Salt Effects on Solvolysis Reactions of *p*-Nitrophenyl Alkanoates Catalyzed by 4-(Dialkylamino)pyridine-Functionalized Polymer in Buffered Water and Aqueous Methanol Solutions

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Abstract: Specific salting-in effects that lead to striking substrate selectivity were observed for the hydrolysis of *p*-nitrophenyl alkanoates **2** ($n = 2-16$) catalyzed by 4-(dialkylamino)pyridine-functionalized polymer **1** in aqueous Tris buffer solution at pH 8.0 and 30 °C. Macromolecule **1** was found to exhibit clear substrate preference for **2** ($n = 6$) in 0.05 M aqueous Tris buffer solution, as contrasted with the corresponding reaction in 0.05 M aqueous phosphate or borate buffer solutions where the substrate selectivity is absent. The formation of a reactive catalyst−substrate complex, **1·2**, appears to be promoted by the presence of tris(hydroxymethyl)methylammonium ion, an efficient salting-in agent, from the Tris buffer system. The salting-in effect on formation of **1·2** complex is presumed responsible for the substrate specificity. The salting-out effects of sodium chloride on the solvolysis of **2** catalyzed by **1** were also investigated in 1:1 (v/v) methanol−water solution at pH 8.0 and 30 °C. The rate of **1**-catalyzed solvolysis of **2** ($n = 10-16$) was found to vary inversely with NaCl concentration (0−1.0 M). The magnitude of the salting-out effects is dependent on the alkyl chain length in **2** and the concentrations of **1** and NaCl. At 7.5×10^{-5} unit mol L^{-1} **1** and 0−1.0 M NaCl the order of reactivity for **2** ($n = 10-16$) was $n = 10 > 12 > 14 > 16$. However, at 5.0×10^{-6} unit mol L^{-1} **1**, a revised reactivity order, **2**, $n = 14 > 12 > 16$, was obtained at [NaCl] < 0.15 M. A significant decrease in the substrate preference for **1**-catalyzed solvolysis of **2** ($n = 10-16$) was observed at higher NaCl concentrations. We suggest that the reduced catalytic efficiency and selectivity expressed by **1** in the presence of sodium chloride should be attributed to changes in the morphology and composition of aggregates containing **1** and **2** in aqueous methanol solution that lead to decreased dependence of aggregate formation on the hydrophobicity of the substrate.

Introduction

The chemical behavior of biological systems is known to be based on the presence of highly organized molecular assemblies.[1] Hydrophobic interactions play a pivotal role in the formation of these assemblies and constitute an important driving force for substrates binding to enzymes and the self-association of amphiphiles in micelles or membranes.[2] Substances such as urea and guanidinium chloride (GnCl) decrease the association of hydrocarbon species in water and act as "salting-in" agents that increase water solubility of hydrocarbons such as benzene or butane[3,4] and decrease effectiveness of surfactant catalysts toward their substrates.[5] In contrast to the salting-in effects, electrolytes such as LiCl and NaCl tend to increase hydrophobic interactions[6] by electrostriction of water that decreases the solubility of hydrocarbons in the salt solution. They are well-known as "salting-out" agents.[3,4]

Recently there has been much discussion about relationships between such salting-in and salting-out effects and reaction mechanisms.[7−16] Bunton and his co-workers have observed kinetic salt effects on bimolecular nucleophilic displacement reaction between 2,4-dinitrochlorobenzene and hydroxide ion or aniline in water or in aqueous ethanol solution.[17] The charge densities of salt ions are the dominant factor in determining the direction of the salt effects.[17] The low charge densities of GnCl favor salting-in, and the high charge densities of LiCl and NaCl favor salting-out of nonpolar reactants. Very recently, Minoru and Masaru have reported that tris(hydroxymethyl)-aminomethane buffer increases the stability of glucosidase in aqueous solution, and the activity of the enzyme shows no appreciable reduction even after standing for 6 months. They attribute the exceptional stability of the protein in aqueous Tris buffer solution to salting-in effects.[18] Few studies have explored the influence of a salting-out agent such as NaCl on the reactivity

