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Zn^{2+}-Catalyzed Methanolysis of Phosphate Triesters: A Process for Catalytic Degradation of the Organophosphorus Pesticides Paraoxon and Fenitrothion

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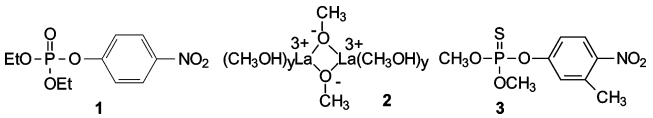
The methanolyses of two neutral phosphorus triesters, paraoxon (**1**) and fenitrothion (**3**), were investigated as a function of added $Zn(OTf)_2$ or $Zn(ClO_4)_2$ in methanol at 25 °C either alone or in the presence of equimolar concentrations of the ligands phenanthroline (**4**), 2,9-dimethylphenanthroline (**5**), and 1,5,9-triazacyclododecane (**6**). The catalysis requires the presence of methoxide, and when studied as a function of added $NaOCH_3$, the rate constants (k_{obs}) for methanolysis of Zn^{2+} alone or in the presence of equimolar **4** or **5** maximize at different $[^-OCH_3]/[Zn^{2+}]_{total}$ ratios of 0.3, 0.5, and 1.0, respectively. Plots of k_{obs} vs $[Zn^{2+}]_{total}$ either alone or in the presence of equimolar ligands **4** and **5** at the $[^-OCH_3]/[Zn^{2+}]_{total}$ ratios corresponding to the rate maxima are curved and show a nonlinear dependence on $[Zn^{2+}]_{total}$. In the cases of **4** and **5**, this is explained as resulting from formation of a nonactive dimer, formulated as a bis-μ-methoxide-bridged form (**L**:$Zn^{2+}(^-OCH_3)_2Zn^{2+}$:**L**) in equilibrium with an active monomeric form (**L**:$Zn^{2+}(^-OCH_3)$). In the case of the Zn^{2+}:**6** system, no dimeric forms are present as can be judged by the strict linearity of the plots of k_{obs} vs $[Zn^{2+}]_{total}$ in the presence of equimolar **6** and $^-OCH_3$. Analysis of the potentiometric titration curves for Zn^{2+} alone and in the presence of the ligands allows calculation of the speciation of the various Zn^{2+} forms and shows that the binding to ligands **4** and **6** is very strong, while the binding to ligand **5** is weaker. Overall the best catalytic system is provided by equimolar Zn^{2+}, **5**, and $^-OCH_3$, which exhibits excellent turnover of the methanolysis of paraoxon when the substrate is in excess. At a concentration of 2 mM in each of these components, which sets the ^s_spH of the solution at 9.5, the acceleration of the methanolysis of paraoxon and fenitrothion relative to the methoxide reaction is 1.8×10^6-fold and 13×10^6-fold, respectively. A mechanism for the catalyzed reactions is proposed which involves a dual role for the metal ion as a Lewis acid and source of nucleophilic Zn^{2+}-bound $^-OCH_3$.

Introduction

We recently reported a method for the decomposition of paraoxon (**1**) via a methanolysis reaction catalyzed by $La(OTf)_3$.[1] That metal ion proves to be remarkably effective in accelerating the methanolysis of unactivated and activated carboxylic acid esters,[2] activated amides such as β-lactams,[3] acetyl imidazole and its pentaminocobalt(III) derivative,[4] and certain phosphate diesters such as diphenyl phosphate, methyl *p*-nitrophenyl phosphate, bis(*p*-nitrophenyl) phosphate,[5a] and 2-hydroxypropyl *p*-nitrophenyl phosphate.[5b] In the case of neutral substrates such as carboxylate esters, β-lactams, and paraoxon, the dominantly active form of the catalyst is a La^{3+} dimer with two methoxides (formulated as **2**), although other forms such as $La^{3+}{}_2(^-OCH_3)_1$ and $La^{3+}{}_2(^-OCH_3)_3$ also have activity.



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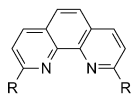
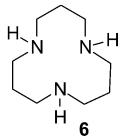
Activated neutral organophosphate, phosphinate, and phosphonate esters are acetylcholinesterase inhibitors,[6] and some of them have important uses as agricultural protectants[7] and as chemical warfare (CW) agents.[8] This family includes the insecticides parathion, malathion, and fenitrothion (**3**), as well as the alkylphosphonofluoridate G and alkylphosphonothioate V nerve agents. Considerable effort has been directed toward methods of facilitating the controlled decomposition of organophosphorus materials, particularly through hydrolysis and oxidation.[9,10] Transition-metal ions and lanthanides and certain mono- and dinuclear complexes thereof are known to promote the hydrolysis of neutral phosphate and/or phosphonate esters,[11,12] and quite recently Pt and Pd metallocycles were shown to be efficacious for thiophosphate pesticide hydrolysis.[13] However, in many cases the hydrolytic reactions of phosphate triesters or phosphonates promoted by the transition-metal ions present problems and are not truly catalytic because the products of hydrolysis (an anionic phosphate diester or an anionic phosphonic acid derivative, respectively) bind to the metal ion, thereby inhibiting further turnover. Moreover, at high pH values where the metal-containing complexes have activity, insolubility of $M^{x+}(^{-}OH)_n$ is a problem which often necessitates the use of complexing ligands to ensure homogeneity.[11,12]

We have demonstrated that some of these problems can be overcome by switching the decontamination methodology from a metal-promoted hydrolytic reaction to a metal-promoted alcoholysis reaction.[1] Since the leaving group (for example, *p*-nitrophenoxy in the case of paraoxon) is replaced by an alkoxy group, the products are neutral and noninhibitory because they will not bind to the metal ions substantially better than does the starting material. Alcoholysis reactions also may proceed with different selectivity than hydrolysis as is known for methanolysis of the V agents, where the reaction with methoxide proceeds largely to displace the SR^{-} group, leading to phosphonate methoxyesters.[8,14,15] Finally, aside from the increased substrate solubility in alcohols relative to H_2O, we have found that most metal ions are soluble at all $^{s}_{s}$pH values surrounding the $^{s}_{s}pK_a$ for ionization of the metal-bound alcohols.

Herein we expand our earlier study[1] to the case of a transition-metal ion by reporting a kinetic study of the Zn^{2+}-catalyzed methanolysis of two pesticides, namely, paraoxon and fenitrothion, in the absence and presence of the complexing agents phenanthroline (**4**), 2,9-dimethylphenanthroline (**5**), and 1,5,9-triazacyclododecane (**6**). As will be seen, switching to Zn^{2+} from La^{3+} allows for the rapid degradation of the P═S systems, providing an important methodology for the destruction of this class of pesticides.



4 R=H
5 R=CH3



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Experimental Section

a. Materials. Methanol (99.8% anhydrous), sodium methoxide (0.5 M solution in methanol), zinc perchlorate ($Zn(ClO_4)_2$), paraoxon, phenanthroline, 2,9-dimethylphenanthroline, and 1,5,9-triazacyclododecane were purchased from Aldrich and used without any further purification. Zinc triflate ($Zn(OTf)_2$) was purchased from Strem Chemicals Inc. $HClO_4$ (70% aqueous solution) was purchased from BDH. Fenitrothion was a gift from Prof. Erwin Buncel of the Department of Chemistry, Queen's University. *Caution: paraoxon and fenitrothion are toxic acetylcholinesterase inhibitors, with oral LD_{50} values of 1.8 and 250 mg/kg, respectively, in rats.*

b. Methods. ^{1}H NMR spectra were determined at 500 MHz and referenced to the CD_2H peak of d_4-methanol appearing at δ 3.31 ppm. ^{31}P NMR spectra were referenced to an external standard of 70% phosphoric acid in water, and upfield chemical shifts are negative. The $CH_3OH_2^{+}$ concentration was determined using an autotitrator equipped with a Metrohm 6.0255.100 combination (glass/calomel) electrode calibrated with standardized aqueous buffers (pH 4.00 and 10.00) as described in our recent papers.[2−5,16] Values of $^{s}_{s}$pH[17] were calculated by subtracting a correction constant of −2.24 from the experimental meter reading as reported

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by Bosch et al.[18] The $^{s}_{s}pK_a$ values of buffers used for the present kinetic studies were obtained from the literature[18] or measured at half-neutralization of the bases with 70% $HClO_4$ in MeOH.

