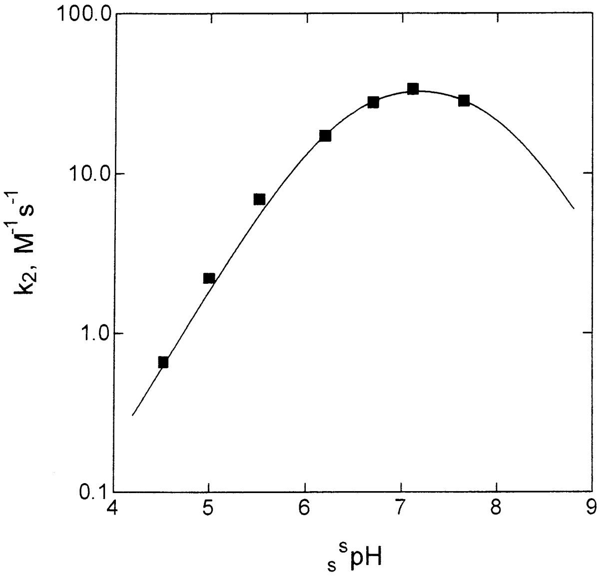
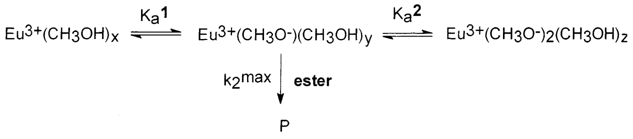


Figure 4. Plot of second-order rate constant (k_2) vs ${}_{s}^{s}$pH for Eu(OTf)$_3$-catalyzed methanolysis of **1**, T = 25 °C. Solid line is calculated from NLLSQ fit of the data to eq 1.

Scheme 2



NLLSQ fitting of the k_2 vs ${}_{s}^{s}$pH kinetic data to the expression in eq 1, derived on the basis of the mechanism

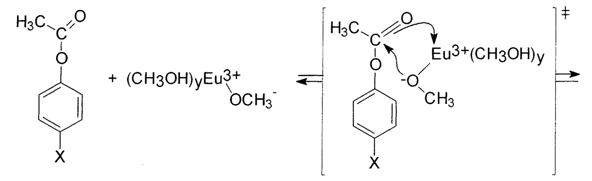
$$k_2 = k_2^{\max}\,{}_{s}^{s}K_a^{\mathbf{1}}[\mathrm{H}^+]/\left({}_{s}^{s}K_a^{\mathbf{1}}\,{}_{s}^{s}K_a^{\mathbf{2}} + {}_{s}^{s}K_a^{\mathbf{1}}[\mathrm{H}^+] + [\mathrm{H}^+]^2\right) \quad (1)$$

given in Scheme 2, gives $k_2^{\max}$ = 42 ± 2 M^{-1} s^{-1}, a kinetic ${}_{s}^{s}$p$K_a^{\mathbf{1}}$ of 6.33 ± 0.06, and ${}_{s}^{s}$p$K_a^{\mathbf{2}}$ = 8.02 ± 0.10 and generates the solid line through the data shown in Figure 4. The two kinetic ${}_{s}^{s}$pK_a values are in good agreement with the titrimetric macroscopic ${}_{s}^{s}$pK_a values given in Table 1 for a 1 mM concentration of Eu(OTf)$_3$, bearing in mind that the kinetic data are determined in the presence of buffers having 5 × 10^{-3} M [ClO$_4^-$] as counterion.

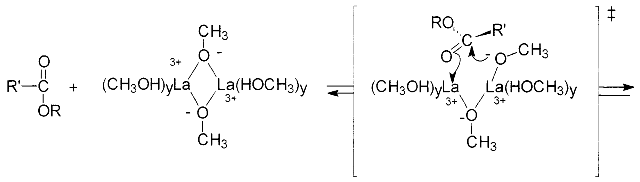
We undertook a similar kinetic study with ester **2**, but due to the limited change in absorbance that accompanies this reaction at 279 nm, we could only study the reaction in buffered solutions in a narrow range above ${}_{s}^{s}$pH 7 (see Table 2). Nevertheless, fitting the three available k_2 values to eq 1 using the two kinetic ${}_{s}^{s}$pK_a values determined for ester **1** gives a $k_2^{\max}$ value for methanolysis of **2** catalyzed by Eu^{3+}(CH$_3$O$^-$) of 11.7 ± 1.5 M^{-1} s^{-1}.

