JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2001; **14:** 823–831
DOI:10.1002/poc.441

Optimization of micellar catalysis of nucleophilic substitution reactions in buffered solutions of cetyltrimethylammonium halide surfactants, part 2: buffers in the pH range 7–8

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Received 26 May 2001; revised 18 July 2001; accepted 24 July 2001

ABSTRACT: Binding of the phosphate, tris-(hydroxymethyl)-methylamine, aminomethylpropanediol, and glycinemethylester buffers by cetyltrimethylammonium chloride (CTACl) in aqueous solutions has been probed by investigating: (1) the dependence of the buffer pH (starting pH 7.9) on [CTACl], and (2) the micellar effect on the kinetics of dephosphorylation of *p*-nitrophenyldiphenylphosphate (PNDPP) by the anion of isonitrosoacetylacetone (INAA) in CTACl solutions in the presence of the same buffers. The pH–[CTACl] profiles showed a marked dependence on the buffer employed and the coion, Y^-, of its acidic component, $RNH_3^+Y^-$. The sizeable pH decrease observed with phosphate buffer (0.43 pH units for [Buffer] = 10^{-2} M at [CTACl] = 2×10^{-2} M) indicates that *both* buffer components, namely $H_2PO_4^-$ and HPO_4^{2-}, exchange with the surfactant counterion, Cl^-. This ion exchange occurs at the expense of the nucleophile (anion of INAA)–Cl^- counterpart. Indeed, the micellar acceleration of the phosphate-buffered reaction is the smallest, $k_{max}/k_w = 410$ (k_{max} and k_w are the maximum pseudo first-order rate constants in buffered micellar solutions and bulk water, respectively). Although CTACl micelles do not seem to incorporate the neutral component of amino buffers, the pH–[CTACl] profiles were found to depend on the nature in Y^- (F^-, Cl^- or AcO^-). The micellar accelerations ($k_{max}/k_w \approx 600$), however, were not strongly altered by a change in the buffer coion, except where $Y^- = F^-$. In the interfacial region, the partially desolvated fluoride ion behaves as a nucleophile, competing with INAA anion for the dephosphorylation of PNDPP. The rate–[surfactant] profiles were interpreted in terms of the pseudophase ion-exchange model, as applied to a reaction scheme involving competitive exchanges of the oximate and Y^- for the surfactant counterion. The second-order rate constant of the micelle-mediated reaction, smaller (*ca* one-third) than that in bulk aqueous solution, is discussed in terms of the properties (ionic strength and microscopic polarity) of interfacial water. Copyright © 2001 John Wiley & Sons, Ltd.

INTRODUCTION

The study of acid–base equilibria in solutions of ionic surfactants is of fundamental importance to rationalizing micellar catalysis, e.g. of pH-dependent reactions involving ionic species.[1,2] However, the 'buffering' of aqueous micellar solutions is a deceptively simple problem that has not been conveniently solved for several situations of interest.[3–6] For example, use of 'well-behaved' buffers has been recommended. This term refers to buffers whose binding to the micellar interface is much weaker than that of the surfactant counterion and are capable, therefore, of maintaining their buffering capacity of the aqueous pseudophase. A typical example is to use boric acid/borate to buffer cetyltrimethylammonium (CTA^+) halide micellar solutions in the pH range 8–10. Absence of a significant surfactant-induced pH change has been interpreted in terms of a negligible micelle binding of the buffer.[6] However, we have recently shown that pH constancy may also arise from similar binding of both buffer components by the CTA^+ micelle.[7]

The following aspects of buffered micellar solutions have been addressed by using the pseudophase ion-exchange (PIE) model,[1,8] the Poisson–Boltzman equation,[1,9] the Brönsted–Bjerrum equation,[3,4,10] as well as other models:[11,12] (i) micelle-induced pH changes of aqueous buffers;[1] (ii) micelle-induced p*K* changes of an acid and its conjugate base;[1,2,6] (iii) buffer-induced changes of the properties of organized assemblies, e.g. their critical micelle concentrations (CMCs), degrees of

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Contract/grant sponsor: FAPESP.

dissociation α, and geometry;[1,13] (iv) buffer-induced changes of the nature of the interfacial region, especially hydration and ionic strength.[8,12–14]

There is only scant information on the above-mentioned buffer-induced changes [points (iii) and (iv)] that can be considered in the general context of salt effects on organized assemblies.[12,14,15] With regard to the first two points, most authors employ the PIE model and its recent extensions.[7,11a,15] These assume that pH or pK changes are due to preferential micellar incorporation of one of the buffer components, due to a combination of 'medium' and electrostatic effects. The former stems from differences between the properties (e.g. microscopic polarity and ionic strength) of bulk and interfacial water, whereas the latter is due to electrostatic interactions between the charged interface and the buffer components.[5,7,16]

A more complex situation arises, however, when the reactants (in the buffered micellar solution) are themselves weak acids/bases, as in nucleophilic substitutions.[1] Consider the reaction of a hydrophilic anionic nucleophile Nu^- with a lipophilic substrate in the presence of CTACl micelles. The micellar kinetic effect depends on $[Nu^-]_m$, the concentration of the nucleophile in the interfacial region. This concentration depends, in turn, on the ion exchange of Nu^-, as well as the buffer components with the surfactant counterion [Eqns (1) and (2)]:

$$CTACl + Nu^- \overset{K_{Cl}^{Nu}}{\rightleftharpoons} CTA\ Nu + Cl^- \qquad (1)$$

$$CTACl + Buf \overset{K_{Cl}^{Buf}}{\rightleftharpoons} CTABuf + Cl^- \qquad (2)$$

where K_{Cl}^{Nu} and K_{Cl}^{Buf} are the exchange constants of the nucleophile and the buffer, respectively, with the surfactant counterion. Consequently, the larger the buffer binding, the smaller is $[Nu^-]_m$ and the smaller is the micellar effect on the rate. Moreover, because of the buffer–surfactant ion exchange, the surfactant present is a mixture of CTACl and CTABuf,[1,7,11] as shown in Scheme 1, where S is the substrate.