Potentiometric titrations of $Zn(OTf)_2$ (5×10^{-4} to 2×10^{-3} M) were performed under Ar at 25 °C according to the general methods described for the titration of metal ions in methanol.[16] A known amount of perchloric acid, 0.6 equiv per Zn^{2+}, was added to the solution to obtain titration data in the lower $^{s}_{s}pH$ region. The exact concentration of the stock solution of the metal ion was determined by EDTA/Eriochrome Black-T titration,[19] and all potentiometric titrations were performed in duplicate using sodium methoxide solutions standardized by titration against 3,5-dinitrobenzoic acid to the equivalence point.

The potentiometric data were analyzed using the computer program Hyperquad 2000 (version 2.1 NT).[20] Titrations were subsequently performed with the metal ion in the presence of equimolar **4**−**6**, and the data analyzed as described in the Results, with all the associated stability constants being given in Table 2.

c. Kinetics. UV−vis kinetics of methanolysis were monitored at 25 °C by observing the rate of loss of **1** or **3** at 268 nm or the rate of appearance of *p*-nitrophenol or 3-methyl-4-nitrophenol between 312 and 335 nm at [**1**] or [**3**] between 4×10^{-5} and 12×10^{-5} M using an OLIS-modified Cary 17 UV−vis spectrophotometer or Cary 100 spectrophotometer. The $[Zn(OTf)_2]$ was varied from 0.2×10^{-3} to 2.0×10^{-3} M. All reactions were followed to at least three half-times and found to exhibit good pseudo-first-order rate behavior. The pseudo-first-order rate constants (k_{obs}) were evaluated by fitting the absorbance vs time traces to a standard exponential model.

The kinetics were all determined under conditions where the $^{s}_{s}pH$ was controlled by a constant $[Zn^{2+}]/[Zn^{2+}(^{-}OCH_3)]$ ratio. In the cases with ligands **4**−**6**, these were added in amounts equivalent to $[Zn^{2+}]_{total}$. Due to the fact that added counterions can ion-pair with Zn^{2+} ions and affect the speciation in solution,[16] the ionic strength was not controlled, but varied with the total $[Zn^{2+}]$ between values of 2×10^{-4} and 20×10^{-4} M. All derived kinetic parameters are given in Table 1.

Table 1. Kinetic Constants for the Methanolysis of **1** and **3** Catalyzed by Zn^{2+} in the Absence and Presence of Ligands **4**−**6**, $T = 25$ °C

catalyst	K_{dis}[a] (mM)	k_m^1[a] ($M^{-1}\,min^{-1}$)	k_m^3[a] ($M^{-1}\,min^{-1}$)
$^{-}OCH_3$	NA	0.66	0.043 ± 0.001
Zn^{2+}[b]	<0.005	72.5 ± 1.5	11.2 ± 0.4
Zn^{2+}:**4**[c]	<0.005	124 ± 2.5	19.0 ± 0.6
Zn^{2+}:**4**$(^{-}OCH_3)_2$[d]	NA	29.5 ± 0.7	2.7 ± 0.1
Zn^{2+}:**5**[e]	0.6 ± 0.2	101 ± 1	48.0 ± 0.7
Zn^{2+}:**6**$(^{-}OCH_3)$[f]	NA	50.8 ± 0.8	2.9 ± 0.1
$La^{3+}{}_2(^{-}OCH_3)_2$[g]	NA	2830 ± 140	*h*

[a] Dimer dissociation constant (K_{dis}) and conditional second-order rate constant (k_m) for the monomer defined as in eq 1. NA means nonapplicable since there is no observable dimerization under the specific conditions. [b] Based on NLLSQ fits of k_{obs} vs $[Zn^{2+}]_{total}$ data to eq 2 at a [methoxide]/$[Zn^{2+}]_{total}$ ratio of 0.3. [c] Based on NLLSQ fits of k_{obs} vs $[Zn^{2+}$:**4**$]_{total}$ data to eq 2 at a [methoxide]/$[Zn^{2+}]_{total}$ ratio of 0.5. [d] Based on linear fits of k_{obs} vs $[Zn^{2+}$:**4**$]_{total}$ data at a [methoxide]/$[Zn^{2+}]_{total}$ ratio of 2.0. [e] Based on NLLSQ fits of k_{obs} vs $[Zn^{2+}$:**5**$]_{total}$ data to eq 2 at a [methoxide]/$[Zn^{2+}]_{total}$ ratio of 1.0. [f] Based on linear fits of k_{obs} vs $[Zn^{2+}$:**6**$(^{-}OCH_3)]_{total}$ data at [methoxide] = $[Zn^{2+}]_{total}$ = [**6**]. [g] From ref 1. [h] No catalysis observed.

Table 2. Formation Constants for Various Species Determined by Potentiometric Titration

	log $^{s}_{s}K$		
equilibrium	**L** = **4** system	**L** = **5** system	**L** = **6** system
[**L**−H^+]/[**L**][H^+]	5.63	6.43	14.92
[**L**:Zn]/[**L**][Zn]	10	4.25	10.11
$[Zn_2$: $\mathbf{L}_2(OMe)_2]/[\mathbf{L}]^2[Zn]^2[OMe]^2$	36.33	28.05	
[Zn:$\mathbf{L}(OMe)_2]/[\mathbf{L}][Zn^{2+}][OMe]^2$	20.58		21.67
[Zn:$\mathbf{L}$(OMe)]/[**L**][Zn][OMe]			17.79

d. ^{31}P NMR Experiment To Ascertain Turnover using Zn^{2+}:5($^{-}OCH_3$). To 0.6 mL of dry methanol (with 20% CD_3OD as an NMR lock signal) containing 1 mM each of $Zn(OTf)_2$, ligand **5**, and $NaOCH_3$ at ambient temperature was added 2.54 mg of paraoxon. At this point, the concentration of paraoxon was 15 mM and that of Zn^{2+}:**5**($^{-}OCH_3$) was taken as 1.0 mM, with the measured $^{s}_{s}pH$ of the methanol solution being 8.75, close to neutrality (8.38, autoprotolysis constant of MeOH $10^{-16.77}$).[18] The ^{31}P NMR spectrum of the solution was monitored periodically for ~160 min, after which time it indicated complete disappearance of the paraoxon signal at δ −6.35 ppm and appearance of a new signal at δ 0.733 ppm corresponding to $(EtO)_2P(=O)(OMe)$. The ^{1}H NMR spectrum of the same solution also indicated complete disappearance of the starting material and full release of free *p*-nitrophenol.

Results

a. Kinetics. Figure 1 displays a plot of the pseudo-first-order rate constants (k_{obs}) for methanolysis of **1** in the presence of 1 mM $Zn(OTf)_2$ as a function of added $NaOCH_3$. The plot maximizes and plateaus at a relatively low and nonstoichiometric $[^{-}OCH_3]/[Zn^{2+}]$ ratio (0.1−0.4) with further added $NaOCH_3$, causing a reduction in catalytic activity suggestive of a complex equilibrium of various forms of "free" Zn^{2+}, $Zn^{2+}(^{-}OCH_3)$, and $Zn^{2+}(^{-}OCH_3)_2$ and their possible dimers and oligomers.

A second set of methanolysis experiments was performed with three substrates, namely, **1**, **3**, and *p*-nitrophenyl acetate, as a function of total added $Zn(ClO_4)_2$, maintaining the $[(^{-}OCH_3)]/[Zn^{2+}]_{total}$ ratio at 0.3 with added $NaOCH_3$, which corresponds to the midpoint of the plateau region where the maximum catalytic activity is realized. The three plots shown in Figure 2 exhibit a similar curvature independent of the

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(15) Three organophosphonothioates studied in ref 14 were shown to react with methoxide to give 93−96% P−S cleavage, while under similar hydroxide concentrations in water, P−S cleavage proceeds to the extent of 74−88%. In the case of hydrolysis, the reaction products from P−S cleavage ($RP(=O)O^{-}(SR')$) are toxic in their own right and relatively resistant to further reaction, while P−S cleavage in the methanolysis reactions yields $RP(=O)OCH_3(SR')$, which undergoes further reaction to give $RP(=O)(OCH_3)_2$.