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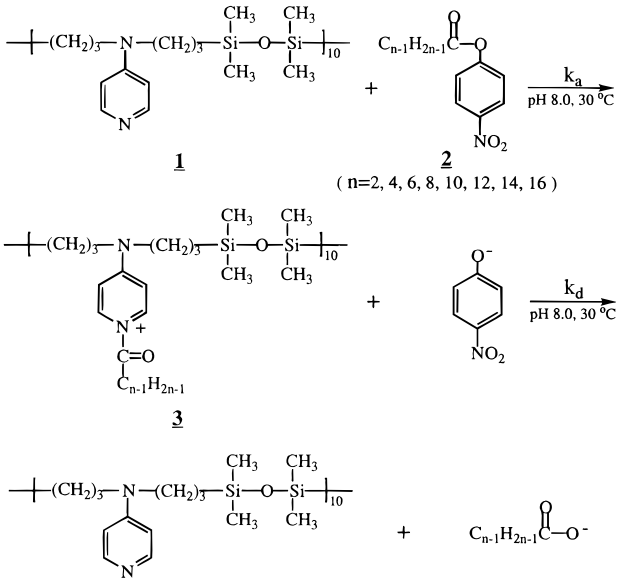
Scheme 1



of hydrophobically associating catalyst−substrate systems that attempt to identify the optimum substrate structure. And no previous study has investigated the influence of electrolytes on the specificity of a "catalyst" that carries the 4-(dialkylamino)-pyridine function, a true turnover catalyst.[14−17,19−21]

4-(Dimethylamino)pyridine and its derivatives are widely recognized as highly reactive supernucleophilic acyl-transfer catalysts in nonaqueous media.[22,23] Polymers and surfactants bearing the 4-(dialkylamino)pyridine group have recently become the subject of extensive research.[24−34] Most studies have focused on the evaluation of these macromolecules as nucleophilic catalysts for solvolysis of *p*-nitrophenyl alkanoates **2** in aqueous and mixed aqueous−organic solvent.[25,26,29] The results from these studies have made essential contributions toward understanding the origins of efficiency and selectivity in biological and chemical catalysis. Macromolecule **1** containing the 4-(dialkylamino)pyridine functionality and a bis-(trimethylene)disiloxane backbone exhibits enzyme-like substrate selectivity for the solvolysis of **2**.[29] This synthetic polymer shows highest levels of activity toward *p*-nitrophenyl tetradecanoate when it is used as a nucleophilic catalyst for the solvolysis of a series of **2** in 1:1 (v/v) methanol−water solution[29] (Scheme 1). Such catalytic reactions are appreciably accelerated by the presence of the anionic surfactant SDS which binds both substrate and catalyst within micellar aggregates and influences reactivity by a combination of catalyst−substrate proximity[5] and micellar microenvironment.[35a]

In the present study, we report an initial example of specific salting-in effects leading to striking substrate selectivity for the hydrolysis reaction of *p*-nitrophenyl alkanoates **2** catalyzed by **1** in 0.05 M aqueous Tris buffer solution. These results provide new insight into catalytic efficiency and substrate selectivity in our enzyme-mimic model systems. We propose that the direct interactions between buffer component and salting-in agent, tris-(hydroxymethyl)methylammonium ion, and catalyst **1** permit use of **1** in aqueous solution and contribute to optimum reactivity with the hexanoate ester **2**. A detailed kinetic characterization of the salting-out effects of sodium chloride on the solvolysis of **2** catalyzed by **1** in 1:1 (v/v) methanol−water solution is also reported.

Experimental Section

Materials and Reagents. Synthesis of the poly(siloxane−bis-(trimethylene)) supported 4-(diallylamino)pyridine (**1**) has been described previously.[30] *p*-Nitrophenyl alkanoates **2** ($n = 2-16$) and 1,4-dioxane were purchased from Sigma Chemical Co. Tris(hydroxymethyl)aminomethane, sodium borate, hydrochloric acid, sodium chloride, methanol, and buffer solution (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) were used as received from Aldrich and Fisher.

