Physicochemical Properties and Supernucleophilicity of Oxime-Functionalized Surfactants: Hydrolytic Catalysts toward Dephosphorylation of Di- and Triphosphate Esters

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S *Supporting Information*

ABSTRACT: Aggregation and kinetic studies have been performed to understand the hydrolytic potencies of the series of oxime-functionalized surfactants, viz., 3- hydroxyiminomethyl-1-alkylpyridinium bromide (alkyl = C_nH_{2n+1}, n = 10, 12, 14, 16, 18) in the cleavage of phosphate esters, p-nitrophenyl diphenyl phosphate (PNPDPP) and bis(2,4-dinitrophenyl) phosphate (BNDPP), in mixed micelles with cetylpyridinium bromide (CPB). Micellization and surface properties of mixed micelles functional surfactants with CPB

were studied by conductivity and surface tension measurements. Acid dissociation constants (pK_a) were determined, the effect of functional surfactant alkyl chain length and pH on the observed rate constant (k_{obs}) for phosphate ester cleavage has been discussed, and the effect of substrate on the supernucleophilicities of the studied oximes was monitored. Functionalized oxime-based surfactants were proved to be supernucleophiles to attack on the P=O center of tri- and diphosphate esters. Oximes with hexadecyl alkyl chain length (3-C_{16}) showed maximum micellar effect on the rate constants toward PNPDPP. Micellar effects were analyzed in terms of the pseudophase model.
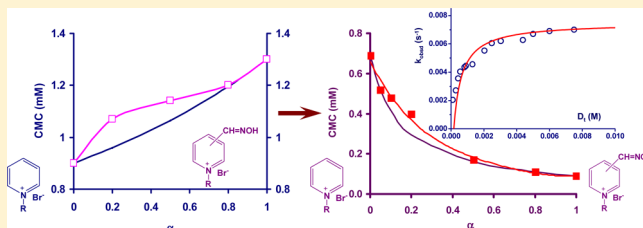
INTRODUCTION

Organophosphorus (OP) compounds are widely used as pesticides, insecticides, and chemical warfare agents (CWA), exhibit high acute toxicity, and can irreversibly inhibit acetylcholinesterase (AChE) which is essential for the proper functioning of the central nervous system.[1−6] This is why possible large-scale use of OPs by terrorist groups round the globe remains a great threat to human race. Thus, intense global efforts are being witnessed toward developing efficient reactivators of OP-deactivated acetylcholinesterases. From this standpoint, amphiphilic systems composed of surfactant and nucleophilic moiety such as oximes,[7] hydroxamates,[8] peroxides[9] o-iodosyl carboxylates,[10] hydroxybenzotriazoles,[11] and hypochlorite,[12] etc., are of great significance. A promising method includes introduction of a nucleophilic moiety into the headgroup of surfactants to produce so-called "functionalized surfactants" with high solubilizing power.[13−15] Nucleophilic functionalized surfactants are among the most powerful reactants in cleavage of organophosphorous compounds.[16−18] The most useful are α-nucleophilic moieties which are to be deprotonated in their reactive anionic form, and pure

functionalized micelles are zwitterionic.[19−21] Although it has long been known that cationic micellar mediums enhance the reaction rates, much interest has been devoted to the study of cosurfactants and mixed surfactant systems that are required to enhance solubility of sparingly soluble substrates and reduce the cost of mixed surfactant systems, and to find additional tools for tuning reactivity.[22−24] Micellar properties of functionalized micelles and pK_a are the most sensitive to the micelle composition parameter that can be changed in the mixed systems.[25] The higher the cationic surfactant content, the lower is the pK_a, and, thus, "milder" the decontamination micellar system.[26] Over the past few decades,[27,28] the role of oximes as well-known AChE reactivators has been expanded to the search and design of supernucleophilic systems for ecotoxic ester cleavage. Physicochemical and kinetic aspects of tertiary oximes (monoisonitrosoacetone and 2,3-butanedione monoxime) and quaternary oximes (mono- and bisquaternary pyridinium

oximes) are the most interesting and challenging areas of research worldwide.[29,30]

Sufficient efforts have been made to study the mechanisms involved with functionalized surfactant-assisted hydrolysis of phosphate esters. Tecilla et al. presented an excellent review on amphiphilic metalloaggregates.[31] Hampl and co-workers have synthesized several amphiphilic quaternary pyridinium ketoximes and examined their efficiency for phosphate ester cleavage.[17b] Simanenko et al.[19,32b] performed a detailed kinetic analysis of nucleophilic cleavage of some phosphate and sulfonate esters in the presence of new imidazolium surfactants bearing moieties of α-nucleophiles, namely oximate,[19,32a,b] hydroxamate,[32a] and amidoximate[32a] groups. Recently, this research team has studied a series of imidazole[32] and pyridinium[33] based functional amphiphiles for decomposition of phosphate ester. The reactivities of these functional surfactants have been described in terms of the nonlinear Brønsted relationship similar to that for nonmicellized oximates.[16b] Alkoxide compounds have been reported by Bunton et al.[34] to study the size versus reactivity of functionalized assemblies for deacylation and dephosphorylation reactions. In order to obtain more reactive systems, functionalized aggregates were extensively investigated by Tonellato and co-workers.[35] Bhattacharya and research group discussed metal ligand functionalized micelles for ester hydrolysis[36] and also reported highly efficient turnover systems based on 4-N,N'-(dimethylaminopyridine) derivatives as hydrolytic micellar catalysts.[37] The purpose of this paper is to estimate the physicochemical parameters of a series of oxime-based functionalized surfactants in mixed micelles of CPB and provide a general kinetic treatment for reactions catalyzed by functional micelles by studying the factors responsible for observed catalytic effects. Herein, we have studied micellar properties, acid dissociation constants, and hydrolytic efficacy of 3-hydroxyiminomethyl-1-alkylpyridinium bromide (alkyl chain length octadecyl, 3-C_{18}; hexadecyl, 3-C_{16}; tetradecyl, 3-C_{14}; dodecyl, 3-C_{12}; and decyl, 3-C_{10}) toward the cleavage of phosphate esters, i.e., p-nitrophenyldiphenyl phosphate (PNPDPP) and bis(2,4-dinitrophenyl)phosphate (BDNPP) in comicelles of cetylpyridinium bromide (CPB) in aqueous medium (Schemes 1 and 2).