Consequently, the usual rate–[surfactant] profiles from which micellar rate constants, k_m and K_{Cl}^{Nu}, are calculated cannot be readily analyzed in terms of the PIE equation [Eqn. (3)] since the composition of the organized assembly changes as a function of increasing [CTACl]. In Eqn. (3), $k_{2,w}$ is the second-order rate constant in the aqueous pseudophase, $[Nu^-]_T$ is the total nucleophile concentration, K_s is the micelle–substrate binding constant and $[D_n] = [CTACl] - CMC$:

$$k_{obs} = \frac{k_{2,w}[Nu^-]_T + (k_m K_s - k_{2,w})[Nu^-]_m}{1 + K_S[D_n]} \qquad (3)$$

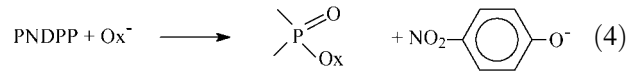
In practice, the above-mentioned complications can be avoided if the buffer components do not bind to the micelle, i.e. $K_{Cl}^{Buf} \ll K_{Cl}^{Nu}$ [i.e. no competition from Eqn. (2)], so that the buffer capacity is maintained, and $[Nu^-]_T$ and the micelle composition are kept constant.

The objectives of the present work were to identify 'well-behaved' buffers in order to obtain large micellar accelerations and to interpret the experimental rates in terms of the PIE model. In a recently published paper,[7] the dephosphorylation of *p*-nitrophenyldiphenyl phosphate[6c] (PNDPP) by butanedione monoximate was studied in the presence of buffered solutions of CTABr, CTACl and CTAOAc. Comparison of pH and/or k_{obs} versus [CTACl] profiles showed that hydroxyamines, ethanolamine in particular, but not borate are well-behaved buffers in the pH range 9–10. By using a different oxime and other buffers, we have now extended this pH range to *ca* 8. It is shown that phosphate binds significantly to CTA^+, and that amine buffers, and tris-(hydroxymethyl)-methylamine (tris) in particular, give rise to marked micellar accelerations, with some dependence on the counterion of the protonated amine.

RESULTS AND DISCUSSION

Choice of the reaction and system components

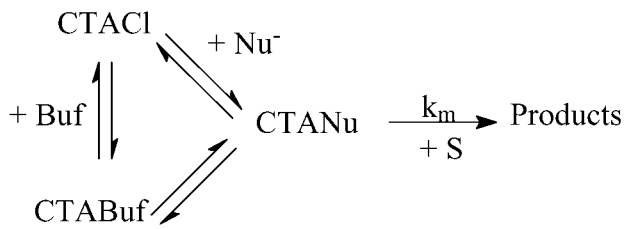
We have used a dephosphorylation reaction, namely the nucleophilic esterolysis of PNDPP by oximate anions (Ox^-) in CTACl buffered solutions, Eqn. (4), in order to compare buffer effects on pH and reactivity in micellar solutions.



(4)

PNDPP is a convenient substrate because the liberated *p*-nitrophenolate ion is readily monitored. Additionally, this ester is very hydrophobic (with CTA^+ $K_s \approx 10^4\ M^{-1}$),[17] so that its reaction in the aqueous pseudophase is negligible.

Oximates are strong α-nucleophiles.[18] Consequently, the reaction of PNDPP with other nucleophiles present, including H_2O, OH^- and amines, can be neglected.



Scheme 1

Table 1. Composition of the aqueous buffer solutions at pH 7.90 and pH dependence on the addition of [CTACl] $\leq 2 \times 10^{-2}$ M

Run	Buffer[a]	[B]/[BH$^+$][b]	[Buffer]$_T$ (M)[c]	[Coion] (M)[d]	ΔpH[e,f]
1	Phosphate (7.21)	4.68	10^{-1}	–[g]	0.0
2		4.68	10^{-2}	–[h]	−0.43
3	Tris (8.1)	0.60	10^{-1}	[Cl$^-$] = 6.1×10^{-2}	0.0
4		0.60	10^{-2}	[Cl$^-$] = 6.1×10^{-3}	0.0[i]
5		0.60	10^{-2}	[AcO$^-$] = 6.1×10^{-3}	0.0[j]
6		0.60	10^{-2}	[F$^-$] = 6.1×10^{-3}	0.0[k]
7	AMP[l] (8.8)	0.12	10^{-1}	[AcO$^-$] = 9×10^{-2}	0.0
8		0.12	10^{-2}	[AcO$^-$] = 9×10^{-3}	0.0
9		9.8[m]	10^{-2}	[AcO$^-$] = 9×10^{-4}	0.0
10	GME[n] (7.75)	1.35	10^{-1}	[Cl$^-$] = 10^{-1}[o]	−0.15[p]
11		1.35	10^{-2}	[Cl$^-$] = 10^{-2}[o]	−0.20[p]

[a] pK in water, in parentheses.
[b] [base]/[acid] ratio at [CTACl] = 0.
[c] [B] + [BH$^+$].
[d] Counterion of the acidic protonated amine.
[e] ΔpH = pH (of the water pseudophase at [CTACl] = 2×10^{-2} M) −pH (at [CTACl] = 0).
[f] Reproducibility better than 0.05 pH units.
[g] [HPO_4^{2-}] = 8.2×10^{-2}M; [H_2PO_4] = 1.8×10^{-2} M.
[h] [HPO_4^{2-}] = 8.2×10^{-3}M; [$H_2PO_4^-$] = 1.8×10^{-3} M.
[i] ΔpH = −0.25 at [CTACl] = 10^{-3} M.
[j] ΔpH = −0.40 at [CTACl] = 10^{-3} M.
[k] Whatever [CTACl].
[l] 2-aminomethyl-1,3-propanadiol.
[m] At pH 9.80; Ref 7.
[n] glycinemethylester.
[o] The buffered solutions are obtained by addition of KOH to $RNH_3^+Cl^-$.
[p] This ΔpH is for [CTACl] = 10^{-3} M and is unchanged by addition of larger [CTACl]; see Fig. 1.