Kinetic Measurements. The cuvette was filled with 2.5 mL of a fresh solution containing catalyst in 0.05 M aqueous buffer solutions at pH 8.0, and the solution was equilibrated for 10 min at 30 ± 1 °C in the thermostated cell compartment of a Hewlett-Packard Model 8450 spectrophotometer. A fresh stock solution (usually 5 μL) of *p*-nitrophenyl alkanoates **2** ($n = 2-16$, 2.5×10^{-2} M) in dioxane was added by microsyringe. The fresh catalyst solutions containing sodium chloride for kinetic experiments were prepared in 1:1 (v/v) methanol−aqueous buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) solution, where the 4-(dialkylamino)pyridine group of **1** is partially protonated. The pK_a of **1** increases from 6.9 to 7.2 as NaCl concentration is increased to 0.50 M in 1:1 (v/v) methanol−water solutions as a result of an increase in shielding of protonated pyridinium cation by chloride counterion. The reaction mixture was quickly mixed by shaking, and the absorbance at 400 nm was recorded as a function of time. The reactions were performed for 4−5 half-lives, and the pseudo-first-order rate constants (k_{obsd}) were obtained as slopes of plots of $\ln[A_\infty/(A_\infty - A_t)]$ vs time, where A_∞ and A_t are the absorbances at infinite time and time t, respectively. The first-order rate constants (k_{obsd}) represent the average of two or three runs, and the experimental error is less than 5%.

Results and Discussion

We have examined the effects of the buffers on the solubility of **1** in aqueous solution at pH 8.0 and 30 °C. In 0.05 M phosphate and borate aqueous buffer solutions, the solubility of **1** was found to be similar to its solubility in pure water, and aqueous solutions of **1** show appreciable turbidity when the concentration of **1** is increased beyond 2.5×10^{-5} unit mol L^{-1}. In contrast, we found that in 0.05 M aqueous Tris buffer solution the solubility of **1** shows a more than 10-fold increase over that in pure water. An aqueous solution of **1** at 2.5×10^{-4} unit mol L^{-1} and 0.05 M Tris buffer remains clear even after standing for prolonged periods. These results clearly suggest that tris(hydroxymethyl)methylammonium ion is a salting-in ion in water in accord with previous observations that the anions and cations of low charge density tend to salt-in organic solutes while the ions of high charge density tend to salt-out such solutes.[3,7,17] Therefore, tris(hydroxymethyl)-methylammonium chloride increases the solubility of the hydrocarbons and other hydrophobes in water.

The Salting-In Effects of Tris(hydroxymethyl)methylammonium Cation. We have investigated the hydrolysis of **2** (*n*

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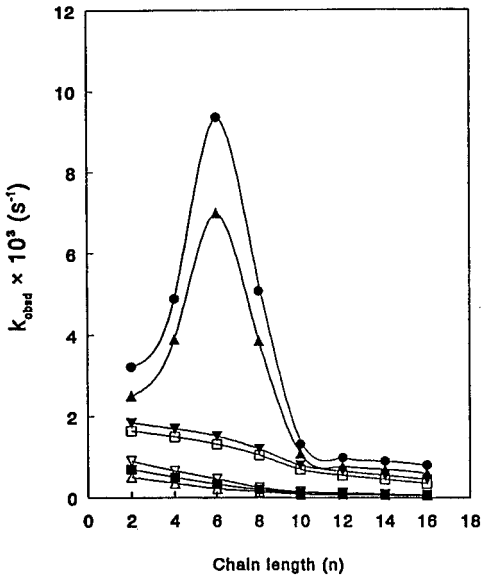

Figure 1. Pseudo-first-order rate constants (k_{obsd}) for the hydrolysis of *p*-nitrophenyl alkanoates **2** ($n = 2-16$, 5.0×10^{-5} M) in the absence and in the presence of **1** as a function of alkanoate chain length (n), catalyst concentration, and buffer system in 0.05 M aqueous buffer at pH 8.0 and 30 °C: ●, 7.5×10^{-5} unit mol L^{-1} **1** in Tris buffer solution; ▲, 2.5×10^{-5} unit mol L^{-1} **1** in Tris buffer solution; ▼, 2.5×10^{-5} unit mol L^{-1} **1** in phosphate buffer solution; □, 2.5×10^{-5} unit mol L^{-1} **1** in borate buffer solution; ▽, in Tris buffer solution only; ■, in phosphate buffer solution only; △, in borate buffer solution only.