Scheme 1. General Structures of the Investigated Surfactants

R= C_nH_{2n+1}

n = 10 (3-C_{10}), 12 (3-C_{12}),
14 (3-C_{14}), 16 (3-C_{16}), 18 (3-C_{18})

3-hydroxyiminomethyl-1-alkylpyridinium bromide

n = 10 (4-C_{10}), 12 (4-C_{12}), 14 (4-C_{14}), 16 (4-C_{16})

4-hydroxyiminomethyl-1-alkylpyridinium bromide

Cetylpyridinium bromide (CPB)
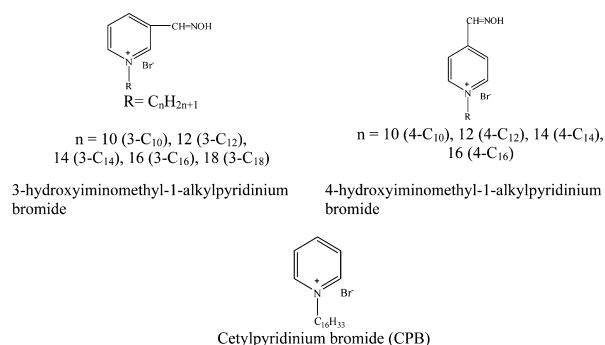
To follow the substrate effect on nucleophilic potency of oximate ions sulfonate ester, p-nitrophenyl p-toluenesulfonate (PNPTS) was used. In our previous investigations,[38] the surfactants with longer alkyl chain lengths (C_{16} and C_{18}) had not been studied due to solubility issues in aqueous solution.

Herein, we solve this problem by using the cationic cosurfactant CPB.

EXPERIMENTAL SECTION

Materials. Bis(2,4-dinitrophenyl)phosphate (BDNPP) was obtained from Department of Chemistry, Federal University of Santa Catarina, Florianopolis-SC, Brazil. p-Nitrophenyldiphenyl phosphate (PNPDPP) and p-nitrophenyl p-toluenesulfonate (PNPTS) were prepared at the Vertox laboratory of Defense Research Development Establishment, Gwalior (India). 3- and 4-hydroxyiminomethyl-1-alkylpyridinium bromide series of functionalized surfactants were prepared in the laboratory of Dr. Kamil Kuca by quaternization of pyridine aldoxime with the corresponding alkyl bromides.[39] Cetylpyridinium bromide was procured from Sigma, Aldrich. All solutions were prepared in triple distilled water.

Methods. *Conductivity Method.* Conductometric measurements were carried out using a Systronics direct reading conductivity meter (Type 306). The conductivity cell was calibrated with KCl solutions in the appropriate concentration range. A concentrated surfactant solution (∼10−20 times the critical micelle concentration (cmc)) was progressively added, using a micropipet, to 20 mL of water−organic solvent medium in a water-jacketed cell whose temperature was carefully controlled by a thermostat (having a temperature accuracy of ±0.01 °C). After thorough mixing and temperature equilibration of 300−320 K was ensured, the specific conductance (κ) was measured.

Surface Tension Measurement. The surface tension of aqueous solutions of surfactants at various concentrations was determined with a surface tensiometer (Jencon, India) using ring detachment (Du Nouy) technique. The tensiometer was calibrated against triple distilled water. Platinum ring was thoroughly cleaned and dried before each measurement. Each experiment was repeated several times until good reproducibility was achieved. The results were accurate within ±0.1 mN m^{-1}.

Kinetic Measurements. The rate of nucleophilic reaction was determined at 300 K by monitoring the increase in the absorption of p-nitrophenoxide anion (400 nm) using a Varian Cary 50 UV−visible spectrophotometer equipped with a Peltier temperature controller unit. The kinetic study was performed under pseudo-first-order conditions with the concentration of nucleophile in excess over the substrate concentration and at an ionic strength of 0.1 M (with KCl). The initial concentration of the substrate was 0.5×10^{-4} M for all reactions. Borate buffer was employed to control the pH of the media. The pH of the reaction medium was measured using Systronics (Type-362) pH-meter. p-Nitrophenoxide ion was liberated quantitatively and identified as one of the products by comparing the UV−visible spectrum at the end of the reaction with the authentic sample under the experimental condition. Each experiment was repeated twice, and the observed rate constants were reproducible within a precision of better than 5%. For all of the kinetic runs, the absorbance/time results fit very well to the first-order rate eq 1

$$\ln(A_\infty - A_t) = \ln(A_\infty - A_0) - kt \tag{1}$$

where A_0, A_t, and A_∞ are the absorbance readings at zero, t, and infinite time, respectively. A representative graph for the hydrolysis of BDNPP with 3-C_{12} at 0.5 mM CPB showing increase in absorbance of p-nitrophenoxide ion at 412 nm is presented in Figure 1.
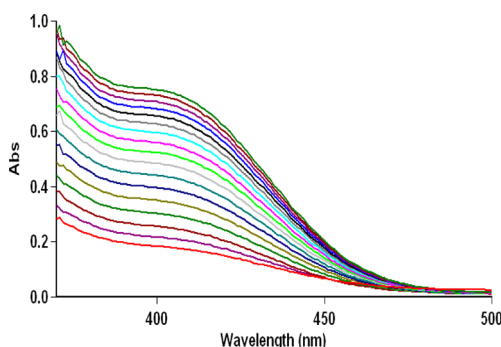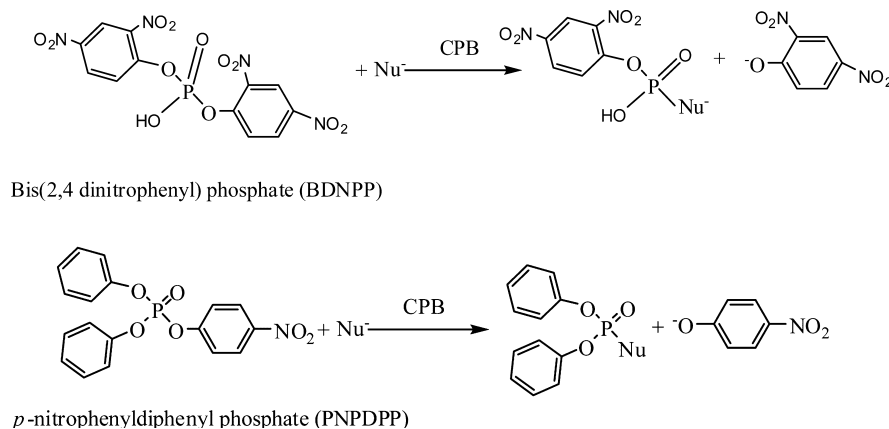
Scheme 2. Nucleophilic Reactions Studied