Isonitrosoacetylacetone [INAA, $(CH_3CO)_2$—C═NOH, also called hydroximinoacetylacetone] was employed because its pK_a in water (7.38)[19] lies within the pH range chosen for the present study, i.e. 7 to 8.

Finally, CTACl has been employed as surfactant. The strong binding of the counterion of CTABr leads only to a small micellar acceleration, due to unfavorable oximate–Br^- exchange.[6c,7] Although the acetate ion of CTAOAc is more readily exchangeable,[20] this surfactant has not been investigated because its effect on the rate is similar to that of CTACl,[7] and the micellar properties of the latter surfactant have been studied in detail.

The buffers employed, phosphate and amines, differ widely with regard to their binding to CTA^+. In the pH range studied, both forms of the phosphate buffer, namely $H_2PO_4^-$ and HPO_4^{2-}, are anions and should, in principle, bind to CTA^+. It is frequently assumed, however, that binding of the former component to CTA^+ can be neglected.[20,21] With amine buffers, the basic component, i.e. the amine, carries no charge and, therefore, is not expected to interact electrostatically with the CTA^+ head-group. It can be incorporated into the micelle, however, by hydrophobic interactions, akin to other moderately hydrophilic nonionic solutes.[22] Contribution of this interaction is expected to be small, however, because the buffers employed, *viz*. ethanolamine, tris, and 2-aminomethyl-1,3-propanediol (AMP), carry the hydrophilic OH group.[23] With regard to the acidic component of the amine buffer, $RNH_3^+Y^-$, RNH_3^+ is not prone to micellar binding due to electrostatic repulsion with CTA^+, although Y^-, its coion, may exchange for the surfactant counterion.

pH versus [CTACl] profiles of the buffers employed

Table 1 and Figs 1–3 show the effects of [CTACl] on buffer pH, at total buffer concentration [Buffer]$_T$ = 10^{-1} and 10^{-2} M, with different Y^-. Except for glycinemethylester (GME), no significant pH dependence on [CTACl] (concentration range $\leq 2 \times 10^{-2}$ M) has been observed at [Buffer]$_T$ = 10^{-1} M, see Table 1 and Fig. 2. That is, the buffer maintains its capacity, even if both components exchange for the surfactant counterion, because concentrations of micelle-bound buffer components are too small compared with [Buffer]$_T$.

Addition of CTACl to 10^{-2} M buffer solution has resulted either in no pH change, or a pH decrease. This shows that micellar binding of the acidic component of the buffer (which should have lead to a pH *increase*) is smaller than, or is equal to that of its basic partner. These pH profiles, however, exhibit a number of interesting features specific to the buffer employed, as discussed below.

(1) With phosphate buffer (Table 1, entry 2, and Fig.

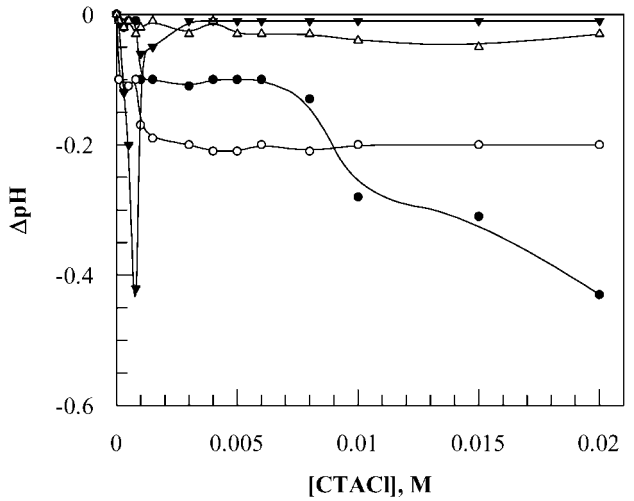


Figure 1. Dependence of pH of the aqueous buffer solution on [CTACl], under the following conditions: $pH_o = 7.9$, 25 °C, $[Buffer]_T = 10^{-2}$ M. The plots are for the following buffers: phosphate (●), GME/Cl^- (○), AMP/AcO^- (△), tris/AcO^- (▼). In this and subsequent figures, the solid lines were drawn to guide the eye

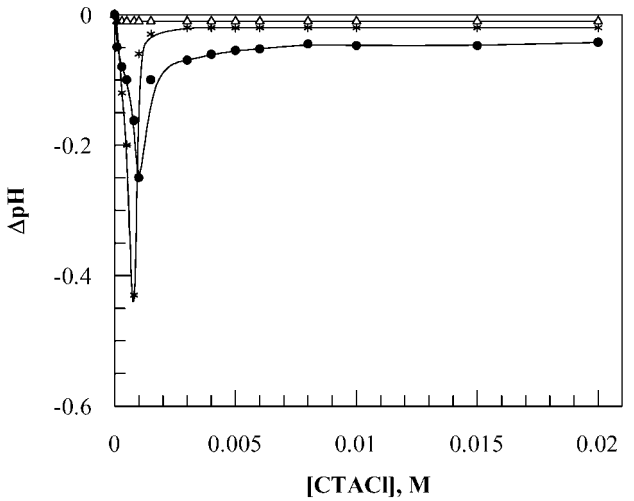


Figure 3. Dependence of pH of aqueous solutions of tris buffer on [CTACl] and the buffer coion, at $pH_o = 7.9$, 25 °C and $[tris]_T = 10^{-2}$ M. The plots refer to the following Y^- of $RNH_3^+Y^-$: acetate (*), chloride (●), and fluoride (△)

2), addition of CTACl decreases the solution pH noticeably, in agreement with the chloride–phosphate dianion exchange constant,[20] $K_{Cl}^{HPO_4^{2-}} = 0.78$. The experimental pH-profile, however, does not correspond to that based only on this ion exchange (Fig. 2). Addition of CTACl ($\leq 10^{-3}$ M) leads to a small pH drop (0.1 pH unit) followed by a plateau in the concentration range $10^{-3} < [CTACl] < 6 \times 10^{-3}$ M. The pH then decreases at $[CTACl] = 8 \times 10^{-3}$ M, i.e. well above the surfactant CMC in the presence of buffers (*ca* 5×10^{-4} M).[7,15a,24] A constant pH