The value for the $k_2^{\max}$ for Eu^{3+}($^-$OCH$_3$)(CH$_3$OH)$_m$-catalyzed methanolysis of the two esters is close to, or even exceeds, the second-order rate constant for attack of meth-

Scheme 3



Scheme 4



oxide on these ($42\ M^{-1}\ s^{-1}$ vs $220 \pm 100\ M^{-1}\ s^{-1}$[13] for **1** and $11.7\ M^{-1}\ s^{-1}$ vs $2.66\ M^{-1}\ s^{-1}$[14] for **2**), even though the basicity of the Eu^{3+}-bound methoxide is approximately 10^{10}-fold lower. We propose that the additional catalytic effect of $Eu^{3+}(^{-}OCH_3)$ arises from a bifunctional behavior involving a simultaneous Lewis acid and nucleophilic role for the complex as in Scheme 3.

It is interesting to compare the second-order rate constants for $Eu^{3+}(CH_3O^-)$ catalyzed methanolysis of **1** and **2** with the $72\ M^{-1}\ s^{-1}$ and $58 \pm 3\ M^{-1}\ s^{-1}$ that we determined previously [2] for the k_2^{max} for La^{3+}-catalyzed methanolysis of the same esters. Detailed kinetic analysis of the La^{3+}-catalyzed methanolysis of **1** clearly indicates that the active species has the stoichiometry $(La^{3+})_2(CH_3O^-)_2$, which we proposed as reacting through an open form as shown in Scheme 4.

While all the above evidence points to the fact that the $Eu^{3+}(CH_3O^-)$ form is catalytically active, addition of the second CH_3O^- to Eu^{3+} not only produces a far less reactive or inactive form (see Scheme 2) but drastically changes the kinetic behavior. Indeed, at ${}^{s}_{s}pH$ values higher than 8.3 (above ${}^{s}_{s}pK_a^{2}$) the kinetic profiles of k_{obs} vs $[Eu(OTf)_3]$ have a definite nonlinear behavior as exemplified in Figure 5 (${}^{s}_{s}pH$ 9.05). After an initial increase in k_{obs}, the value plateaus above $[Eu(OTf)_3]$ of $\sim 2 \times 10^{-4}$ M, depending upon the ${}^{s}_{s}pH$, and this effect is observed for both esters **1** and **2**. It is difficult to envision any preequilibrium saturation binding of the ester to the metal ion as being responsible for this effect, and kinetic analysis indicates that the curve is more complex than what is required for such behavior. One possible explanation of this is formation of higher-order Eu^{3+} aggregates as illustrated in Scheme 1, which can be promoted by a weblike coordination between two bridging methoxide anions and Eu^{3+} that can be expected to occur above ${}^{s}_{s}pK_a^{2}$. Similar aggregates are known for lanthanides in water[9,15] and usually lead to the formation of precipitates at high pH, but in methanol no precipitates are observed.

c. Eu^{3+}-Catalyzed Methanolysis of 3. To show that the Eu^{3+} catalytic system is active toward nonactivated esters and also has high catalytic turnover, we investigated the methanolysis of 1 M ethyl acetate (**3**) in MeOH-d_4 by NMR at 25 °C. Shown in Figure 6 is a plot of the pseudo-first-order rate constant for establishment of the equilibrium in eq 2 in the presence of 10^{-2} M $Eu(OTf)_3$ with added $NaOCD_3$ such that the $[CD_3ONa]/[Eu^{3+}]$ ratio varies between 0.0 and 2.4.

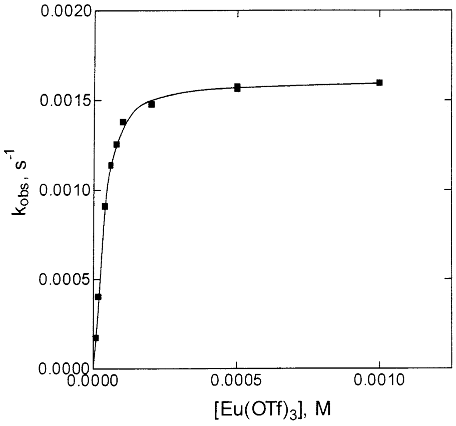


Figure 5. Plot of pseudo-first-order rate constants for the methanolysis of **1** vs $[Eu(OTf)_3]$ at 25 °C, *N*-ethylmorphiline buffer, ${}^{s}_{s}pH$ 9.05.