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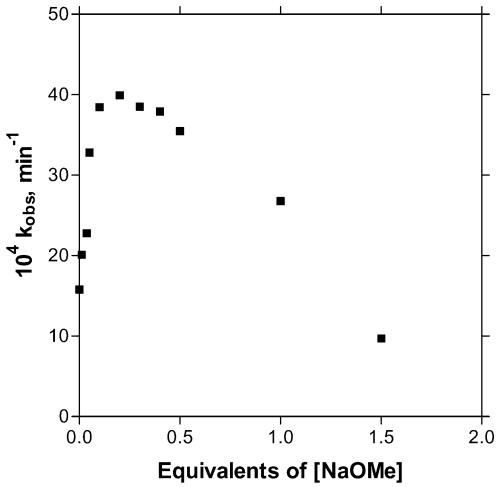


Figure 1. k_{obs} for the methanolysis of **1** vs added $NaOCH_3$ in the presence of 1 mM $Zn(OTf)_2$, $T = 25$ °C.

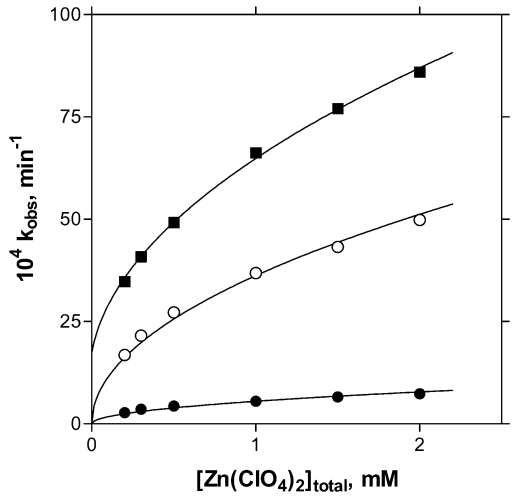
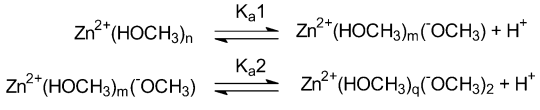


Figure 2. k_{obs} for the methanolysis of **3** (●), **1** (○) and *p*-nitrophenyl acetate (■) vs $[Zn(ClO_4)_2]$ at a constant $[Zn^{2+}(^{-}OCH_3)]/[Zn^{2+}]_{total}$ ratio of 0.3, $T = 25$ °C. Lines through the data are calculated on the basis of eq 2. Note the nonzero intercept for the most reactive substrate, *p*-nitrophenyl acetate, attributable to the background reaction, which at ^{s}pH 10.00 is $k_{obs} = 2.2 \times 10^{-3}$ min^{-1}.

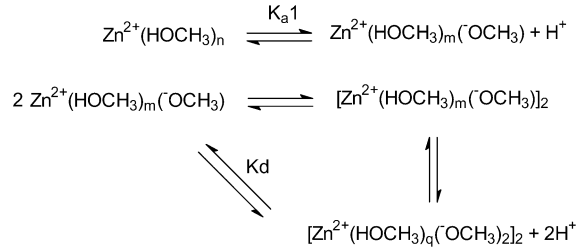
Scheme 1



nature of the substrate, which suggests that this originates with the speciation of the Zn^{2+} ions in solution.

In a first attempt to anayze the data, we considered a simple set of equilibria outlined in Scheme 1, involving sequential formation of $Zn^{2+}(^{-}OCH_3)$ and $Zn^{2+}(^{-}OCH_3)_2$ from Zn^{2+} as was proposed previously on the basis of potentiometric titration.[16] In Part 1 of the Supporting Information we have presented a mathematical analysis to determine the dependence of the concentration of the catalytically active form ($Zn^{2+}(^{-}OCH_3)$) on total $[Zn^{2+}]$ and total [methoxide]. That analysis shows that this simple scheme cannot explain the experimental kinetic data in Figure 1 since the maximum kinetic rate is predicted to occur at a $[^{-}OCH_3]/[Zn^{2+}]$ ratio of 1 (not 0.2−0.4 as observed in Figure

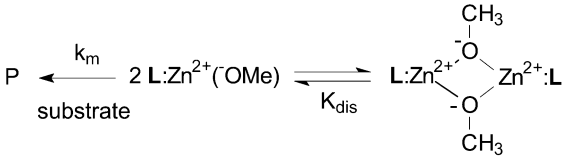
Scheme 2



1) while the predicted dependence of k_{obs} on total $[Zn^{2+}]$ is linear, not curved as shown in Figure 2.

To address the appearance of the experimental plots shown in Figures 1 and 2, a more complex process shown in Figure 2 is required, the key point of which is the requirement to limit the overall $[Zn^{2+}(^{-}OCH_3)]$ through the formation of dimeric species. Given in Part 2 of the Supporting Information is a mathematical treatment of Scheme 2, where K_d represents a complex step involving dimerization and second proton dissociation, both processes being necessary to model the data successfully. The simplified analytical solution shown in the Supporting Information allows us to emulate the characteristic graphical shapes given in Figures 1 and 2, which are not attainable using Scheme 1. In particular, the rate maximum of Figure 1 is now successfully emulated to occur at a $[^{-}OCH_3]/[Zn^{2+}]$ ratio of 0.2−0.4, and the curvature in the plots of k_{obs} vs $[Zn^{2+}]_{total}$ is also successfully reproduced.

While the treatment is, admittedly, simplified with respect to possible formation of higher order aggregates, the successful emulation of the Figures 1 and 2 kinetic plots using the process shown in Scheme 2 strongly supports the formation of one or more inactive dimeric species which are in equilibrium with a catalytically active monomer. Unfortunately, the analytical solution (see the Supporting Information) is too complex to be used successfully for the complete analysis of the kinetic data. To perform the analysis of the k_{obs} vs $[Zn^{2+}]_{total}$ data (Figure 2) where the $[^{-}OCH_3]/[Zn^{2+}]_{total}$ ratio is held constant, we have chosen to simplify further the analysis as in eq 1, where all the dimeric forms are proportional to $[Zn^{2+}{}_2(^{-}OCH_3)_2]$, which is in equilibrium with the active form $Zn^{2+}(^{-}OCH_3)$. It is important to note that at a constant $[^{-}OCH_3]/[Zn^{2+}]_{total}$ ratio the equilibrium distribution of $Zn^{2+}{}_2(^{-}OCH_3)_2$ and $Zn^{2+}{}_2(^{-}OCH_3)_4$ should not be significantly perturbed. In its general form, eq 1 may include ligands bonded to the Zn^{2+}, which extends its utility to the cases of the phenanthrolines **4** and **5** discussed below. Also below we show that this approach allows us to analyze the experimental kinetic data for any of the systems that involve monomer/dimer equilibria in a way which is consistent with the chemical behavior.



(1)

$$k_{obs} = \{k_m K_{dis} (\sqrt{1 + 8[Zn^{2+}]_t / K_{dis}} - 1)/4\} + k_o \quad (2)$$

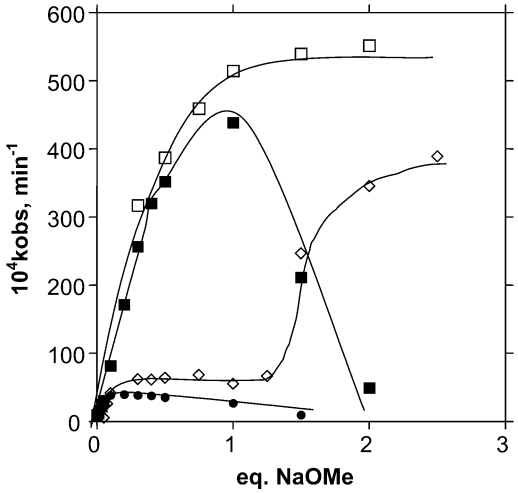


Figure 3. k_{obs} vs number of equivalents of added $NaOCH_3$ for the methanolysis of paraoxon in the presence of 1 mM $Zn(ClO_4)$ with no added ligand (●), with 1 mM **4** (◇), with 1 mM **5** (■), and with 1 mM **6** (□). Lines through the data were drawn as a visual aid only.