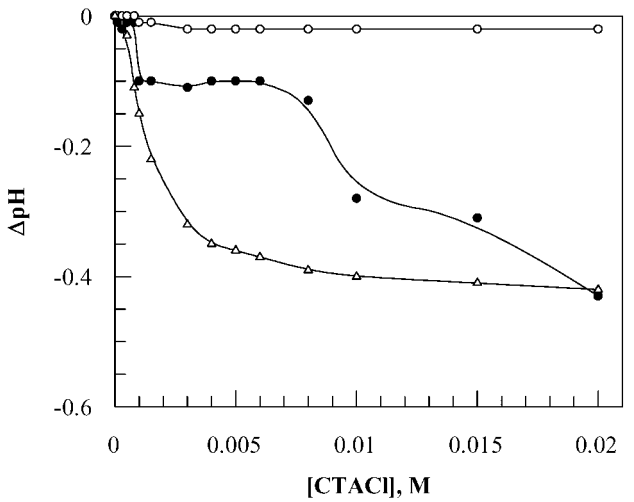


Figure 2. Dependence of pH of aqueous solutions of phosphate buffer on [CTACl], at $pH_o = 7.9$ and 25 °C. The plots are for $[Phosphate]_T = 10^{-1}$ M (○), $[Phosphate]_T = 10^{-2}$ M (●). The symbol △ refers to pH values calculated with the PIE model, by using $K_{Cl}^{HPO_4^{2-}} = 0.78$ and assuming no binding of $H_2PO_4^-$ (see text)

implies that *both* components of the buffer exchange for the surfactant counterion. Therefore, the pH profile of the phosphate buffer suggests strongly that not only the basic dianionic phosphate but also the acidic monophosphate anion exchange for the chloride ion of the surfactant, with $K_{Cl}^{H_2PO_4^-}$ smaller[22c] than $K_{Cl}^{HPO_4^{2-}}$. However, a quantitative analysis of the observed pH profile is not possible with these data only.

(2) The hydroxymethyl amines show quite different pH–surfactant profiles. Thus no pH change has been observed with AMP solutions:[23] Table 1. A similar behavior has been observed for AMP at pH 9.8, i.e. at a very different [acid]/[base] ratio.[7] The obvious conclusion is that there is no micellar incorporation of both components of this buffer.

(3) A similar conclusion on buffer incorporation can be drawn for tris at $[CTACl] \geq 4 \times 10^{-3}$ M. This is consistent with the marked hydrophilicity of solutes carrying the hydroxymethyl group.[22,25] However, close to $[CTACl] = 8 \times 10^{-4}$ M, i.e. close to the CMC of the surfactant, the pH-profiles of 10^{-2} M tris buffers exhibit 'dips', Figs 1 and 3. The depth of the dip depends on the nature of Y^-, and in particular on its solvation energy.[21,26] It is deep (−0.40 pH unit) for the poorly solvated acetate ion, less pronounced (−0.25 pH unit) for the chloride ion, and disappears for the strongly solvated fluoride ion. The reason for the dependence of ΔpH on the solvation of Y^- is unclear at the moment, but it may be due to specific interactions within sub-micellar aggregates,[11a] since the dip disappears above the CMC.

(4) Finally, the pH profile of GME is different from other amine buffers in two respects: (i) the pH becomes independent of [CTACl], after an initial decrease

of *ca* 0.2 pH unit, caused by addition of 10^{-3} M surfactant (Fig. 1): (ii) this profile was observed at $[Buffer]_T = 10^{-2}$ and 10^{-1} M (plot not shown). As in the case of borate,[7] the absence of pH dependence at higher [surfactant] suggests a similar incorporation of the acid and base components of GME, an aminoester less hydrophilic than the hydroxymethyl amines.[22] Moreover, the large concentrations of chloride ions added to the aqueous pseudophase (Table 1) can also affect the structure of the micellar aggregates and their ion-binding ability.[13a]

In conclusion, each of the buffers studied exhibits a specific pH response to addition of CTACl. Even if the acid component of the amine buffers is not incorporated into the micelle, its coion appears to affect ΔpH. These results bear on general and specific salt effects on micellar interfacial regions.[8,12,13]

PNDPP–INAA reaction in bulk aqueous solution

In aqueous solution, the pK_a of INAA is 7.38, i.e. there will be comparable concentrations of the oxime and oximate ion (the reactive nucleophile in the dephosphorylation reaction) in the aqueous pseudophase at the pH of the present study, i.e. 7.9.[19,27] The oxime, however, is unstable in bulk water at this pH because of a reaction between its anionic and neutral forms that produces pyruvic acid, among other products.[28] Accordingly, we were unable to obtain reliable rate data for the reaction of PNDPP with INAA in this medium. In contrast, reproducible pseudo first-order kinetics were observed in bulk aqueous solution at pH 9.8, i.e. where the concentration of the oxime is negligible compared with that of the oximate. The second-order rate constant for the reaction of INAA anion with PNDPP in buffered bulk aqueous solution was found to be $k_{2,w} = 0.27 \pm 0.01$ M^{-1} s^{-1}.

PNDPP–INAA reaction in micellar pseudophase

In our previous work,[7] the rate constant $k_{2,m}$ for the reaction of PNDPP with 2,3-butanedione monoximate [Eqn. (4) with $Ox^- = CH_3COC—(CH_3)=NO^-$] in the presence of CTACl was determined with the oxime–oximate system itself acting as buffer. The reason was to avoid ion exchange, other than that between Cl^- and the oximate. This procedure was unsuccessful with INAA, because of the above-mentioned decomposition at pH 7.9 in the aqueous pseudophase. This reaction is probably responsible for the unreasonably large pH drop (*ca* three units) that has been observed in the pH–[CTACl] profile for the oxime/oximate buffer, due to the formation of acidic species, e.g. pyruvic acid (in water, $pK_a = 2.50$). For INAA, $k_{2,m}$ and K_{Cl}^{Ox} are, therefore, inaccessible by this method.