Bis(2,4 dinitrophenyl) phosphate (BDNPP)

p-nitrophenyldiphenyl phosphate (PNPDPP)

Figure 1. Typical kinetic behavior for the reaction of BDNPP with 3-hydroxyiminomethyl-1-dodecylpyridinium bromide. Reaction conditions: $[\text{BDNPP}] = 0.5 \times 10^{-4}$ M, $[\text{3-}C_{12}] = 0.5 \times 10^{-3}$ M, $[\text{CPB}] = 0.5 \times 10^{-3}$ M, ionic strength, $\mu = 0.1$ M KCl, pH = 9.0, temperature = 300 K.
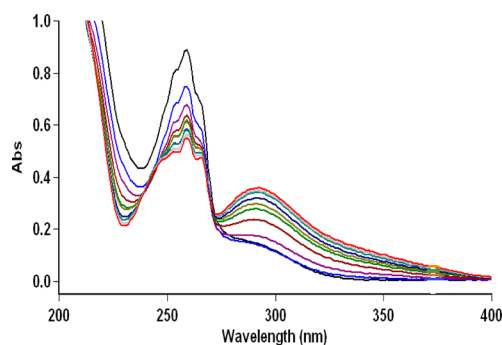
Figure 2. Absorbance spectra of 3-hydroxyiminomethyl-1-tetradecyl-pyridinium bromide (3-C_{14}) in 0.5 mM CPB at 300 K.

Determination of Acid Dissociation Constant (pK$_a$). The acid dissociation constant (pK_a) values of all the functionalized oximes in 1.0 mM of CPB were determined spectrophotometrically by using the well-known method described by Albert and Sergeant.[39] The method depends on the direct determination of the ratio of molecular species (protonated) to dissociated (deprotonated) species in buffer solutions. An aliquot (3 mL) of a stock solution (5×10^{-4} M) of oxime in triple distilled water was diluted with 25 mL phosphate buffer solution. Different pH values ranging from 7.12 to 10.5 were selected to determine the pK_a of oximes. The pH of the solution was measured using Systronics (Type-362) pH-meter, and the spectrum was recorded using buffer solution as a blank. The absorption spectrum was recorded using Varian Cary 50 UV−vis spectrophotometer in the range of 200−400 nm in the solution of different acidity. The average values of 10 measurements were considered as the pK_a of the compound with respect to oximino functionality. The spectrophotometric determination of pK_a of 3-C_{14} is reproduced in Figure 2 at 300 K. The pK_a calculations were made around half-neutralization using the following equation:

$$pK_a = pH_{exp} - \log \frac{Abs_\Psi - Abs_{Hox}}{Abs_{ox} - Abs_\Psi} \quad (2)$$

where Abs_{HOx} is the absorbance of the un-ionized form of compound, Abs_Ψ is the absorbance of the partially ionized form

of compound, and Abs_{Ox} is the absorbance of the completely ionized form of compound.

■ **RESULTS AND DISCUSSION**

Herein, we have studied physicochemical properties of functionalized aggregates and their efficiencies as powerful micellar catalyst for phosphorylitic reactions due to their practical significance. Taking the best example of aqueous medium, a particular organic substrate is transferred from bulk solvent (water) to the aggregate pseudophase where it may experience a different, less polar environment and proximity of other reactant species, which can be observed as kinetic benefits.

Physicochemical properties of cationic functionalized 3- and 4-hydroxyiminomethyl-1-alkylpyridinium bromide surfactants (3-C_n and 4-C_n) were studied in the presence/absence of nonfunctionalized cationic surfactant cetylpyridinium bromide (CPB). The mixed micellar system of oxime-functionalized and conventional surfactant (CPB) was used to study the cleavage of *p*-nitrophenyldiphenyl phosphate and bis(2,4-dinitrophenyl)phosphate. The pH and surfactant concentration-dependent first-order rate constants were determined for the reaction of PNPDPP and BDNPP with nucleophiles in excess.

Physicochemical Properties. *Micellar and Surface Properties.* Mixed micellar systems in water undergo various physicochemical changes in micellar aggregates to provide better interfacial and surface properties.[40,41] The cmc values and interaction parameters of pure and mixed 3-C_n (n = 10, 12, 14, 16, 18) + CPB systems determined by conductometric and surface tension measurements are presented in Table 1 and

Table 1. Critical Micelle Concentrations (Cmc),[a] Micellar Ionization Degree (α), Micellar Mole Fraction (X_1),[b] and Interaction Parameter (β) of 3-Series Functionalized Surfactants with CPB by Conductivity and Surface Tension at 300 K (pH = 7.1)

	conductivity						surface tension				
	3-C_n		3-C_n + CPB[c] (1:1)					3-C_n	3-C_n + CPB[c] (1:1)			
F. S.	cmc (mM)	α	cmc_m (mM)	A	cmc_i (mM)	X_1	β	cmc (mM)	cmc_m (mM)	cmc_i (mM)	X_1	β
C_{10}	2.10[b]	0.40	1.30	0.49	1.26	0.28	0.15	2.03	1.49	1.24	0.20	0.92
C_{12}	1.30[b]	0.39	1.15	0.43	1.06	0.39	0.32	1.20	1.07	1.03	0.42	0.18
C_{14}	0.60[b]	0.48	0.82	0.41	0.72	0.63	0.54	0.65	0.82	0.75	0.59	0.34
C_{16}	0.05[b]	0.21	0.049	0.30	0.095	0.71	−4.60	0.08	0.09	0.15	0.72	−3.27
C_{18}	–	–	–	–	–	–	–	0.04	0.06	0.08	0.81	−2.55

[a]Cmc_m = cmc mixture, cmc_i = cmc ideal, F.S. = functionalized surfactant (C_n). [b]Reference 38a. [c]Cmc of CPB by surface tension is 0.90 mM at 300 K.