$= 2-16$) in the absence and in the presence of **1** in 0.05 M Tris, phosphate, or borate aqueous buffer solutions at pH 8.0 and 30 °C. The results are presented in Figure 1. In the absence of **1**, the hydrolysis rate of **2** ($n = 2-16$) is virtually independent of both substrate chain length and buffer system for Tris, phosphate, or borate buffer solutions. In the presence of 2.5×10^{-5} unit mol L^{-1} **1** the hydrolysis rates for **2** ($n = 2-16$) were also very slow and differed from each other by only small factors in phosphate or borate buffer solutions, indicating that no appreciable catalysis is observed in these systems when the solvent is water. Increasing the alkanoate chain length in **2** causes small decreases in the hydrolysis rate in conformity with results from aqueous buffer solutions that contain no catalyst. At high concentrations, **1** is not soluble in these buffer solutions, and therefore, its catalysis could not be examined. However, in aqueous Tris buffer solution, the rates for the hydrolysis of **2** ($n = 2-8$) with 2.5×10^{-5} unit mol L^{-1} **1** are much faster than those in aqueous phosphate or borate buffer solutions. Strikingly, macromolecule **1** demonstrates clear substrate preference for **2** ($n = 6$) and exhibits little effect on hydrolysis of **2** ($n \geq 10$). Such substrate preference for **2** ($n = 6$) is also observed for cholesterol esterase in the same hydrolysis reaction.[36] This suggests that similar structure−activity effects may be operative in the two systems. As the concentration of **1** is increased to 7.5×10^{-5} unit mol L^{-1}, the hydrolysis rate increases significantly for **2** ($n = 2-8$). But the impact on longer chain esters remains insignificant, and the preference of **1** for **2** ($n = 6$) remains unchanged in Tris buffer solution. Therefore, Tris buffer has a significant effect on the catalytic activity of **1** for the hydrolysis of **2** in aqueous solution. To confirm the true catalytic performance of **1** in Tris buffer solution, kinetic runs were carried out in the presence of excess substrate. Importantly, the catalytic effectiveness is maintained to complete reaction in the hydrolysis of 10-fold excess substrate.

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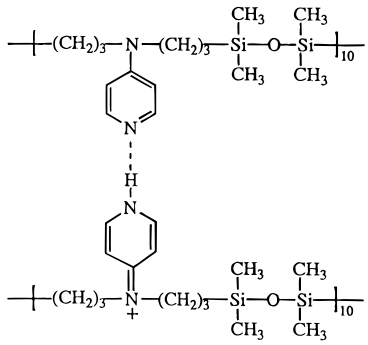
Since the homologues of **2** differ in the chain length of their alkanoate component only, the selectivity obtained presumably originates, at least in part, as a consequence of hydrophobic−lipophilic interactions between **1** and **2**. The correlation of the kinetic performance of **1** with its solubility suggests that distribution of both **1** and **2** among solution and aggregate phases controlled by the salting-in effects of tris(hydroxymethyl)-methylammonium ion could be a major factor affecting hydrolysis rates of **2** in Tris buffer solution. The reaction medium composed of solvent and added electrolytes is known to control micellization, conformations of proteins, and equilibria of enzymes, substrates, and their association complexes. The complexation equilibria involving **1** and **2** and subsequent catalysis of reactions of substrate as illustrated in Scheme 1 may be controlled by the nature of aggregate phases[37,38] and the conformational changes of **1** induced by changes in the reaction medium.[39] Previous studies have suggested that Tris buffer is not a reactant for the deacylation of the acylpyridinium intermediate **3** (Scheme 1) in catalytic hydrolysis reactions.[24,35b] This conclusion is supported by the lack of significant rate enhancement of hydrolysis of **2** ($n = 2$, $n \geq 10$) in uncatalyzed reactions and reactions catalyzed by **1** in aqueous phosphate or borate buffer (Figure 1). The presence of Tris makes a significant impact only on rates of hydrolysis of **2** ($n = 4$, 6, and 8) when catalyzed by **1**. The direct solvation interactions[7] by salting-in agent tris(hydroxymethyl)methylammonium ion with **1** may contribute to efficient binding and/or phase transfer dynamics involving **1** and **2** that is optimum at **2** ($n = 6$) in aqueous Tris buffer at pH 8.0. The structure (**1**-H···**1**)$^+$, which