However, in agreement with published data on bimolecular reactions in micellar media,[1,6,7,11a] it is expected that $k_{2,m}/k_{2,w}$, the ratio between the rate constants of the reaction in micellar and aqueous pseudophases, is smaller than unity, as found for the butanedione monooximate–PNDPP reaction.[7] Therefore, it is estimated that $k_{2,m}$ for the INAA–PNDPP reaction is in the order of 0.1 M^{-1} s^{-1}, corresponding to $k_m = 0.7$ s^{-1} with $k_m = k_{2,m}/V_m$ (micellar volume, $V_m = 0.14$ M).[1c] The expected K_{Cl}^{Ox} value for INAA oximate should be either similar to that for butanedione monooximate,[7] if electrostatic interactions dominate the ion exchange, or slightly smaller if hydrophobic interactions play a role. With regard to the latter, INAA appears to be more hydrophilic than butanedione monoxime, based on values of log P_{oct}[22d,22e] (the partition coefficient of nonionic solutes between *n*-octanol and water, a measure of their hydrophobic character) of 0.86 and 0.02 respectively.

Dependence of the micellar acceleration on buffer

In contrast to the reactions at pH 7.9 in bulk water, or in CTACl solution buffered solely by INAA, there is no significant oxime decomposition in the reaction in CTACl solutions buffered by phosphate, tris or AMP. This is evidenced by the quality of the rate data,[†] and the absence of a pH drop at the end of the reaction. The INAA stability may arise from: (i) the reaction of the oximate with PNDPP in the micellar pseudophase being faster than its reaction with the oxime in the aqueous pseudophase, resulting in a protection of INAA against decomposition (*vide infra*); (ii) the total oxime concentration in buffered CTACl solution ($[Ox]_T = 10^{-3}$ M) is smaller than that employed in the absence of surfactant ($[Ox]_T = 10^{-2}$ M). The second explanation seems unlikely, however, since INAA decomposition occurs in CTACl solutions buffered by GME (*vide infra*).

The observed rate–[surfactant] profiles in buffered CTACl solutions are shown in Fig. 4. They are consistent with second-order micelle-mediated ion–molecule reactions. With the three buffers, the largest acceleration occurs at [CTACl] close to $(1 \pm 0.2) \times 10^{-3}$ M, i.e. at [CTACl] slightly higher than the experimental CMC (5×10^{-4} M in the presence of buffers), as has been observed elsewhere.[11a] The corresponding k_{max} values and micellar accelerations (k_{max}/k_w) are reported in Table 2. The effect of buffer concentration is small, $k_{0.01M}/k_{0.1M} = 6$ for phosphate and 3 for tris and AMP, and can be attributed to a 'medium' effect arising from differences between the properties (including ionic strength and polarity) of the aqueous pseudophase and interfacial

[†]The pseudo first-order experiments afford excellent monoexponentials with correlation coefficient $R \geq 0.999$ and a reproducibility better than ±2%. Calculated [*p*-nitrophenoxide] was in excellent agreement with $[PNDPP]_0$.

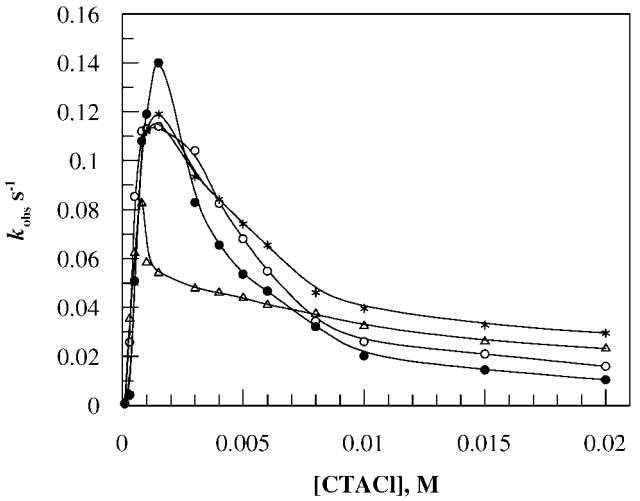


Figure 4. Rate–[surfactant] profiles for the PNDPP–INAA reaction [Eqn. (4)] at 25 °C in the presence of buffers, under the following conditions: $[Ox^-]_T = 7.5 \times 10^{-4}$ M; $[Buffer]_T = 10^{-2}$ M; $pH_o = 7.9$. The plots refer to: tris/Cl^- (○), tris/AcO^- (●), AMP/AcO^- (*), and phosphate (△)

water,[1,11–15,29] and/or an interfacial binding of the buffer, in the case of phosphate in particular. Tris/F^- exhibits an unexpected behavior, since the rate increases with [Buffer] instead of decreasing as for the other buffers, Table 2. This result is readily understood in view of the high nucleophilicity of dehydrated fluoride ions, and the possibility of a fluoride-ion-catalyzed dephosphorylation of PNDPP.[30] That is, the partially desolvated F^- in the interfacial region is likely to compete with micellized oximate. Although the chloride–fluoride exchange constant is small,[20] $K_{Cl}^{F} = 0.22$, the total fluoride ion concentration ($[F^-]_T = 6.2 \times 10^{-2}$ M and 6.2×10^{-3} M with tris/$F^- = 10^{-1}$ M and 10^{-2} M, respectively, Table 1) is large compared with that of the oximate, $[Ox^-]_T = 7.5 \times 10^{-4}$ M. From the relative values of $K_{Cl}^{F^-}$ and $K_{Cl}^{Ox^-}$, at $[tris/F^-] = 10^{-2}$ M, we estimate that $[F^-]_m$ is at least 1.7 times larger than $[Ox^-]_m$; this concentration difference may compensate for differences in reactivity between the two nucleophiles.