Figure 3. Cmc values of CPB + 3-C_{16} and CPB + 3-C_{18} mixed systems can be predicted from Figure S1 of the Supporting Information.
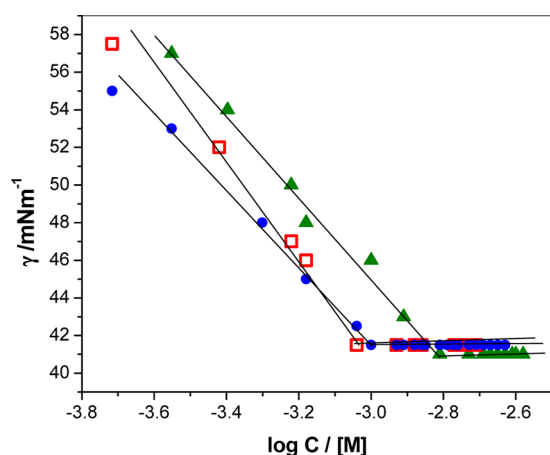

Figure 3. Plots of the surface tension vs concentration of CPB + 3C_{10} (□), CPB + 3C_{12} (○), and CPB + 3C_{14} (△) mixed systems (0.5 mole fraction) at 300 K (pH 7.1).

It can be clearly inferred from Table 1 that the cmc values of pure components and mixed systems depend on hydrophobic chain length of the surfactants. With rise in alkyl chain length, cmc values of the surfactants decrease significantly in the order 3-C_{10} > 3-C_{12} > 3-C_{14} > 3-C_{16} > 3-C_{18}. Micellization depends on the hydrophobicity of surfactants and polarity of the bulk medium. The hydrophobicity of the surfactants increases with the chain length, resulting in thermodynamic threshold required for the formation of the micelles to be reached at lower surfactant concentration in the case of higher alkyl chain length surfactants. The cmc values in mixed system of 3-C_n + CPB lie between the cmc values of individual components. Nome et al.[42] observed decrease in cmc of the mixed micelles of DTAB with a functionalized surfactant, laurylhydroxamic acid (LHA). Cmc of DTAB in water was 1.5×10^{-2} M, but for the mixture of DTAB and LHA, cmc = 3.0×10^{-3} M. The aggregation in mixed surfactant systems is different from single surfactant systems. Therefore, mixed systems can strengthen the hydrophobic environment, resulting in the onset of micellization at lower cmc in comparison to pure surfactants.

Although all the present binary mixtures are cationic combinations, nonideal mixing behavior is expected on the basis of a significant difference between their hydrophobic tails, which have otherwise identical head groups. The Clint equation

can be used to determine the ideality in the mixed micelle formation at the cmc, which relates the theoretical ideal mixed cmc with the experimental cmc of the pure components using the following equation in the case of ideal mixing,

$$\frac{1}{cmc_{ideal}} = \sum_{i=1}^{n} \left(\frac{\alpha_i}{cmc_i} \right) \tag{3}$$

where cmc_i and cmc_{ideal} are the critical micellar concentrations of the ith component and the mixture, respectively; α_i is the mole fraction of component i in solution. From Table 1 it can be observed that cmc_m values are slightly higher than cmc_i over the whole range of alkyl chain length except in the case of 3-C_{16} and 3-C_{18} for 3-C_n + CPB mixtures. This suggests that the mixed micelles are formed due to synergistic interactions in the 3-C_{16} or 3-C_{18} + CPB mixtures whereas interactions were antagonistic in the rest of the systems. The extent of favorable or unfavorable interactions can be evaluated with the help of a Rubingh[43] phase separation model of micellization and regular solution approximation as derived in eq 4

$$\frac{(X_1)^2 \ln(\alpha_1 C_{mix}/X_1 C_1)}{(1 - X_1)^2 \ln[(1 - \alpha_1)C_{mix}/(1 - X_1)C_2]} = 1 \tag{4}$$

where X_1 is the mole fraction of surfactant 1 in the mixed micelle. Equation 4 can be solved iteratively to obtain the value of X_1, from which the interaction parameter β can be evaluated using eq 5

$$\beta = \frac{\ln(\alpha_1 C_{mix}/X_1 C_1)}{(1 - X_1)^2} \tag{5}$$

From conductivity and surface tension measurements, the β value for all the mixed systems were positive except 3-C_{16} and 3-C_{18} as they have negative β values. Positive β value suggests antagonistic mixing in the former cases, and the negative β value in the latter case demonstrates mixed micelle formation due to attractive interaction. During the formation of mixed micelles, both ideal and nonideal mixing can occur.[44] Since the hydrophobic effect, which drives the aggregation process, is not specific to surfactant headgroup, the formation or randomly mixed surfactant aggregate will be favored and this leads to the ideal component of mixing but in the case of mixture comprising different surfactants, the electrostatic and steric repulsion between the head groups lead to nonideal mixing in the aggregates.[45,46] Stern layer and delocalization may reduce the compactness of the mixed micelle. The antagonism was not much pronounced in the investigated mixed systems, and synergism was observed in the more hydrophobic environment

Table 2. Critical Micelle Concentration, Cmc_m, Cmc_I, Micellar Mole Fraction (α), X_1, X_I, Interaction Parameter, β, for CPB + 3-C_{12}, Mixtures (T = 300 K) by Conductivity and Surface Tension at pH 7.1

	conductivity						surface tension				
α 3-C_{12}	$cmc_m{}^a$ (mM)	α	$cmc_i{}^a$ (mM)	X_1	X_I	β	$cmc_m{}^a$ (mM)	$cmc_i{}^a$ (mM)	X_1	X_I	β
0.0	0.90		0.90				0.90	0.90			
0.2	1.07	0.56	0.96	0.05	0.14	1.28	0.99	0.95	0.125	0.15	0.36
0.5	1.14	0.72	1.06	0.39	0.40	0.29	1.07	1.03	0.42	0.42	0.18
0.8	1.18	0.43	1.19	0.72	0.73	−0.05	1.13	−	−	−	−
1.0	1.30		1.30				1.20	1.20			

^{a}Cmc_m = experimental cmc of mixed micelle, cmc_i = ideal cmc calculated from eq 3.