(**1**−H····**1**)$^+$

represents a low-barrier hydrogen bond between a 4-(dialkylamino)pyridine group and its conjugate acid, has been suggested as a stabilizing force that supplements hydrophobic forces in catalyst **1**.[40,41]

The Salting-Out Effects of Sodium Chloride. The behavior of sodium chloride as a salting-out agent, leading to increased hydrophobic effects and decreased solubilities of hydrocarbons in water and polar solvents, has been well documented in the literature.[3,6,7] We have also examined the salting-out effects of sodium chloride on the **1**-catalyzed solvolysis of **2** ($n = 10-16$) in 1:1 (v/v) methanol−water solution in order to probe the relationship between the rate of the model reaction and changes in hydrophobic effects. The kinetic data for the salting-out effects on **1**-catalyzed solvolysis of **2** ($n = 10-16$) that result from added sodium chloride in 1:1 methanol−water solution are summarized in Table 1 and displayed in Figures 2−4. The

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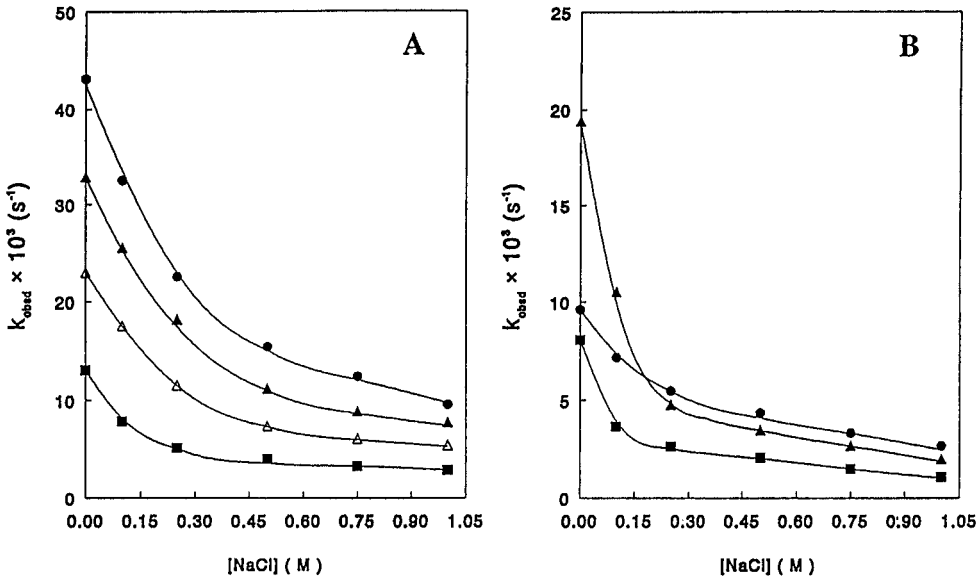

Figure 2. Pseudo-first-order rate constants (k_{obsd}) for the solvolysis of *p*-nitrophenyl alkanoates **2** ($n = 10-16$, 5.0×10^{-5} M) catalyzed by **1** in the presence of varied concentration of sodium chloride in 1:1 (v/v) methanol−aqueous buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) solution at 30 °C: (A) 7.5×10^{-5} unit mol L^{-1} **1**: ●, $n = 10$; ▲, $n = 12$; △, $n = 14$; ■, $n = 16$. (B) 5.0×10^{-6} unit mol L^{-1} **1**: ●, $n = 12$; ▲, $n = 14$; ■, $n = 16$.