Table 2. Dependence of maximum micellar accelerations k_{max} of the PNDPP–INAA reaction on buffer in the presence of CTACl, at 25 °C[a]

Buffer[b]	$[Buffer]_T$	k_{max}[c] (s^{-1})	k_{max}/k_w[d]
Phosphate	10^{-1}	0.013	65
	10^{-2}	0.083	410
AMP/AcO^-	10^{-1}	0.037	185
	10^{-2}	0.119	590
Tris/AcO^-	5×10^{-2}	0.107	530
	10^{-2}	0.140	690
Tris/Cl^-	10^{-1}	0.040	200
	10^{-2}	0.110	540
Tris/F^-[e]	10^{-1}	0.280	
	10^{-2}	0.210	–

[a] Eqn. (4) with Ox^- = INAA oximate.
[b] Buffer composition of Table 1.
[c] At ± 2%; for $[CTACl] = 1 \times 10^{-3}$ M.
[d] k_w/s^{-1} calculated with $k_{2,w} = 0.27$ M^{-1} s^{-1} at $[Ox^-] = 7.5 \times 10^{-4}$ M.
[e] Competition between dephosphorylation by Ox^- and F^-; see text.

The trend of the micellar acceleration (k_{max}/k_w in Table 2) and its dependence on the buffer is not fully consistent with the conclusions of the pH-metric study of the buffers. Whereas the micellar kinetic effect in the presence of phosphate, the most strongly CTACl-bound buffer, is, as expected, the smallest (Table 2), significant differences in k_{max}/k_w were observed with amino buffers, although the pH–[CTACl] profiles imply no buffer incorporation. These differences can be readily interpreted in the following terms: the changes in micellar effects result, unambiguously, from changes in the concentration of micellized oximate anions $[Ox^-]_m$, which are related to $K_{Cl}^{Ox^-}$ rather than to changes in the micellar rate constant k_m. (k_m can vary with the *buffer-dependent* hydration and ionic strength of the interface. However, the corresponding k_m variations are likely to be within the error range of the k_m value measured in this work.) The smaller the interfacial binding of the buffer components, and in particular the coion Y^-, the larger is the concentration of micellized oximate $[Ox^-]_m$ and the larger is the micellar acceleration.

The role of the buffer coion in determining $[Ox^-]_m$ is evidenced by comparing the micellar effects where tris/AcO^- and tris/Cl^- were used as buffers. With the more strongly CTA-bound chloride, the rate increase is slightly smaller and, as expected, $[Ox^-]_m$ is smaller. In contrast, the micellar acceleration is large with AMP/AcO^- and tris/AcO^-. This agrees[‡] with the large concentrations of acetate ions added (6.08×10^{-3} M and 9×10^{-3} M for AMP and tris respectively; Table 1), readily exchangeable for the surfactant counterions, *vide infra*.

No reliable kinetic data were obtained for the GME-buffered micellar reaction, because the release of *p*-nitrophenolate was erratic and very slow. As in bulk aqueous solution buffered solely by the oxime buffer, the main reaction is the decomposition of INAA. This is strong evidence for an insignificant micellization of oximate ions. The inhibition of oximate micellization cannot result from the large concentrations of chloride ions introduced, since with this buffer the $[Cl^-]$ is not markedly higher (10^{-2} M) than with tris ($[Cl^-] = 6.1 \times 10^{-3}$ M). Therefore, inhibition of the oximate micellization is consistent with a saturation of the micellar interface by incorporation of both components of this

[‡]For tris/AcO^-, it is interesting to note that the dip in the pH–[CTACl] profile and the maximum acceleration occur at the same [CTACl] (1×10^{-3} M), i.e. where $[Ox^-]_m$ is the largest. In other words, the sizeable pH decrease of the tris/AcO^- buffer solution (attributed to ion-pair interactions in the aqueous pseudophase) did not provoke a significant decrease in $[Ox^-]_T$.

relatively hydrophobic buffer, as suggested by the pH data.

In summary, the micellar acceleration depends on $[Ox^-]_m$. This concentration, in turn, is determined by the interplay of the following factors: K_{Cl}^{Ox}; ion-exchange of buffer components (e.g. phosphate) or buffer coion (e.g. amines) for the surfactant counterion; inclusion of the amine itself (e.g. GME) into the micellar pseudophase; small specific salt effects. The latter effect is measurable because the buffer concentration in our study (10^{-2} M) is large compared with those of the surfactant and the oximate.

Extension of the PIE model to three-ion exchange reactions

The rate–[CTACl] profiles analogous to those of Fig. 4 are generally analyzed with the equation [Eqn. (3)] derived from the pseudophase ion-exchange model with $[Nu^-]_m = [Ox^-]_m$, calculated as m^{Ox} ($m^{Ox} = [Ox^-]_m/[D_n]$) from Eqn. (5), in which $[Cl^-]_T$ is the concentration of chloride ions, i.e. that of the surfactant, $[Ox^-]_T$ is the total oximate concentration, $K_{Cl}^{Ox} = ([Ox^-]_m[Cl^-]_w)/([Ox^-]_w[Cl^-]_m)$ and β is the micellar charge:

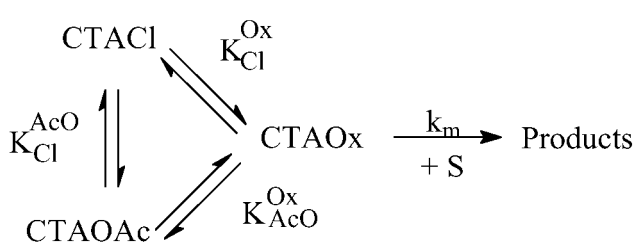
$$(m^{Ox})^2 - m^{Ox}\left(\frac{[Cl^-]_T + K_{Cl}^{Ox}[Ox^-]_T}{[D_n](K_{Cl}^{Ox} - 1)} + \beta\right) + \frac{\beta K_{Cl}^{Ox}[Ox^-]_T}{[D_n](K_{Cl}^{Ox} - 1)} = 0 \quad (5)$$

For the PNDPP–INAA reaction that occurs only at the micellar interface (K_s of PNDPP is large), Eqn. (3) simplifies to Eqn. (6), where m^{Ox} can be obtained from Eqn. (5) for a given K_{Cl}^{Ox}:

$$k_{obs} = k_m m^{Ox} = k_m \frac{[Ox^-]_m}{[D_n]} \quad (6)$$

According to Eqn. (6), the relationship between k_{obs} and m^{Ox} should be linear, the slope of which affords k_m. Therefore, K_{Cl}^{Ox} has to be iterated until the best regression coefficient R for the k_{obs}–m^{Ox} relationship is obtained.