of longer chain length surfactants (3-C_{16} and 3-C_{18}) as displayed in Table 1. This fact was supported by literature data[45] where synergism increased with increase in hydrophobicity of mixed systems. Increase in the hydrophobic tail length of 3-C_n might have increased the hydrophobic character of the core coupled by the neutralization of polar headgroup repulsions and this might have generated synergism. Slight antagonism in the case of 3-C_{10} to 3-C_{14} mixed systems can also be explained on the basis of less difference in the cmc values of individual components whereas in the higher chain lengths cmc difference was much pronounced.[47]

Table 2 shows micellar parameters of 3-C_{12} + CPB system studied at different mole fractions (0.2, 0.5, and 0.8) by conductivity and surface tension measurements at 300 K and pH 7.1. The results are also depicted in Figure 4. With
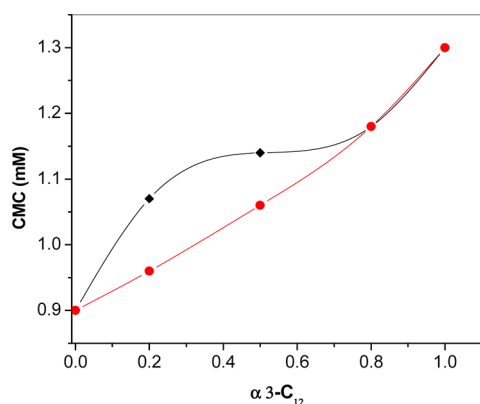

Figure 4. Variation of the cmc 10^3 C (mol dm^{-3}) with the mole fraction (α) of CPB + 3-C_{12} systems (red ●) cmc_I and (◆) cmc_m at temperature 300 K and pH 7.1.

increasing mole fraction of 3-C_{12} in the mixture, β values decrease constantly (Table 2). At 0.2 and 0.5 mole fraction, the mixture showed slight antagonism (repulsive interaction) but at 0.8 mole fraction interactions were attractive (synergism). Enhancement of synergism with increase in mole fraction of one of the components is quite a well-known trend[48] in mixed micellar systems.

Interfacial properties and thermodynamic parameters of 3-series functionalized surfactants in presence and absence of CPB in aqueous medium at 300 K and pH 7.1 are listed in Table S1 as Supporting Information. The values of different surface properties Π_{cmc} (the surface pressure at the cmc), Γ_{max} (the maximum surface excess), and A_{min} (the minimum surface area per molecule) and thermodynamic parameters, $\Delta G^\circ{}_m$ (Gibbs free energy of micellization) and $\Delta G^\circ{}_{ads}$ (the standard Gibbs energy of adsorption), were obtained at 0.5 mole fraction

of CPB. Π_{cmc} and Γ_{max} (Table S1) do not follow any regular trend with chain length or mole fraction. Both $\Delta G^\circ{}_m$ and $\Delta G^\circ{}_{ads}$ are negative, and their magnitudes reveal the latter to be more spontaneous due to hydrophobicity of amphiphiles, which leads them toward air/water interface.[49]

Effect of pH is very significant while studying micellar kinetics and hence surface studies were done at pH 8.0 for better understanding of morphological changes in the mixed systems. Cmc determination of various cationic surfactants (including CPB) at pH 8.0 has been reported in our previous work.[50] At pH > 7.5 functionalized surfactants behave as zwitterionic species. CPB + 3-C_{12} system (1:1) was studied at pH 8.0 (Table 3) with the aim of reproducing the kinetic

Table 3. Critical Micelle Concentration (cmc_m) and Cmc ideal (cmc_i) for CPB + 3-C_{12} Mixtures (T = 303 K) by Surface Tension at pH 8.0

α 3-C_{12}	cmc_m (mM)	cmc_i (mM)
0.0	0.69	0.69
0.05	0.52	0.52
0.1	0.48	0.41
0.2	0.40	0.30
0.5	0.17	0.16
0.8	0.11	0.11
1.0	0.09	0.09

conditions, and favorable interactions were reported to demonstrate synergism (i.e., negative β). Hence, it can be assumed that the CPB + 3-C_n mixed systems at considerably higher pH (>8.0) will show favorable interactions and enhanced surface properties (Figure 5).
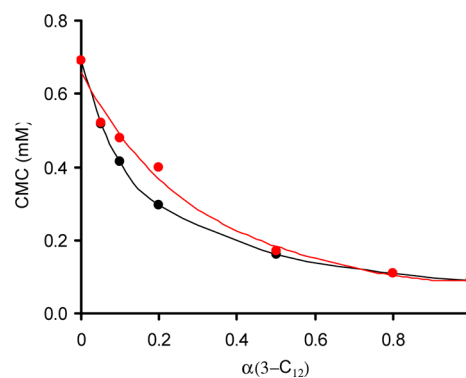

Figure 5. Variation of the cmc 10^3 C/mol dm^{-3} with the mole fraction (α) of CPB + 3-C_{12} systems (●) cmc_i and (red ●) cmc_m by surface tension at pH 8.0 and temperature 300 K.

E

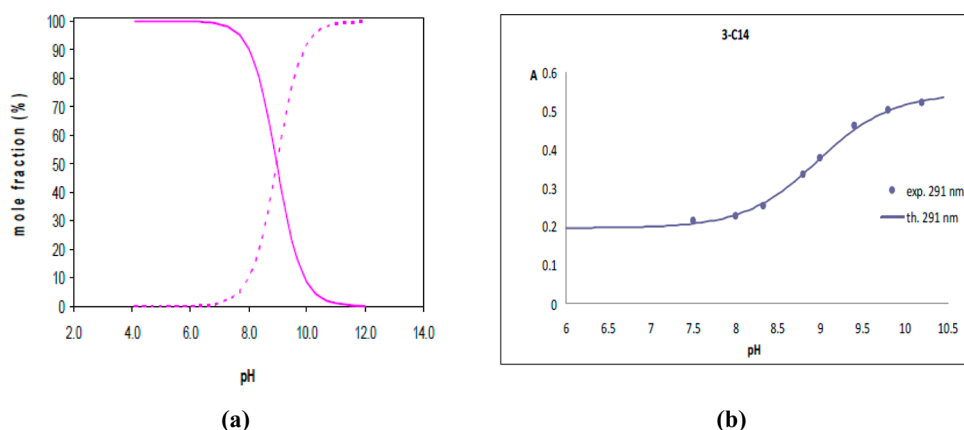dx.doi.org/10.1021/jp310010q | J. Phys. Chem. B XXXX, XXX, XXX−XXX

Figure 6. (a) pH vs mole fraction profile, showing protonated (---) and deprotonated (—) species for 3-C_{14}. (b) Absorbance dependence of 3-C_{14} on pH; experimenta data λ_m = 291 nm; solid line, nonlinear regression ([3-C_{14}] = 2.0×10^{-5} M).