pseudo-first-order rate constants (k_{obsd}) for the solvolysis of **2** ($n = 10-16$) catalyzed by **1** in the presence of varied amounts of sodium chloride in 1:1 (v/v) methanol−aqueous buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$) at pH 8.0 and 30 °C are presented graphically in Figure 2. At 7.5×10^{-5} unit mol L^{-1} **1** (Figure 2A), the rate was found to decrease approximately 4-fold when the concentration of sodium chloride was increased from 0 to 1.0 M for each of the four substrate esters. The order of reactivity for **2** ($n = 10-16$) was $n = 10 > 12 > 14 > 16$. At 5.0×10^{-6} unit mol L^{-1} **1** (Figure 2B), without sodium chloride, the solvolysis rate of **2** ($n = 14$) was much faster than that of **2** ($n = 12$ and 16) under the same experimental conditions. The order of reactivity was **2** ($n = 14 > 12 > 16$). A 10-fold decrease, a surprisingly large decrease, of the rate constant for solvolysis of **2** ($n = 14$) (Table 1) was found to accompany the increase in NaCl concentration (0−1.0 M), and approximately 70% of the decrease occurs over the concentration range 0−0.15 M NaCl. Clearly, the magnitude of salting-out effects is dependent on the alkyl chain length in **2**, and the effects are especially large for **2** ($n = 14$). The results displayed in Figure 2 also indicate that the salting-out effects depend upon the concentration of **1**. Further support for these conclusions is provided by additional experiments that monitor effects of sodium chloride concentration on **1**-catalyzed solvolysis of **2** (Table 1). As the concentration of NaCl was increased from 0.10 to 0.75 M, the rate decrease, which is expressed as a ratio of $k_{0,obsd}$ to $k_{s,obsd}$ for **1**-catalyzed solvolysis of **2** in the absence and in the presence of NaCl, varied from 1.9-fold to 7.4-fold for **2** ($n = 14$) at 5.0×10^{-6} unit mol L^{-1} **1**, while the reduction in the solvolysis rate of **2** ($n = 14$) varied from 1.3-fold to 4.1-fold at 5.0×10^{-5} unit mol L^{-1} **1**. The magnitude of the salting-out effects for each of the four esters increases with the concentration of NaCl in 1:1 methanol−water solution. We suggest that reduced catalytic activity and substrate preferences for **2** ($n = 10-16$) that accompany increasing NaCl concentration may be ascribed to the changes of the morphology and/or composition of aggregates containing **1** and **2** and decreased dependence of the aggregate formation on the hydrophobicity of the substrate.[39,42] This response is believed to be due primarily to enhanced hydrophobic self-association of **1** and **2** and increased stabilization of N-acylpyridinium intermediate **3** within hydrophobic self-aggregates.[38]

Table 1. Salting-Out Effects of Sodium Chloride on 1-Catalyzed Solvolysis of 2 ($n = 10-16$) in 1:1 (v/v) Methanol−Aqueous Buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) Solution at 30 °C

1 (unit mol L^{-1})	**2**[a]	NaCl (M)	$k_{s,obsd} \times 10^3$ (s^{-1})[b]	$k_{0,obsd}/k_{s,obsd}$[c]
5.0×10^{-6}	$n = 12$	0.10	7.14	1.34
	$n = 12$	0.25	5.45	1.76
	$n = 12$	0.50	4.35	2.21
	$n = 12$	0.75	3.30	2.91
	$n = 12$	1.00	2.65	3.62
5.0×10^{-6}	$n = 14$	0.10	10.50	1.85
	$n = 14$	0.25	4.75	4.08
	$n = 14$	0.50	3.45	5.62
	$n = 14$	0.75	2.64	7.35
	$n = 14$	1.00	1.96	9.90
5.0×10^{-6}	$n = 16$	0.10	3.65	2.20
	$n = 16$	0.25	2.62	3.07
	$n = 16$	0.50	2.05	3.93
	$n = 16$	0.75	1.48	5.44
	$n = 16$	1.00	1.05	7.67
1.0×10^{-5}	$n = 12$	1.00	3.99	4.18
	$n = 14$	1.00	2.85	7.30
	$n = 16$	1.00	1.50	6.80
2.5×10^{-5}	$n = 10$	1.00	3.95	5.19
	$n = 12$	1.00	5.75	5.29
	$n = 14$	1.00	3.75	5.60
	$n = 16$	1.00	1.98	5.51
5.0×10^{-5}	$n = 10$	0.10	22.00	1.39
	$n = 10$	0.25	15.90	1.91
	$n = 10$	0.50	11.50	2.65
	$n = 10$	0.75	9.25	3.30
	$n = 10$	1.00	7.42	4.11
5.0×10^{-5}	$n = 12$	0.10	24.80	1.27
	$n = 12$	0.25	17.65	1.78
	$n = 12$	0.50	10.45	3.01
	$n = 12$	0.75	8.10	3.89
	$n = 12$	1.00	6.74	4.67
5.0×10^{-5}	$n = 14$	0.10	16.60	1.33
	$n = 14$	0.25	10.85	2.03
	$n = 14$	0.50	6.68	3.29
	$n = 14$	0.75	5.35	4.11
	$n = 14$	1.00	4.65	4.73
5.0×10^{-5}	$n = 16$	0.10	7.12	1.69
	$n = 16$	0.25	4.65	2.58
	$n = 16$	0.50	3.50	3.43
	$n = 16$	0.75	2.85	4.21
	$n = 16$	1.00	2.45	4.90
7.5×10^{-5}	$n = 10$	1.00	9.56	4.49
	$n = 12$	1.00	7.72	4.25
	$n = 14$	1.00	5.36	4.27
	$n = 16$	1.00	2.85	4.56