When applied roughly to all the rate data of Fig. 4 and to those obtained previously for the PNDPP–butanedione monooximate,[7] this procedure does not provide any acceptable linear relationship, independently of the value of K_{Cl}^{Ox}.



Scheme 2

Table 3. Interfacial distribution, $m = [anion]_m/[D_n]$, of the three micellized anions, Cl^-, AcO^- and Ox^-, in CTACl solutions in the presence of AMP/AcO^- buffer ($[Buffer]_T = 10^{-2}$ M; $[AcO^-]_T = 8.93 \times 10^{-3}$ M; $[Ox^-]_T = 7.5 \times 10^{-4}$ M), calculated from Scheme 2 with $K_{Cl}^{Ox} = 2$ and $K_{AcO}^{Ox} = 4$

$10^3[D_n]$ (M)[a]	m^{Ox}	m^{AcO}	m^{Cl}	$10^2 k_{obs}$ (s^{-1})[b]
1	0.19	0.38	0.04	11.3
2.5	0.16	0.37	0.09	9.33
3.5	0.14	0.37	0.11	8.42
4.5	0.13	0.36	0.14	7.42
5.5	0.12	0.35	0.16	6.55
7.5	0.10	0.34	0.19	4.61
9.5	0.09	0.33	0.22	3.96
14.5	0.07	0.30	0.27	3.28
19.5	0.05	0.28	0.31	2.95

[a] $[D_n] = [CTACl] - CMC$ with $CMC = 5 \times 10^{-4}$ M; Ref. 24.
[b] At ± 2%.

In contrast, Eqn. (6) fits fairly well the experimental rate profile with tris/Cl^-, for which Scheme 1 simplifies to Eqn. (1), where $[Cl]_T$ of Eqn. (5) refers to the chloride ions from CTACl *and* the buffer. The better fit ($R = 0.998$) was observed over a rather large range of K_{Cl}^{Ox}, and k_m was obtained with an acceptable accuracy: $K_{Cl}^{Ox} = 2 \pm 1.5$, $k_m = 2 \pm 0.7 s^{-1}$, $k_{2,m}/k_w = 1 \pm 0.5$. These values are in reasonable agreement with those estimated above (*vide supra*).

For the two amine buffers with $Y^- = AcO^-$, Scheme 2 should be considered. According to Scheme 2, the oximate micellization arises not only by exchange with CTACl but also with CTAOAc. Therefore, not only K_{Cl}^{Ox} but also K_{AcO}^{Ox} must be taken into account. The relevant constants are: $K_{Cl}^{AcO} = 0.5, K_{AcO}^{Ox} = K_{Cl}^{Ox}/K_{Cl}^{OAc} = 2K_{Cl}^{Ox}$ with $0.5 < K_{Cl}^{Ox} < 3.5$. With these values, the balance between the three micellized anions, $[Cl^-]_m$, $[AcO^-]_m$ and $[Ox^-]_m$, is readily calculated§ for each K_{Cl}^{Ox} at each total surfactant concentration, as shown in Table 3, for example. Then, K_{Cl}^{Ox} is optimized by using Eqn. (6), under the form of $k_{obs}[D_n] = k_m[Ox^-]_m$, which provides a k_m value independent of [surfactant] and/or buffer type (tris or AMP). The best k_m value, 0.54 ± 0.05 s^{-1}, was obtained with $K_{Cl}^{Ox} = 1.5 \pm 0.5$ and 2.0 ± 0.5 for tris/AcO^- and AMP/AcO^- respectively. Therefore, for the PNDPP–INAA reaction, $k_{2,m} = 7.6 \times 10^{-2}$ M^{-1} s^{-1} and $k_{2,m}/k_{2,w} = 0.3$.

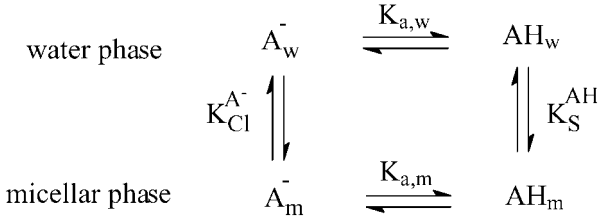
§In Scheme 2, the relative concentrations of the two surfactants present, namely CTACl and CTAOAc, do not depend on [oximate], since neither Cl^- nor AcO^- are consumed during the reaction. Therefore, $[Cl^-]_m$ and $[AcO^-]_m$ are first calculated at each $[CTA^+]_T$ with K_{Cl}^{AcO} only, without considering the presence of $[Ox^-]$. Then, $[Ox^-]_m$ is calculated as the sum of the micellized oximate concentrations, arising from its exchanges for $[Cl^-]_m$ and $[AcO^-]_m$ independently, at each $[CTA^+]$.

PNDPP-INAA reaction in micelles

We now consider the significance of the results obtained. The decrease of about one-third in the second-order rate constant for the PNDPP–INAA reaction on going from the aqueous pseudophase to the micellar interface is consistent with that found for the PNDPP–butanedione monooximate reaction ($k_{2,m}/k_{2,w} = 0.4$) and agrees with those usually obtained in nucleophilic substitutions.[1] The rate constant decrease of the oximate reactions in micellar media is likely to be attributed to the small polarity of the interfacial region, rather than to partial desolvation of the oximates at the interface. Indeed, it is now known that the high reactivity of these α-nucleophiles in water is due to their poor hydration,[18] i.e. further dehydration on going to the micellar interface should have an insignificant effect on their reactivity.