Given in eq 2 is the appropriate kinetic expression based on eq 1, which also includes a k_o term for the background reaction which is present for the most reactive substrate (in the case of Zn^{2+} alone, *p*-nitrophenyl acetate) but is not important for the less reactive phosphate triesters. This expression, derived from consideration of the equations for the conservation of total Zn^{2+} mass, the monomeric/dimeric Zn^{2+} species, and the rate and dissociation constants defined in eq 1, shows a complex dependence including a square-root term which leads to a nonlinear dependence on $[Zn^{2+}]_{total}$, similar to that observed with the more complicated analytical solution for the process in Scheme 2 given in the Supporting Information. NLLSQ fitting of the k_{obs} vs concentration data for each substrate to eq 2 generates the lines through the data in Figure 2, with the k_m and K_{dis} constants being presented in Table 1.

b. Effect of Ligands. Shown in Figure 3 are plots of the k_{obs} for methanolysis of **1** in the presence of 1 mM Zn^{2+} as a function of added $NaOCH_3$ in the presence of equimolar ligands **4**−**6**. For ease of visual comparison, the Figure 1 data for Zn^{2+} alone are also presented. For all systems there are two domains corresponding to the addition of the first, and then second, equivalent of $^-OCH_3$ per Zn^{2+}. The ^s_spH range encountered during the consumption of the first equivalent of methoxide is in the neutral region, ∼8−10 (neutral ^s_spH in methanol 8.38[17]), this being the most interesting region in terms of catalysis and the one on which we will concentrate. Upon addition of the second equivalent of methoxide, the overall behavior is more sporadic depending on the nature of the ligand as can be seen from Figure 3 and as will be analyzed in a later section. Addition of ligand is seen to have important consequences on the overall activity of the complexed Zn^{2+}.

Shown in parts a and b of Figure 4 are the concentration dependencies for the methanolysis of paraoxon and fenitrothion catalyzed by Zn^{2+} alone and in the presence of ligand **4** or **5**, where the $[(^-OCH_3)]/[Zn^{2+}]_{total}$ ratio is kept at a constant value corresponding to the plateaued rate shown in

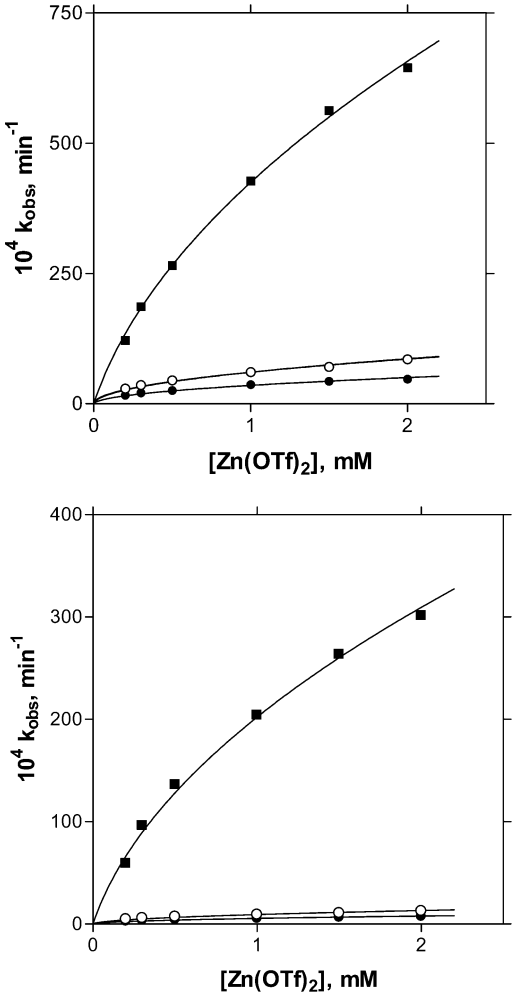


Figure 4. (a, top) k_{obs} for the methanolysis of paraoxon as a function of $[Zn^{2+}]_{total}$ alone and in the presence of equimolar **4** or **5** at constant $[(^-OCH_3)]/[Zn^{2+}]_{total}$ ratios corresponding to plateaued activity (no ligand, ●, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 0.3$; **4**, ○, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 0.5$; **5**, ■, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 1.0$). (b, bottom) k_{obs} for the methanolysis of fenitrothion as a function of $[Zn^{2+}]_{total}$ alone and in the presence of equimolar **4** or **5** at constant $[(^-OCH_3)]/[Zn^{2+}]_{total}$ ratios corresponding to plateaued activity (no ligand, ●, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 0.3$; **4**, ○, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 0.5$; **5**, ■, $[(^-OCH_3)]/[Zn^{2+}]_{total} = 1.0$).

Figure 3 (i.e., 0.3 for Zn^{2+} alone, 0.5 for **4**, and 1.0 for **5**). These data are also curved, not due to a saturation binding of the phosphorus triesters to the metal, but due to the monomer/dimer equilibrium given in eq 1. The lines through the Figure 4 data are derived on the basis of NLLSQ fits to eq 2 and yield the kinetic constants given in Table 1. As shown in Figure 5a, the kinetic dependence in the presence of ligand **6** is strictly linear and shows no evidence of monomer/dimer equilibrium.

c. ^{31}P NMR Turnover Experiments. The ^{31}P NMR spectrum of a solution containing 15 mM paraoxon and 1 mM each of $Zn(OTf)_2$, $NaOCH_3$, and ligand **5** was continuously monitored at ambient temperature over a period of ∼160 min. The spectra were summed every 15 min to produce the time profile given in Figure 6, which displays the disappearance of **1** and the appearance of a new signal at δ 0.733 ppm attributed to diethyl methyl phosphate. Fitting of these two time profiles to a first-order expression gave an average pseudo-first-order rate constant of $(4.5 \pm 0.1) \times$