[a] [**2**] = 5.0×10^{-5} M. [b] $k_{s,obsd}$, pseudo-first-order rate constant in the presence of NaCl. [c] $k_{0,obsd}$, pseudo-first-order rate constant in the absence of NaCl.

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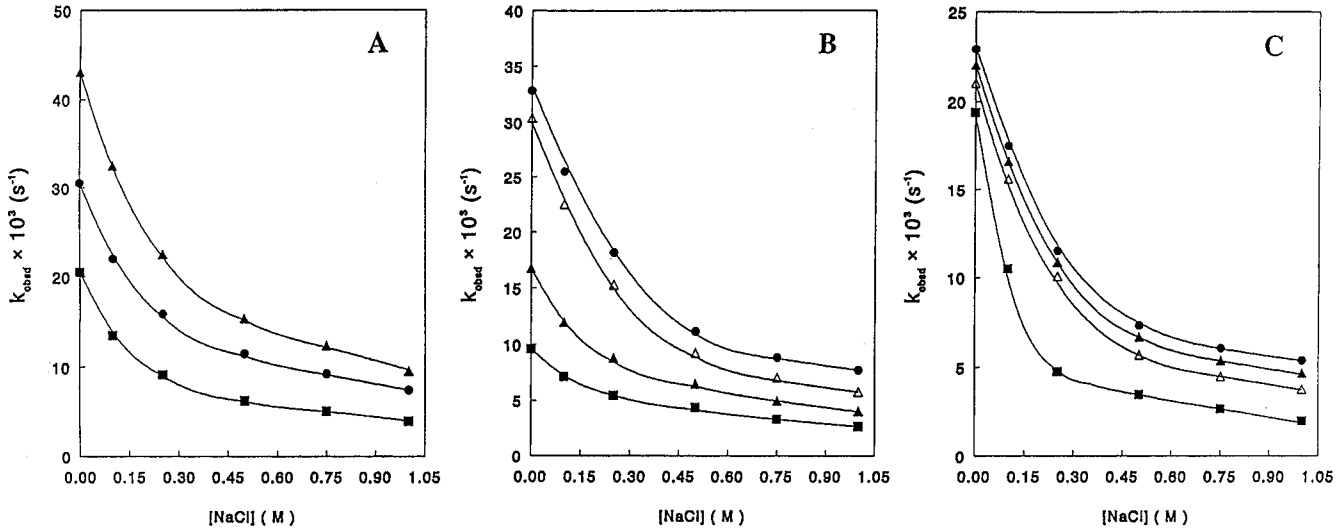

Figure 3. Effects of **1** concentration on pseudo-first-order rate constants (k_{obsd}) for **1**-catalyzed solvolysis of **2** ($n = 10-14$, 5.0×10^{-5} M) in the presence of varied concentration of sodium chloride in 1:1 (v/v) methanol−aqueous buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) solution at 30 °C: (A) **2** ($n = 10$): ▲, 7.5×10^{-5} unit mol L^{-1}; ●, 5.0×10^{-5} unit mol L^{-1}; ■, 2.5×10^{-5} unit mol L^{-1}. (B) **2** ($n = 12$): ●, 7.5×10^{-5} unit mol L^{-1}; △, 2.5×10^{-5} unit mol L^{-1}; ▲, 1.0×10^{-5} unit mol L^{-1}; ■, 5.0×10^{-6} unit mol L^{-1}. (C) **2** ($n = 14$): ●, 7.5×10^{-5} unit mol L^{-1}; ▲, 5.0×10^{-5} unit mol L^{-1}; △, 2.5×10^{-5} unit mol L^{-1}; ■, 5.0×10^{-6} unit mol L^{-1}.