Mixed micellar systems change their cmcs dramatically when going from cationic (protonated oxime) to zwitterionic (deprotonated oximate ion, i.e., reactive form of the functionalized surfactant) micelle. Thus, at pH 7.1 with $\alpha_{3\text{-}C12}$ 0.5 decreases from ca. 1 mM (reactive oximate ion is not present) toward 0.17 mM at pH 8.0 (oximate ion is deprotonated incompletely). Therefore, a difference in charge distribution at the micellar interface can be used as a tool for tuning micellar properties followed by switching mixed micellar system from its inert (promotes alkaline hydrolysis only) to reactive (promotes oximolysis).

Acid Dissociation Constant (pKa). The determination of the effect of [surfactant] on the pK_a of nucleophiles is essential for analyzing quantitatively the effects of surfactant aggregates on reaction rates if the nucleophile is the dissociated species of the weak acid. In our previous work,[38] we reported pK_a of 3- and 4-series of hydroxyiminomethyl-1-alkylpyridinium bromide functionalized detergents. Prokop'eva et al.[33] have reported pK_a of 4-hydroxyiminomethyl-1-tetradecylpyridinium bromide by spectrophotometric (pK_a = 7.92), kinetic (pK_a = 7.86) and potentiometric (pK_a = 8.61) methods. These literature values are quite well in agreement with the pK_a of 4-C_{14} (pK_a = 8.61) determined in the present investigation. To estimate pK_a under defined reaction conditions, we monitored the effect of CPB on the pK_a of the investigated surfactants by spectrophotometric and nonlinear regression methods. The pK_a values calculated by both the techniques were in good agreement with each other (pK_a of 3-C_{14} = 8.97, 4-C_{10} = 9.10, and 4-C_{12} = 8.48 by curve-fitting method).

Equation 6 was applied for pyridinium-based oxime-functionalized surfactants

$$\text{HOx} \overset{K_a}{\rightleftarrows} \text{H}^+ + \text{Ox}^- \tag{6}$$

The pH versus mole fraction profile, showing protonated and deprotonated species for 3-C_{14} is shown in Figure 6a. The calculations were performed at both analytical wavelengths, i.e., absorbance maxima of each deprotonated and protonated species of the oxime moiety (Scheme 3).

A nonlinear least-squares fit was applied to eq 6, which led to the absorbance versus pH data as presented in Figure 6b.

It can be concluded from Table 4 that (i) the pK_a's of functionalized surfactants decrease with decrease in alkyl chain length of the surfactant though the effects are not much pronounced, (ii) pK_a's of 4-series surfactants are lower in

Scheme 3. Deprotonation of Oxime Functionality into Oximate Ion
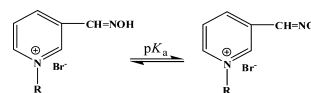

Table 4. Acid Dissociation Constants (pK_a) of 3- and 4-Series Functionalized Surfactants in the Presence and Absence of CPB (1.0 mM) by Spectrophotometric Method at Temperature 300 K

	pK_a			
	3-series		4-series	
F.S.[a]	no CPB	CPB	no CPB	CPB
C_{10}	9.40	9.02	9.20	9.13
C_{12}	9.32	8.80	8.65	8.45
C_{14}	9.10	8.98	8.06	7.91
C_{16}	8.72	8.50	7.83	7.56

[a]F.S. = functionalized surfactants.

magnitude than 3-series which can be accounted for on the basis of spatial obstruction offered by oxime moiety at 3-position in the pyridinium ring, and (iii) pK_a values decrease in the presence of monomeric surfactant CPB. To support this fact, pK_a of 3-C_{14} was studied at various CPB concentrations (Figure 7). At higher CPB concentrations, sufficient reduction in pK_a was observed. This can be explained by the fact that, at concentration lower than the cmc, reduction in pK_a is not significant[51] but at high CPB concentration total cmc of the system reduced and shift in acid−base equilibrium occurred. Micelles induce redistribution of acidic and basic species into the micellar pseudophase, in particular charged micelles. The pK_a in the micellar systems compared with the systems without micelles strongly supports the shift of acid−base equilibria.[20]

Kinetic Studies with Functionalized Surfactants. Effective cleavage of various phosphate and sulfonate esters have been done with aldoxime, ketoxime, and hydroxamate functionalized pyridinium and imidazolium surfactants. Among these, aldoxime-incorporated pyridinium-functionalized surfactants proved to be better nucleophiles for ester hydrolytic reactions.[25] We aimed at cleavage of phosphate (PNPDPP and BDNPP) and sulfonate (p-nitrophenyltoluenesulfonate; PNPTS) esters with 3-series (3-C_n) and 4-series (4-C_n) functionalized surfactants. Effect of conventional surfactant
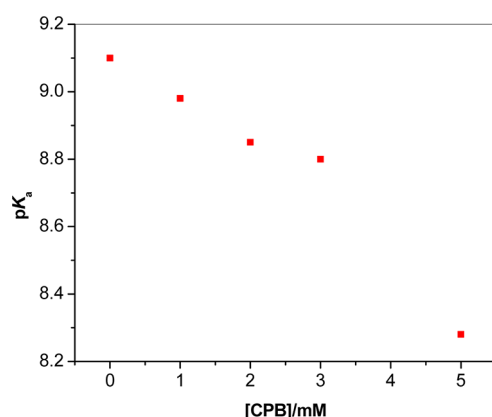
Figure 7. Acid dissociation constant (pK_a) of 3-hydroxyiminomethyl-1-tetradecylpyridinium bromide ($3\text{-}C_{14}$) at various CPB concentrations.

CPB was examined on the rate of esterolytic reactions at pH close to the pK_a of oxime-functionalized surfactants. Also, effect of pH and alkyl chain length of $3\text{-}C_n$ and influence of substrate on pseudo-first-order reaction rates were analyzed.