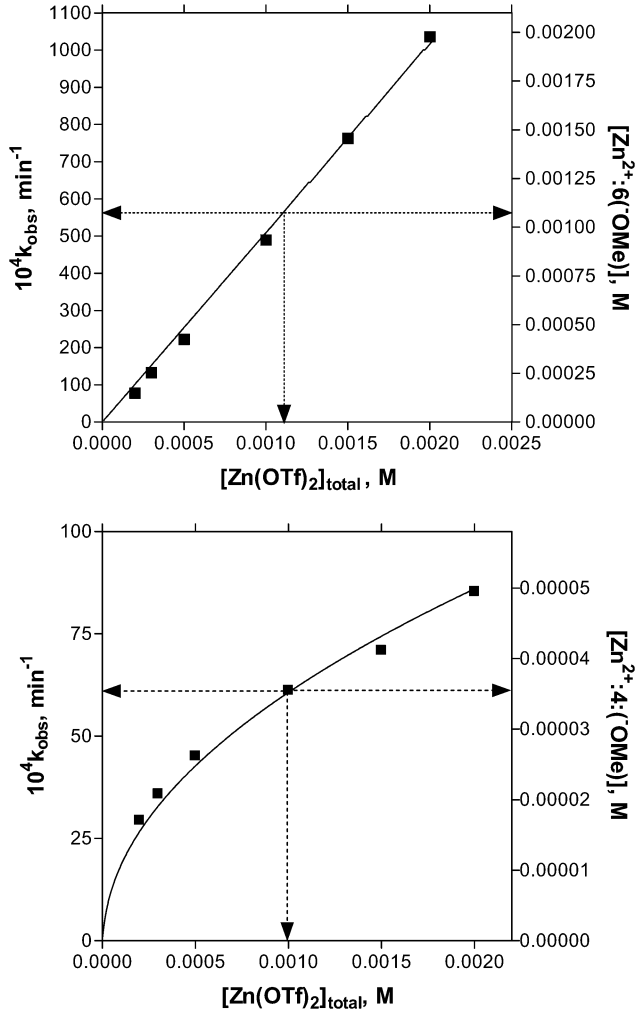


Figure 5. (a, top) k_{obs} for methanolysis of paraoxon as a function of $[Zn(OTf)_2]_{total}$ containing equimolar **6** and $NaOCH_3$, $T = 25$ °C. ■ represents the actual experimental rate constant (left axis). The solid line represents $[Zn^{2+}$:**6**$(^-OCH_3)]$ (right axis) determined by Hyperquad fitting of titration data (see the Results, section d). The arrows are presented as a visual aid to connect the various species concentrations with the kinetic constant. (b, bottom) k_{obs} for the methanolysis of paraoxon as a function of $[Zn(OTf)_2]_{total}$ containing equimolar **4** and 0.5 equiv of $NaOCH_3$, $T = 25$ °C. ■ represents the actual experimental rate constant (left axis). The solid line represents $[Zn^{2+}$:**4**$(^-OCH_3)]$ (right axis) determined by Hyperquad fitting of the titration data (see the Results, section d). The arrows are presented as a visual aid to connect the various species concentrations with the kinetic constant.

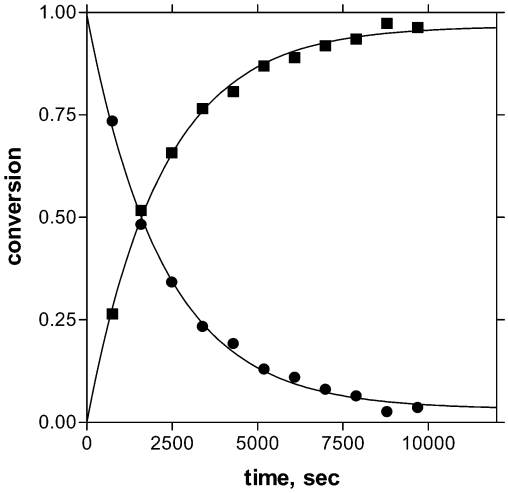


Figure 6. Relative ^{31}P NMR integrated concentrations of starting material, paraoxon (●), and product, diethyl methyl phosphate (■), as a function of time (methanol containing 15 mM paraoxon and 1 mM each of $Zn(OTf)_2$, $NaOCH_3$, and ligand **5**, $T = 25$ °C).

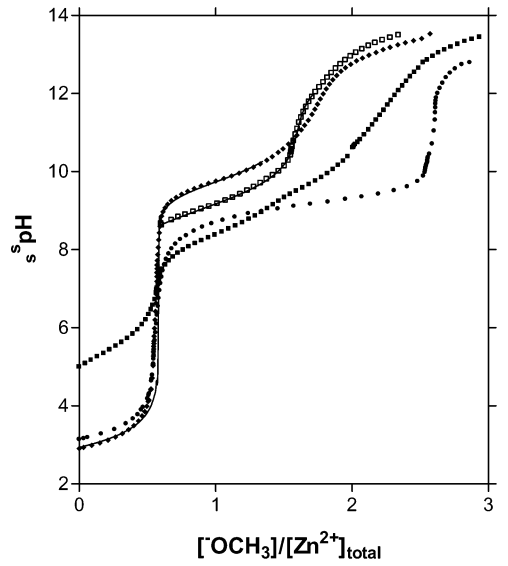


Figure 7. Potentiometric titration of 2 mM $Zn(OTf)_2$ with no added ligand (●), with 2 mM **4** (◆), with 2 mM **5** (■), and with 2 mM **6** (□) with 1.2 mM added $HClO_4$. Lines through the titration curves with **4** and **6** were derived from Hyperquad fitting of the data to models given in the Results, section d.

10^{-4} s^{-1} over 15 turnovers ($t_{1/2} = 25$ min), thus showing the true catalytic nature of the system.

d. Potentiometric Titration and Speciation Analysis. Potentiometric titration of $Zn(OTf)_2$ solutions of varying concentrations (0.5−2 mM) in anhydrous methanol were performed in the absence and presence of equimolar amounts of ligands **4**−**6** to determine the speciation of the Zn^{2+} ions under conditions similar to those of the kinetic experiments. Independent titrations of 1 mM solutions of each ligand were performed, and the resulting data were analyzed using the Hyperquad 2000 fitting routine, providing the $^s_sp$$K_a$ values for the last acid dissociation step, $\mathbf{L}-H^+ \leftrightarrows \mathbf{L} + H^+$, of 5.63 ± 0.01, 6.43 ± 0.01, and >13 for **4**−H^+, **5**−H^+, and **6**−H^+, respectively.

The potentiometric titration curve of $Zn(OTf)_2$ presented in Figure 7 shows the consumption of 2 equiv of methoxide occurring in one rather steep step which was previously analyzed in terms of sequential dissociation of two protons, pK_{a1} and pK_{a2}, with the second being lower than the first due to cooperativity arising from a change in coordination number or/and a monomer/dimer/oligomer equilibrium.[16] From the present kinetic results (see above) the $Zn^{2+}(^-OCH_3)$ system must at least exist in a monomer/dimer equilibrium, but the situation is sufficiently complex that we have been unable to analyze the entire profile successfully using the Hyperquad fitting routines. In the presence of ligands **4**−**6** the titration curve changes due to the formation of complexes which simplify the system by preventing the formation of oligomers, and allows us to successfully use the Hyperquad fitting. A number of different dissociation schemes were attempted, and the final adopted ones were selected on the basis of the goodness of fit to the titration profiles along

with due consideration of the various species suggested by the kinetic studies.

The case of triazacrown ether **6** is the simplest to analyze since we have no evidence supporting the presence of any species containing more than one Zn^{2+} ion. This fact, coupled with the high $^{s}_{s}pK$ of **6**−H^+, allows one to define the relevant species in solution as **6**−H^+, Zn^{2+}:**6**, Zn^{2+}:**6**($^-OCH_3$), and Zn^{2+}:**6**($^-OCH_3$)$_2$, which, when fit via the Hyperquad 2000 program, produces a theoretical titration curve (Figure 7) which is in excellent agreement with the observed curve. The best fit formation constants for **6**−H^+, Zn^{2+}:**6**, Zn^{2+}:**6**($^-OCH_3$), and Zn^{2+}:**6**($^-OCH_3$)$_2$ are given in Table 2.[21] The Zn^{2+} speciation diagram constructed from these constants (not shown) indicates that in the $^{s}_{s}$pH region used in our kinetic studies, greater than 95% of the total Zn^{2+} is present as Zn^{2+}:**6**($^-OCH_3$). Shown in Figure 5a is a plot of the pseudo-first-order rate constants for the methanolysis of paraoxon in the presence of $Zn(OTf)_2$ with a right-hand axis depicting the computed [Zn^{2+}:**6**($^-OCH_3$)] as a function of the total [$Zn(OTf)_2$]. The very good correlations between the kinetic data and the speciation data strongly support Zn^{2+}:**6**($^-OCH_3$) as the catalytically active component, with a derived second-order rate constant of 50.4 M^{-1} min^{-1} for the methanolysis of paraoxon.