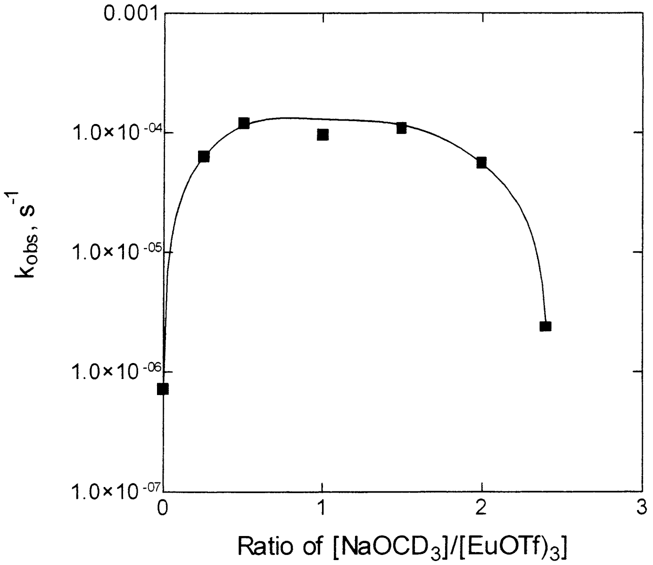


Figure 6. Plot of the observed rate constant for methanolysis of 1 M ethyl acetate in methanol-d_4 in the presence of 10^{-2} M $Eu(OTf)_3$ at various ratios of $[NaOCD_3]/\ [Eu(OTf)_3]$, $T = 25$ °C.

$$CH_3C(=O)OEt + CD_3OD \xrightleftharpoons{Eu^{3+}/CD_3O^-} CH_3C(=O)OCD_3 + EtOD \tag{2}$$

There are three points of note. The first is that the maximum rate constant of $\sim 1 \times 10^{-4}\ s^{-1}$ is attained at a $[CD_3ONa]/[Eu^{3+}]$ ratio between 0.5 and 1.5, consistent with the kinetic analysis for ester **1**, which suggests the active form is $Eu^{3+}(CH_3O^-)$. Second, in all cases the NMR analysis indicates that the equilibrium position has roughly 95% methyl acetate and 5% ethyl acetate. Since the catalyst must be capable of catalyzing the reverse reaction, by implication

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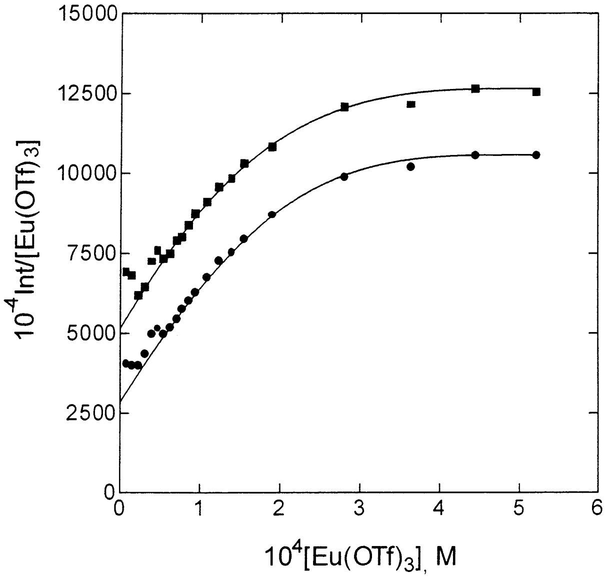

Figure 7. Plot of the luminescence efficiency, defined as intensities of luminescence peaks/[Eu(OTf)$_3$]$_t$ at 617 nm (■) and 626 nm (●) vs [Eu(OTf)$_3$]$_t$ in methanol solutions at ${}^s_s$pH 9.1 (*N*-ethylmorpholine buffer, 0.02 M).

Eu^{3+}-catalyzed ethanolysis reactions are also possible, although we have not investigated these in detail. Finally, from the large excess of **3,** it is also clear that the catalytic system is capable of high turnover and does not suffer the sort of "aging" degradation that is commonly seen for lanthanide catalysis of hydrolysis in water.[9a]

d. Luminescence of Eu^{3+} in Methanol. The nonlinear kinetic dependencies for methanolysis of esters **1** and **2** as a function of [Eu^{3+}] at ${}^s_s$pH values above 8.3 referred to in section b, implying the formation of nonactive $Eu^{3+}(^-OCH_3)_2$ aggregates, required further investigation. It is known[16] that certain lanthanide cations including Eu^{3+} [17] exhibit strong luminescent properties, and luminescence spectroscopy is widely used to investigate coordination chemistry of lanthanide ions in solution. Solutions of Eu(OTf)$_3$ in methanol, when irradiated with 395-nm light, exhibit two emission peaks at λ_{max} 592 and 617 nm. Further experiments showed that both the intensity and shape of these emission peaks are sensitive to ${}^s_s$pH. Addition of sodium methoxide (0.1−2 equiv) to a 4×10^{-4} M solution of Eu(OTf)$_3$ caused differential increases in the intensity of these two luminescence bands, the most sensitive being the one at 617 nm. This provides additional evidence of strong coordination of methoxide to Eu^{3+}. To establish if the speciation in solution is dependent on the [Eu^{3+}], we examined the luminescence spectra of 8×10^{-6} M < [Eu(OTf)$_3$] < 6×10^{-4} M in buffered solution at ${}^s_s$pH 9.1 (*N*-ethylmorpholine, 0.02 M). In Figure 7 are presented plots of the luminescence efficiency of the 617- and 626-nm peaks (defined as peak intensity/[Eu(OTf)$_3$]$_{total}$) as a function of [Eu(OTf)$_3$]$_{total}$. These show an increase followed by a plateau above [Eu(OTf)$_3$]$_{total}$ of 2×10^{-4} M, which is consistent with a concentration-dependent change in coordination sphere of Eu^{3+} as might result from the formation of higher order aggregates. The break in the luminescence profile coincides with the [Eu(OTf)$_3$], where a nonlinear kinetic behavior was observed in the k_{obs} vs [Eu(OTf)$_3$] plot (see above and Figure 5), suggesting that the luminescence and kinetic breaks can be attributed to the same process of formation of higher order aggregates at higher ${}^s_s$pH values.