Effect of Substrates. In the case of amphiphilic molecules featuring covalently bound nucleophiles or other reactive groups, functionalized component is a potential reactant for the hydrolytic cleavage of activated substrates. The main advantage of using functionalized surfactants in cationic form is that they provide large rate enhancements at pH quite near their apparent pK_a. In Table 5 are shown pseudo-first-order rate

Table 5. Pseudo-First-Order Rate Constants for the Hydrolysis of Phosphate and Sulfonate Esters with Functionalized Surfactants ($3\text{-}C_n$)^a

substrate	$10^3 k_{obs}$ (s^{-1})					
	$3\text{-}C_{10}$	$4\text{-}C_{10}$	$3\text{-}C_{12}$	$4\text{-}C_{12}$	$3\text{-}C_{14}$	$3\text{-}C_{16}$
PNPDPP	1.29	2.55	2.78	4.34	9.07	16.2
BDNPP	0.09	1.08	0.50	1.63	3.38	5.77
PNPTS	0.03	0.91	0.14	2.09	2.59	4.10

^{a}Reaction conditions: [substrate] = 0.5×10^{-4} M, $[3\text{-}C_n]$ = 0.5×10^{-3} M, [KCl] = 0.1 M, pH = 9.0, temperature = 300 K.

constants for cleavage of PNPDPP, BDNPP, and PNPTS with $3\text{-}C_n$ and $4\text{-}C_n$ (n = 10, 12) under the conditions of an excessive nucleophile over the substrate at pH 9.0 (0.01 M borate buffer). From the data obtained, order of ester cleavage may be presented as PNPDPP > BDNPP > PNPTS. PNPDPP being a triester can be more easily hydrolyzed than a diester (BDNPP). The nucleophilic efficiency of oximate ions is lower toward S═O centers (PNPTS) which supports that S═O possess lower electrophilicity as compared to P═O centers for substrates studied.[8a] It is evident from Table 5 that the observed rate constants for $4\text{-}C_n$ are higher than that of $3\text{-}C_n$. Less spatial obstruction and low cmc and pK_a values of $4\text{-}C_n$ may be responsible for the better kinetic advantage provided by these surfactants.

Effect of Alkyl Chain Length of Oxime-Functionalized Surfactants ($3\text{-}C_n$). Table 5 summarizes the effect of different alkyl chain lengths (C_{10}–C_{16}) of the $3\text{-}C_n$ functionalized surfactant on the esterolytic reactions. Surfactant chain length has a significant impact on k_{obs} values for the cleavage of esters. The k_{obs} values increased with increase in the alkyl chain length

of the surfactants. This increase in the order ($3\text{-}C_{10}$ < $3\text{-}C_{12}$ < $3\text{-}C_{14}$ < $3\text{-}C_{16}$) is mainly due to the increase in the electrical surface potential of the micelle and also due to an increase in the hydrophobicity of the palisade layer of micelle. Similarly, Figure S2 in the Supporting Information depicts the effect of alkyl chain length in $4\text{-}C_n$ surfactants ($4\text{-}C_{10}$ < $4\text{-}C_{12}$). The rate enhancement may be accounted for on the basis of critical micelle concentration (cmc) and acid dissociation constant (pK_a) of these functionalized surfactants. pK_a of $3\text{-}C_{16}$ is the least ($3\text{-}C_{16}$, pK_a 8.72; $3\text{-}C_{14}$, pK_a 9.10; $3\text{-}C_{12}$, pK_a 9.32; $3\text{-}C_{10}$, pK_a 9.40) hence, it showed maximum reactivity as a nucleophilic moiety in micellar media. Also, cmc's of these functionalized surfactants are in the order $3\text{-}C_{10}$ > $3\text{-}C_{12}$ > $3\text{-}C_{14}$ > $3\text{-}C_{16}$, which clearly suggests higher reaction rates with $3\text{-}C_{14}$ and $3\text{-}C_{16}$. The observed trend of alkyl chain lengths of $3\text{-}C_n$ in Table 5 is also supported by the results obtained for the effect of CPB as comicelles on rate of BDNPP cleavage (explained further).

Effect of CPB Comicelles. Effect of surfactants on rate of oximolysis has been investigated in a large number of reports using various substrates and oximes. Positively charged surfactants, as a common trend, increase oximolysis rates but quantitative analysis of these effects is seldom reported. The degradation of diester BDNPP with oximate ions from functional micelles of $3\text{-}C_n$ in the presence of cationic surfactant CPB at pH 8.0 and 9.0 is clearly manifested in Figure 8 and in Table S2 in the Supporting Information. With rise in the CPB concentration, the rate of reaction increased and k_{obs} tend to maximum, indicating bimolecular reaction. At pH 9.0, the rate enhancement at 0.5 mM of CPB was 2.9-fold for $3\text{-}C_{16}$, 2.6-fold for $3\text{-}C_{14}$, 16.1-fold for $3\text{-}C_{12}$, and 24.3-fold for $3\text{-}C_{10}$ with respect to the reactions at 0 mM [CPB]. As the functionalized surfactant concentration was maintained at 0.5×10^{-3} M and [CPB] was increased gradually, the reaction rate considerably increased by concentrating α-nucleophile in the micellar phase. When the substrate was completely bound with micelles, the reaction rate was no longer dependent on the surfactant concentration. Subsequent addition of surfactant caused reduction in the observed reaction rate. This might be due to the dilution of the catalyst in the Stern layer of micelles. Nome et al.[42] have reported BDNPP hydrolysis with laurylhydroxamic acid in mixed micelle with CTAB/DTAB at pH 10.0. They observed dephosphorylation of BDNPP to be 10^4-fold faster in a mixture of functionalized laurylhydroxamic acid surfactant and CTAB. Increase in the rate constant was observed as a function of pH.