Potentiometric titration of an equimolar mixture of $Zn(OTf)_2$ and **4** in the presence of 0.6 equiv of perchloric acid showed that all the added H^+ was released in the strong acid region below $^{s}_{s}$pH 3, with one additional step consuming a single equivalent of methoxide around $^{s}_{s}$pH 10. The former indicates strong binding between Zn^{2+} and **4** even at $^{s}_{s}$pH 3, but does not allow us to determine an exact value of the Zn^{2+}:**4** binding constant other than to set a lower limit for its formation constant of 10^{10} M^{-1}, which was used as a fixed value in all subsequent fittings. In the higher $^{s}_{s}$pH region where the kinetic experiments were performed, we employed a model where the Zn^{2+} exists predominantly as {Zn^{2+}:**4**($^-OCH_3$)}$_2$ and Zn^{2+}:**4**($^-OCH_3$)$_2$, both of these being inferred by the kinetic data. Hyperquad 2000 fitting of the full titration profile using the previously determined stability constants for **4**−H^+ and Zn^{2+}:**4** produces a good fit and provides respective stability constants for {Zn^{2+}:**4**($^-OCH_3$)}$_2$ and Zn^{2+}**4**:($^-OCH_3$)$_2$ given in Table 2. Shown in Figure 5b is a plot of the pseudo-first-order rate constants for the methanolysis of paraoxon in the presence of $Zn(OTf)_2$ with a right-hand axis depicting the computed [Zn^{2+}:**4**:($^-OCH_3$)] as a function of the total [$Zn(OTf)_2$].

Finally, potentiometric titration of an equimolar solution of **5** and $Zn(OTf)_2$ was undertaken in an attempt to determine formation constants of the various species. From comparison of this titration profile and the one for **5** alone, it immediately became clear that the binding of this ligand to Zn^{2+} was relatively weak, and that no more than 85% of the available Zn^{2+} was bound to the ligand at any $^{s}_{s}$pH. While it might be assumed that one could fit the available data using a speciation model based on that found for the phenanthroline:Zn^{2+} system, including **5**−H^+, **5**, Zn^{2+}, Zn^{2+}($^-OCH_3$), Zn^{2+}:**5**, Zn^{2+}:**5**($^-OCH_3$), {Zn^{2+}**5**:($^-OCH_3$)}$_2$, and Zn^{2+}($^-OCH_3$)$_2$ and oligomers thereof, the large number of variables precludes our being able to assign values to any of the constants with confidence.

(21) From the formation constants given in Table 2, one can calculate the first and second $^{s}_{s}pK_a$ values of 9.1 and 12.9 for Zn^{2+}:**6** to generate Zn^{2+}:**6**($^-OCH_3$) and Zn^{2+}:**6**($^-OCH_3$)$_2$.

Discussion

The metal alkoxides of Zn^{2+} are generally considered to be oligomeric or polymeric,[22] but in the case of $ZnCl_2$ in methanol can exist as a complex distribution of soluble monomeric or dimeric species including $Zn(OCH_3)_4^{2-}$, {$Zn(OCH_3)_3(HOCH_3)$}$^-$, {$ZnCl(OCH_3)_2$}$_2^-$, and {$Zn_2Cl_2(OCH_3)_2$}$^{2-}$ depending on the molar ratio of the reactants ($ZnCl_2$ and $NaOCH_3$).[23] Several crystal structures are available for dimeric or oligomeric Zn^{2+} species which are bridged by μ-alkoxides.[12d,r,22a,24] Some earlier studies of the hydrolysis of phosphate triesters by Cu^{2+} complexes have demonstrated that a concentration-dependent formation of kinetically less reactive or unreactive μ-$^-$OH-bridged dimers[25] does occur,[11i,n,u,s,26] and there are also reports of the formation of analogous inactive Zn^{2+} dimers in water.[27]

In the present study of the catalysis of the methanolysis of **1** and **3** by $Zn(OTf)_2$ and $Zn(ClO_4)_2$, either alone or in the presence of complexing ligands, we have no structural information, but it is clear that (1) the Zn^{2+} species are appreciably soluble in solution at all $^{s}_{s}$pH values and concentrations employed in the study and (2) equilibria consisting of dimeric species in equilibrium with a kinetically active monomeric species are formed in the case of Zn^{2+}, Zn^{2+}:**4**, and Zn^{2+}:**5**, but not in the case of Zn^{2+}:**6**, where only the kinetically active monomeric form is present. We have used Zn^{2+} with triflate or perchlorate counterions for their relative kinetic inertness since they do not inhibit the Zn^{2+} catalysis unlike the situation with more strongly coordinating anions such as bromide, chloride, or acetate, all of which are significantly inhibitory. We have confirmed this by observing that the methanolysis of paraoxon catalyzed by 1 mM $Zn(OTf)_2$ with 0.3 equiv of added $NaOCH_3$ is relatively unaffected by the addition of up to 5 mM NaOTf or $NaClO_4$, but is drastically inhibited by the addition of 1

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mM NaCl, NaBr, or $Na(O_2CCH_3)$. It may be that the OTf^- or ClO_4^- ions are ion-paired with the Zn^{2+} in a way that enhances the overall solubility but does not impair catalysis,[28] but we have not investigated this in any detail nor included such in our kinetic analyses.

a. Kinetics of Catalyzed Methanolysis of 1 and 3. The kinetics for Zn^{2+}-catalyzed methanolysis of paraoxon and fenitrothion fall into two distinct classes depending on which ligand is coordinated to the metal ion and how much methoxide is added. Without any ligand, as shown in Figure 1, the k_{obs} for methanolysis of **1** in the presence of 1 mM $Zn(OTf)_2$ maximizes between 0.1 and 0.4 mM added $NaOCH_3$. There is an initially very strong dependence on [methoxide], and the slope of the initial linear part up to 0.05 equiv yields a second-order rate constant of $\sim$34 M^{-1} min^{-1} for methanolysis of **1**. Undoubtedly the initially added methoxide is coordinated to Zn^{2+} to establish the $\{Zn(OCH_3)\}_2^{2+} \leftrightarrows 2\{Zn(OCH_3)\}^+$ equilibrium, but as additional methoxide is added, the overall rate drops significantly, suggesting formation of inactive species having a $[(^-OCH_3)]/[Zn^{2+}]$ ratio greater than 1. This fits with our previous observations[16] that the potentiometric titration of Zn^{2+} in methanol displays a steeper-than-normal consumption of two methoxides in an apparent single event having a midpoint of ${}^s_spK_a \approx 9.8$ which, when analyzed by fitting to a model containing only the monomeric species $Zn^{2+}(OCH_3^-)$ and $Zn^{2+}(OCH_3^-)_2$, gives apparent ${}^s_spK_{a1}$ and ${}^s_spK_{a2}$ values of 10.66 and 8.94. While our original fitting did not include dimer and oligomer formation, the fact that the second apparent ${}^s_spK_a$ is lower than the first indicates some cooperative effect facilitating addition of a second methoxide per Zn^{2+} ion before the first addition is stoichiometrically complete. This phenomenon limits the amount of any forms having a methoxide/Zn^{2+} stoichiometry of 1 and shifts the maximum of the kinetic plot in Figure 1 to $[^-OCH_3]/[Zn^{2+}]_{total}$ ratios of less than unity. This is now nicely supported by the analytical solution given in Part 2 of the Supporting Information. Species where the $[(^-OCH_3)]/[Zn^{2+}]$ ratio is >1 may exist in solution as oligomers of $\{Zn^{2+}(^-OCH_3)_{1.5,2}\}_n$ held together with bis-μ-methoxide bridges but without any pronounced catalytic activity. Added bi- or tridentate ligands could, in principle, disrupt this arrangement by capping one face of the Zn^{2+}, favoring the formation of dimers and monomers of stoichiometry $\{Zn^{2+}:\mathbf{L}(^-OCH_3)\}_2$, $Zn^{2+}:\mathbf{L}(^-OCH_3)(HOCH_3)$, or $Zn^{2+}:\mathbf{L}(^-OCH_3)_2$ depending on the [methoxide]/$[Zn^{2+}]$ ratio. Indeed, as shown in Figure 3, ligands **4**−**6** modify the kinetic behavior in two important ways depending on whether the $[(^-OCH_3)]/[Zn^{2+}]$ ratio is less than or greater than 1.