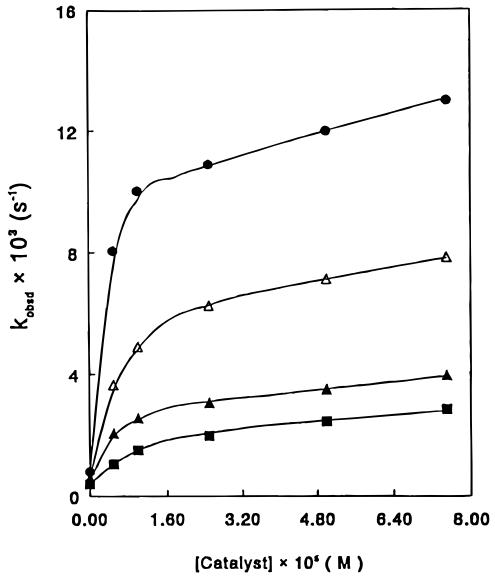

Figure 4. Pseudo-first-order rate constants (k_{obsd}) for **1**-catalyzed solvolysis of **2** ($n = 16$, 5.0×10^{-5} M) as a function of NaCl concentration in 1:1 (v/v) methanol−aqueous buffer (0.05 M $H_2PO_4^-/HPO_4^{2-}$, pH 8.0) solution at pH 8.0 and 30 °C: ●, in the absence of NaCl; △, in the presence of 0.1 M NaCl; ▲, in the presence of 0.5 M NaCl; ■, in the presence of 1.0 M NaCl.

Relevant plots of the pseudo-first-order rate constants vs NaCl concentrations for the solvolysis of **2** ($n = 10$, 12, and 14) catalyzed by **1** as a function of the catalyst concentration in 1:1 methanol−water solution are shown graphically in Figure 3. In the presence of sodium chloride, all solvolysis reactions show an inverse relationship between solvolysis rate and NaCl concentration. Rates of solvolysis remain proportional to the concentration of **1** when determined in the presence of NaCl, and the shapes of the curves (Figure 3) are practically the same for the three substrates, indicative of similar controlling factors in the salting-out effects in these systems.

Figure 4 shows relevant plots of the pseudo-first-order rate constants vs catalyst concentrations for the solvolysis of **2** ($n = 16$) catalyzed by **1** as a function of NaCl concentration. In the absence of sodium chloride, solvolysis rate increases rapidly with an increase in concentration of **1** to 1.5×10^{-5} unit mol L^{-1} as the substrate associates with the catalyst and finally saturation is obtained for high concentrations of **1** when the substrate is fully bound. However, significant decreases of the solvolysis rates are observed with increases in NaCl concentration. It is noted that the plots for saturation kinetics level off with increasing NaCl concentration. This may be due to morphological changes in aggregates of **1** induced by added NaCl which lead to reduced binding surface of the macromolecular aggregates and to more effective partitioning of hydrophobic and hydrophilic species in the aqueous methanol solution.[42] The reaction solutions become turbid when sodium chloride is increased to more than 1.0 M in 1:1 methanol−water solution.

Clearly, there would be increased stabilization of **2** if it formed self-aggregates which buried the ester group in a hydrophobic phase and isolated these reactive species from the 1:1 methanol−water solution.[38] We contend that added NaCl decreases access by substrate to the catalyst surfaces in **1**-catalyzed solvolysis of **2** ($n = 10-16$) and access of intermediate **3** to solvent components and slows exchange rates of reaction components among solution and aggregated phases. This contention is based on the fact that the addition of electrolytes facilitates the formation of hydrophobic aggregates of polymers[43] and the hydrophobic interactions between polymers and organic additives are diminished with increases of electrolyte concentration in aqueous solution.[44]

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