Despite the rate constant decrease, marked accelerations in micellar media are observed. This is consistent with the inappropriately[11a] termed 'micellar catalysis' of nucleophilic reactions, which is currently attributed to an increase in the nucleophile concentration in the small micellar volume and not to a rate constant increase.[1] In this respect, the data of Table 3 and the change in m^{Ox} with the surfactant concentration in the presence of AMP/AcO^- buffer are of interest. The large micellar acceleration in the presence of added acetate ions is readily understood since, at small [surfactant], the main surfactant is CTAOAc, which allows a markedly large micellar incorporation of the oximate: about 20% of the surfactant is present as CTAOx. These data also make it possible to understand why, in our previous work,[7] the micellar acceleration with CTAOAc was very similar to that with CTACl in the presence of added acetate ions.

Finally, the micellar protection of INAA against its decomposition also deserves to be emphasized, since similar results were obtained for dephosphorylation by the highly unstable magnesium monoperoxyphthalate (MMPP) in micellar media.[31] INAA and MMPP decompose by nucleophilic attack of their anionic forms on their neutral precursor.[28] A reasonable interpretation, consistent with the pK decrease of oximes at micellar interfaces (*vide supra*) is, therefore, that the two neutral and anionic species are segregated into two distinct pseudophases: oxime in the water pseudophase and oximate at the interface.



Scheme 3

CONCLUSIONS

The present study shows the complexity of analyzing pH–[surfactant] profiles of aqueous buffered solutions. For the pH region employed, 7–8, only AMP and tris can be considered as 'well-behaved' buffers, since both components, i.e. RNH_2 and RNH_3^+, are not micelle-incorporated. The role of the coion of $RNH_3^+Y^-$ should be taken into account, however, because ion exchange with the micellar counterion means that the surfactant present may be CTAY and not CTACl. In contrast, GME and phosphate, two frequently employed buffers in the pH range 7–8, are not suited for CTACl solutions, since both buffer components are incorporated into the micelle.

Our work bears on the question of micelle-induced pK_a changes ($\Delta pK_{a,m} = pK_{a,m} - pK_{a,w}$), because the relative binding of the buffer components is relevant to $K_{a,m}$, as shown in Scheme 3. According to Scheme 3, the absence of binding of one component implies a sizeable $\Delta pK_{a,m}$, since $K_{a,m}/K_{a,w} = K^{A^-}_{Cl}/K^{AH}_S$. Rate–and pH–[surfactant] profiles have indicated that both buffer components of the two hydroxymethylamines do not bind to the micelle, i.e. $\Delta pK_{a,m}$ values for these buffers are most certainly inaccessible. Our results for the relatively hydrophobic GME, and previous results on similar hydrophobic amines,[2,22] indicate that $\Delta pK_{a,m}$ for this buffer is negative. In agreement with the literature,[2] our data clearly indicate that $\Delta pK_{a,m}$ for phosphate is negative and relatively large, although its magnitude is probably less than that calculated from $K^{HPO_4^{2-}}_{Cl}$ only, since the phosphate monoanion also binds to the micelle. The oximate anion of INAA, but not its neutral form, binds to CTACl; therefore, a negative $\Delta pK_{a,m}$ is implied, in agreement with results of other oximes.[2,6] Significant micellar accelerations can be achieved only with 'well-behaved' buffers that do not inhibit micelle incorporation of the anionic nucleophile. For amine buffers, it is important to use readily exchangeable coions, because this leads to an additional increase of nucleophile micellization; Scheme 1. Independent of the buffer employed, however, salt effects on the organized assembly (including on the properties of interfacial water) are probably significant. Work is in progress to understand better these specific buffer effects.

EXPERIMENTAL

Materials

All reagents were purchased from Aldrich or Merck and were of the purest grade. Buffer solutions were prepared with CO_2-free distilled water. Freshly prepared solutions were used in all experiments. CTACl (≥98%, Fluka) was used without further purification. INAA was synthesized

according to the previously published procedure[19] and purified by sublimation under reduced pressure before use. Freshly prepared solutions were used for the kinetic experiments. The absence of INAA decomposition was checked spectrophotometrically (oxime: $\lambda_{max} = 232$ nm, $\varepsilon_{max} = 9250\ M^{-1}\ s^{-1}$; oximate: $\lambda_{max} = 281$ nm, $\varepsilon_{max} = 10700\ M^{-1}\ s^{-1}$). PNDPP was prepared and purified as previously described.[32]

Kinetic measurements

Rate constants were determined at 25.0 ± 0.01 °C under pseudo first-order conditions in the thermostatic cell of a Perkin Elmer $\lambda 2$ spectrophotometer. The reactions were initiated by injecting 12 µl of 2.3×10^{-3} M solution of PNDPP into 1.2 ml of buffer solution containing the oxime and the surfactant. The rates of PNDPP esterolysis were determined by following the appearance of *p*-nitrophenolate ion at 402 nm. The absence of INAA decomposition during the kinetic run was checked by measuring the pH at the end of the experiment. The pseudo first-order rate constants k_{obs} were obtained by nonlinear regression fitting to the equation $A_t = A_\infty(1 - e^{k_{obs}t})$ where A_t and A_∞ are the absorbances at time t and 'infinity' respectively; k_{obs} values were found to be reproducible within 2%.

pH measurements

pH data were measured under argon atmosphere at 25 ± 0.1 °C using a Methrom pH meter (Model 691) equipped with a Metrohm glass electrode (Ref. 6.0219.100) with a sleeve diaphragm and a double-junction to the Ag/AgCl ([KCl] = 3 M) inner reference. This electrode, specific for pH measurements in surfactant solutions, prevents the clogging of the diaphragm. The glass electrode was standardized by using standard pH 7.0 and 10.0 buffers.

Acknowledgements

O. A. El Seoud thanks the FAPESP for financial support and the CNPq for a research productivity fellowship. This work has been carried out within a CAPES/COFECUB bilateral cooperation project and a CNRS/ASB convention.

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