b. Ligands 4 and 5. As shown by the various formation constants given in Table 2, **4** binds very tightly to Zn^{2+} at all ${}^s_spH$ values in methanol, which is in line with the previously reported strong binding in water.[29] According to our potentiometric titration data, the major species in the ${}^s_spH$ domain surrounding $0 < [^-OCH_3]/[Zn^{2+}]_{total} < 1$ is the dimer $\{Zn^{2+}:\mathbf{4}(^-OCH_3)\}_2$, which is in equilibrium with a small amount of kinetically active monomer, $Zn^{2+}:\mathbf{4}(^-OCH_3)$. Under conditions where $[^-OCH_3]/[Zn^{2+}]_{total} = 0.5$, a plot of k_{obs} vs $[Zn^{2+}]_{total}$ follows the square-root dependence of eq 2 that corresponds to the process presented in eq 1, with the derived kinetic parameters being given in Table 1. The same general phenomenon is seen with ligand **5**, although its binding to Zn^{2+} is weaker than that of **4** (as is known to be the case in water[30]) such that at any given ${}^s_spH$, only about 85% of the Zn^{2+} is bound to **5**. At $[^-OCH_3]/[Zn^{2+}]_{total} = 1$, the k_{obs} vs $[Zn^{2+}]_{total}$ plot is also curved and can be analyzed according to the expression given in eq 2. That the best fits to the kinetic data follow the square-root dependence of eq 2 and not a cube-root or larger dependence indicates that higher order oligomers are not prominent forms under these conditions. The various conditional kinetic constants were determined from these fits, which, in the case of $\{Zn^{2+}(^-OCH_3)\}_2$, and $\{Zn^{2+}:\mathbf{4}(^-OCH_3)\}_2$, required an iterative fitting procedure with a fixed dimer dissociation constant that was progressively reduced until both the standard deviation and correlation between K_{dis} and k_m were minimized. In the case of $\{Zn^{2+}:\mathbf{5}(^-OCH_3)\}_2$, where the dimerization is not as strong, the kinetic parameters were determined by unrestricted fits. The dissociation constant for this dimer at 0.6 ± 0.2 mM is at least 100 times greater than those for $\{Zn^{2+}(^-OCH_3)\}_2$ or $\{Zn^{2+}:\mathbf{4}(^-OCH_3)\}_2$ probably due to a steric buttressing between the opposing 2,9-dimethyl groups.

As shown in Figure 3 for the methanolysis of **1**, the Zn^{2+}:**4** and Zn^{2+}:**5** systems behave differently in the $1 < [(^-OCH_3)]/[Zn^{2+}]_{total} < 2$ domains, with the overall activity increasing and decreasing, respectively. Because of the weak binding inherent in the Zn^{2+}:**5** system, the additional methoxide probably displaces the ligand from the $\{Zn^{2+}:\mathbf{5}(^-OCH_3)\}_{1,2}$ forms to generate uncomplexed **5** and $\{Zn(OCH_3)_2\}_n$ dimers or oligomers, which are not active. However, because of the far stronger binding of **4** to Zn^{2+}, the additional methoxide breaks apart the $\{Zn^{2+}:\mathbf{4}(^-OCH_3)\}_2$ dimer as shown in Scheme 3 to form $Zn^{2+}:\mathbf{4}(^-OCH_3)_2$. The presence of $Zn^{2+}:\mathbf{4}(^-OCH_3)_2$ and its catalytic viability are, respectively, confirmed by the potentiometric titration data and by the fact that a plot of k_{obs} for methanolysis of both substrates vs $[Zn^{2+}]_{total}$ under conditions where the $[Zn^{2+}]/[\mathbf{4}]/[methoxide]$ ratio is 1/1/2 gives a straight line with a slope of $k_{m'}{}^{\mathbf{1}} = 29.5$ M^{-1} min^{-1} for the methanolysis of **1** and $k_{m'}{}^{\mathbf{3}} = 2.7$ M^{-1} min^{-1} for the methanolysis of **3**.

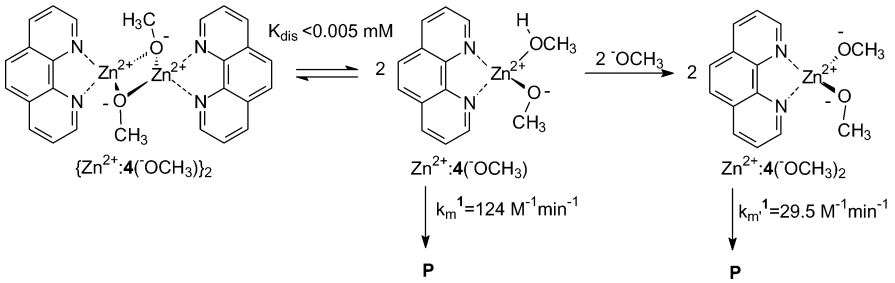
c. Ligand 6. From an analytical standpoint the Zn^{2+}:**6** system is the simplest one because of the very strong binding and the apparent lack of formation of dimers under any of the conditions employed. Kimura has investigated the Zn^{2+}:**6**

(28) H. R. Gut (*Helv. Chim. Acta* **1964**, *47*, 1964) has reported that zinc methoxide is insoluble when it is formed from diethylzinc in methanol but when formed from $ZnCl_2$ and $LiOCH_3$ in methanol is soluble probably because the so-formed complex(es) contains chloride.

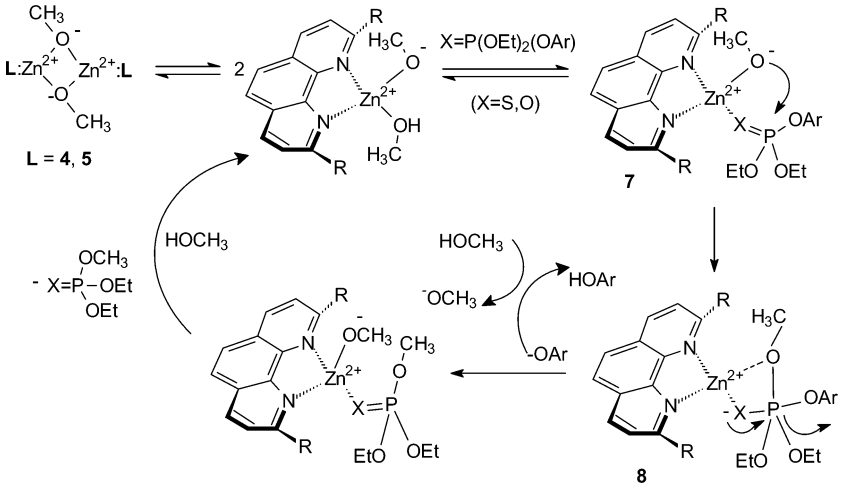
(29) Kolthoff et al. (Kolthoff, I. M.; Leussing, D. L.; Lee, T. S. *J. Am. Chem. Soc.* **1951**, *73*, 390) report a log *K* of 6.4 for the stability constant of **4** + Zn^{2+} ↔ **4**:Zn^{2+} in water.

(30) Yasuda et al. (Yasuda, M.; Sone, K.; Yamasaki, K. *J. Phys. Chem.* **1956**, *60*, 1667) report a log *K* of 3.1 for the stability constant of **5** + Zn^{2+} ↔ **5**:Zn^{2+} in water.