It is important to stress that the putative oligomeric form is not catalytically important for the methanolysis of esters, but its formation results in an interesting kinetic phenomenon, which in our opinion is rarely observed. The k_{obs} vs [Eu(OTf)$_3$]$_{total}$ kinetic data for methanolysis of **1** at higher ${}^s_s$pH is consistent with a process involving catalytically active $Eu^{3+}(CH_3O^-)$ monomers in equilibrium with inactive higher order aggregates of Eu^{3+} ions as suggested in Scheme 1. The system bears strong resemblance to other concentration-dependent phenomena where a monomer is in equilibrium with an aggregate. A close analogy appears to be the behavior of micellar systems where, at total surfactant concentrations above the critical micelle concentration (cmc), aggregates containing *N* surfactant monomers spontaneously form. This behavior is described in eq 3 where *N* is the aggregation number.[18] The concentration of the free surfactant is always limited by the cmc which, by the analogy drawn to our case, is the amount of free $Eu^{3+}(CH_3O^-)$ responsible for catalysis.

$$[\text{micelle}] = ([\text{surfactant}]_t - \text{cmc})/N \qquad (3)$$

Conclusion

In the above we have shown that Eu^{3+} catalyzes the methanolysis of two activated esters and a nonactivated one, ethyl acetate, with high turnover numbers. The catalytically active form is a $Eu^{3+}(CH_3O^-)$ monomer. The Eu^{3+} system is notably different from the La^{3+} system we investigated earlier,[2] where the active form of the catalyst is a dimer of stoichiometry $(La^{3+})_2(CH_3O^-)_2$. Highest activity for the Eu^{3+} system is obtained in a ${}^s_s$pH 7.1−7.2 solution, midway between the two macroscopic kinetic ${}^s_s$pK_a values of ${}^s_s$p$K_a^{\mathbf{1}}$ = 6.33 ± 0.06 and ${}^s_s$p$K_a^{\mathbf{2}}$ = 8.02 ± 0.10. Above the second ${}^s_s$p$K_a^{\mathbf{2}}$, we observe the formation of higher order aggregates of general stoichiometry $(Eu^{3+}(CH_3O^-)_2)_n$, which are not catalytically active.

Catalytically active $Ln^{3+}(CH_3O^-)_x$ complexes for preparative purposes can easily be made by adding the Ln(OTf)$_3$ salts to methanol solution containing the appropriate number of equivalents of NaOCH$_3$.[5] Indeed, the $(La^{3+}(CH_3O^-))_2$ dimer we originally described has been shown recently to be particularly effective for deprotection of acylated alcohols that are sensitive to alkaline or acidic conditions.[19] The catalytically active $Eu^{3+}(CH_3O^-)$ form for preparative purposes can be generated in situ simply by treating a methanol

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solution of $Eu(OTf)_3$ (10^{-2} M) with 1 equiv of $NaOCH_3$. Under these conditions, the acceleration afforded to the methanolysis of **1**, **2,** and **3** by 10^{-2} M of this catalyst relative to the attack of methoxide at $^{s}_{s}$pH 7.12 is 8 530 000-, 195 000 000-, and 7 813 000-fold, respectively.[20] Given the large acceleration and ease of preparation of the catalyst, it can be envisioned that this system will be of value in promoting other transesterifications and for removing acyl protecting groups from alcohols under essentially neutral conditions. Quite possibly the monomeric composition of the Eu^{3+} catalyst will imbue different selectivities than are seen for the dimeric $(La^{3+}(CH_3O^-))_2$, a topic of future research in these laboratories.

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(20) The acceleration is computed relative to the reaction of methoxide at $^{s}_{s}$pH 7.12, where the $[CH_3O^-] = 2.24 \times 10^{-10}$ M, using the second-order rate constants for methoxide attack on **1**, **2**, and **3** of 220, 2.66, and 5.7×10^{-2} M^{-1} s^{-1}, respectively,[2] and the second-order rate constants (k_2^{max}) determined in this work of 42, 11.7, and 1×10^{-2} M^{-1} s^{-1}, respectively.