Scheme 3



Scheme 4



system in water as a model for carbonic anhydrase, where the log K for its formation constant is 8.4 at 25 °C,[31] and also reported on its ability to facilitate the hydrolysis of tris-(4-nitrophenyl) phosphate in 33% ethanol/water.[12d] The catalytic activity in this system is tied to the formation of a $Zn^{2+}-{}^{-}OH$ species (pK_a for $Zn^{2+}-{}^{-}OH_2 = 7.3$[31]). In methanol the formation constant is somewhat larger ($\log {}^{S}_{S}K = 10.11$) ensuring that there is essentially no free ligand in solution, and the ${}^{S}_{S}pK$ for ionization of **6**:$Zn^{2+}-{}^{-}HOCH_3$ is 9.1.[21] The k_{obs} vs $[Zn^{2+}]_{total}$ plot shown in Figure 5 is a straight line consistent with (Zn^{2+}:**6**($^{-}OCH_3$)) being the active and predominant form without intervention of any $\{Zn^{2+}$:**6**($^{-}OCH_3$)$\}_2$ dimer. The lack of dimer formation in this system is perhaps attributable to the instability of a 5-coordinate Zn^{2+} required for the dimer relative to the more stable 4-coordinate Zn^{2+} in the $\{Zn^{2+}$:**4**($^{-}OCH_3$)$\}_2$ and $\{Zn^{2+}$:**5**($^{-}OCH_3$)$\}_2$ dimers.

d. Catalytic Mechanism. In cases where the Zn^{2+}-catalyzed[11a,z,12d,32] or Cu^{2+}-catalyzed[11i,n,s,t,u,x,12a] hydrolysis of phosphate triesters has been studied, the active form of the catalyst is invariably a metal hydroxo species (M^{2+}:**L**(^{-}OH)) that is usually proposed to react with the substrate through a 4-coordinate transition state where the metal ion functions both to deliver the coordinated −OH nucleophile and as a Lewis acid to coordinate the P═O unit.[33] Support for the bifunctional role generally comes from the observation that the second-order rate constant for $M^{2+}-{}^{-}OH$-catalyzed hydrolysis is larger than that for −OH itself,[11a,i,n,s] but this is not always observed.[12d] Our preferred mechanism for the catalyzed methanolysis of **1** and **3**, shown in Scheme 4, is similar to those proposed previously and in the case of the dimeric **4**- and **5**-containing species requires that these dissociate to form monomers prior to the catalytic event. While not explicity obseved in our kinetic studies, the phosphate or thiophosphate must transiently bind to the monomers to form **7**. The structural aspects for such binding are known for Zn^{2+} complexes of phosphine oxides[34] and tritoluoyl phosphate.[35]

Complex **7** can then undergo intramolecular formation of the 5-coordinate phosphorus intermediate **8** from which OAr is expelled either with or without assistance through binding to the metal as has been discussed in our previous study of the La^{3+}-catalyzed methanolysis of paraoxon.[1] A completely analogous mechanism can be proposed for Zn^{2+}:**6**($^{-}OCH_3$) monomer involving the same essential catalytic steps.

What makes our systems unusual is the ability of the Zn^{2+} species to catalytically methanolyze both the P═O and P═S species with second-order rate constants 50−1000-fold larger than the corresponding second-order rate constants for methoxide attack alone. Enhancements of this magnitude to our knowledge are not routinely seen for Zn^{2+}- and Cu^{2+}-

(31) Kimura, E.; Shiota, T.; Kooike, T.; Shiro, M.; Kodama, M. *J. Am. Chem. Soc.* **1990**, *112*, 5805.
(32) (a) Clewley, R. G.; Slebocka-Tilk, H.; Brown, R. S. *Inorg. Chim. Acta* **1989**, *157*, 453. (b) Norman, P. R. *Inorg. Chim. Acta* **1987**, *130*, 1. (c) Norman, P. R.; Tate, A.; Rich, P. *Inorg. Chim. Acta* **1988**, *145*, 211. (d) Breslow, R.; Singh, S. *Bioorg. Chem.* **1988**, *16*, 408.
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(34) Kosky, C. A.; Gayda, J.-P.; Gibson, J. F.; Jones, S. F.; Williams, D. J. *Inorg. Chem.* **1982**, *21*, 3173.
(35) Mikulski, C. M.; Pytlewski, L. L.; Karagannis, N. M. *Inorg. Chim. Acta* **1979**, *32*, 263.

catalyzed hydrolysis reactions in water. Our findings can thus be taken as support for the bifunctional nature of our catalytic systems. We speculate that there are two reasons why exhalted activity is seen in methanol, related to both the reduced dielectric constant of the medium and its reduced solvation of metal ions relative to that of water. These effects should lead to a higher net binding constant between the phosphate and Zn^{2+} complex, producing more of the requisite complex **7** than in water, and perhaps also to an increased nucleophilic activity of the Zn^{2+}-coordinated methoxide.

The systems described above are simple enough that preparatively useful forms of the catalysts can simply be generated by the addition of known amounts of ligand, $Zn(OTf)_2$, and methoxide. The catalytic effacacy of the methanolysis of paraoxon and fenitrothion by these species can be judged by the acceleration afforded by over the background reaction at the $^{s}_{s}$pH where the catalyst is active. For a solution comprising 2 mM each of $Zn(OTf)_2$, ligand **5**, and $NaOCH_3$, which generates a $^{s}_{s}$pH of ~9.5, the acceleration of methanolysis of **1** and **3** is 1.8×10^6-fold and 13×10^6-fold, respectively. On the other hand, a solution comprising 1 mM $Zn(OTf)_2$, ligand **6**, and 0.5 mM $NaOCH_3$ generates a $^{s}_{s}$pH of 9.3 and gives an acceleration for the methanolysis of **1** of 1.7×10^6-fold.

As a final point we note that an enzymatic phosphotriesterase (PTA) isolated from the soil-dwelling bacterium *Pseudomonas diminuta* contains an active site with two Zn^{2+} ions bridged by a water or hydroxide, and a carboxylated lysine. The metal ions are additionally ligated to the protein by four histidine imidazoles and an aspartate COO^-.[36] Apparently this motif is particularly effective for the hydrolysis of paraoxon, the preferred substrate, for which the k_{cat}/K_M value is $\sim 10^8$ M^{-1} s^{-1}.[37] While we have shown earlier that a dimeric form of La^{3+} (**2**) is effective for methanolyzing paraoxon, it is particularly curious that the dimeric forms of Zn^{2+} in this study are not active, or at least far less reactive than the monomeric forms we have identified.

Conclusions

In the above we have shown that a rather simple combination of the triflate or perchlorate salts of Zn^{2+} alone or Zn^{2+} in the presence of equimolar amounts of the commercially available ligands **4**−**6** can serve as a reasonably effective catalytic system for the decomposition of both paraoxon and fenitrothion, suggesting that this system produces an effective method for destruction of both P═O and P═S phosphate triester pesticides and related CW agents. Catalytic activity requires the addition of methoxide, and the active forms of the metal ions are $Zn^{2+}(^-OCH_3)$ with no added ligand and Zn^{2+}:**L**$(^-OCH_3)$ when ligand is present. Added ligands have the effect of increasing the activity by stabilizing $Zn^{2+}(^-OCH_3)$ and limiting the oligomerization of $Zn^{2+}(^-OCH_3)_2$ in solution. However, decreasing the oligomerization through addition of phenanthroline ligands does not prevent the formation of $Zn^{2+}(^-OCH_3)$ dimers since the bulk of the material is now present as **L**:$Zn^{2+}(^-OCH_3)_2Zn^{2+}$:**L**, which itself is not catalytically active but is in equilibrium with an active monomeric form. The propensity to form the inactive dimers can be reduced either by increasing the steric interaction (ligand **5**) or by changing the coordination number (ligand **6**), in which cases the overall activity of the catalytic system increases. Future work will be aimed at creating a higher activity catalyst based on the more strongly binding phenanthroline system, where the dimerization is precluded through the use of alternative methods.

Overall, the Zn^{2+}:**5** system is the best of the present catalysts and affords accelerations of 1.8×10^6-fold and 13×10^6-fold for the methanolysis of paraoxon and fenitrothion at 2 mM each of $Zn(OTf)_2$, ligand **5**, and $NaOCH_3$. The activity toward fenitrothion is significant and potentially important since a large number of pesticides and certain CW agents are sulfur-containing members of the neutral phosphorus ester class. Our previously studied $La^{3+}{}_2(^-OCH_3)_2$ system[1] is better for paraoxon: a 2×10^{-3} M solution of $La(OTf)_3$, containing equimolar $NaOCH_3$, affords a 10^9-fold acceleration relative to the rate of the base reaction ($t_{1/2} \approx$ 20 s), but it shows no significant catalysis of methanolysis of fenitrothion. This points out the importance of matching the relative hard/soft characteristics of the catalyst and substrate, and suggests to us that softer metal ions such as Cu^{2+} and Pd^{2+} could show very much enhanced catalytic activity toward the methanolysis of sulfur-containing phosphorus species, an area of current research in these laboratories.

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Supporting Information Available: Detailed analytical solution for the processes given in Schemes 1 (Part 1) and 2 (Part 2) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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