For better insight into the mechanisms we selected single system ($3\text{-}C_{12}$ + CPB) for BDNPP hydrolysis and the effect of total surfactant concentration on k_{obs} has been investigated (Figure 9). Attention is drawn to the fact that the kinetic cmc of $3\text{-}C_{12}$ at 0.8 mole fraction in mixed micelle mixture as predicted from Figure 9 is 0.82 mM which is quite lower than the individual cmc of $3\text{-}C_{12}$. The overall kinetic behavior of the functional surfactants and their comicelles with CPB is described in the framework of the pseudophase model (PPM) and it was found that the rate enhancement is mainly due to the reagent concentration in the micellar pseudophase. Kapitanov et al.[32c] studied phosphate and sulfonate ester cleavage with surfactants having imidazolium ring in their headgroup in comicelles with CTAB. We found similar trends with pyridinium ring functional micelles for diester cleavage in CPB. The observed rate constant for the decomposition of substrate increases with increase of mole fraction of functional
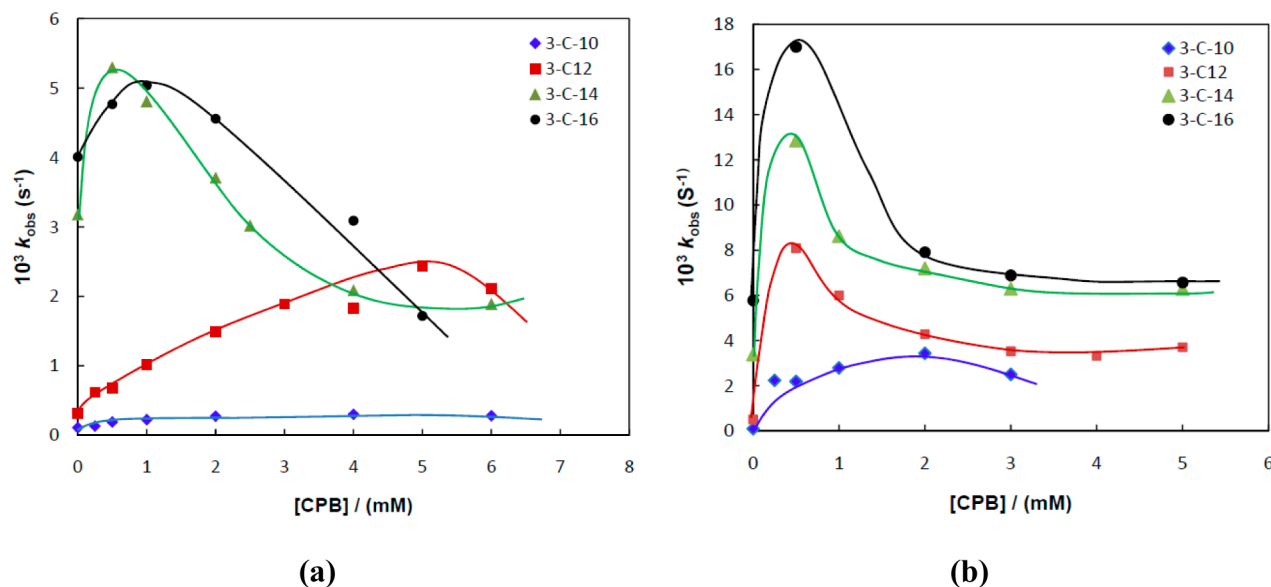
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Figure 8. Rate profile for effect of CPB as comicelle on the hydrolysis of BDNPP with 3-hydroxyiminomethyl-1-alkylpyridinium bromide (a) at pH 8.0 and (b) at pH = 9.0. Reaction conditions: $[\text{BDNPP}] = 0.5 \times 10^{-4}$ M, $[3\text{-C}_n] = 0.5 \times 10^{-3}$ M, ionic strength, $\mu = 0.1$ M KCl, temperature = 300 K.
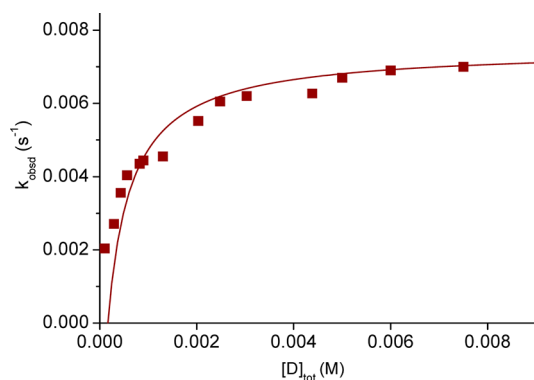

Figure 9. Plot for the effect of total surfactant concentration (3-C$_{12}$ + CPB) for cleavage of BDNPP at 0.8 mole fraction of 3-C$_{12}$. Reaction conditions: $[\text{BDNPP}] = 0.5 \times 10^{-4}$ M, KCl = 0.1 M, pH = 9.0, temperature = 300 K (line is predicted values calculatated from eq 7).

surfactants, total concentration of surfactants, and pH (explained further).

Among kinetic approaches to treat experimental data on reaction occurring in micellar solution there are two most often used by researchers,[22] namely pseudophase ion exchange (PIE) and pseudophase partititoning (PPM). The (PIE) model[52] takes into account an exchange taking place in Stern layer between counterions and added ions including those being capable to interact chemically with a substrate bound at the micellar interface. This model is preferable in the case of small ions whereas PPM (Berezin approach) takes into account the equilibrium partititoning of the substrate and reagent between the water and micellar phase (pseudophase). In general, it gives acceptable results and is very descriptive in determination of factors governing micellar effects. This model is criticized[53] since it does not reflect intimate ionic effects. For example, binding constants for hydrophilic ions are small and they are not constant at different concentration of electrolyte. The two models for description of kinetic data allow us to take into account two different sides of the processes occurring on the

micellar interface. In the case of our system (3-C$_{12}$ + CPB), there are two reactive species: hydroxide ion from the bulk alkaline solution, and oximate generated by oxime surfactants. At pH 9.0, the cleavage of substrate by functionalized surfactant is the main route, and alkaline hydrolysis is negligible. So, using PPM (eq 7) allows us to estimate appropriate parameters of the micellar effect on the reaction rate:

$$k_{obsd} = \frac{\alpha(k_{2,Oxime}^m/V_M)K_S C + k_{OH^-}^w a_{OH^-}}{1 + K_S C}\frac{K_{a,app}}{K_{a,app} + a_{H^+}}$$
$$+ \frac{(1-\alpha)(k_{2,OH}^m/V_M)K_S K_{OH} C + k_{2,OH}^w}{(1 + K_S C)(1 + K_{OH} C)} a_{OH^-} \quad (7)$$

In the eq 7, α is the mole fraction of functional surfactant in comicelle of CPB; k_2^m and k_2^w are the second-order rate constants characterizing the nucleophilicity of the oximate fragments, M$^{-1}\cdot$s^{-1}; K_S is the substrate binding constant, M^{-1}; V_M is the partial mole volume of surfactant, L/mol; C is concentration of micellized surfactant, M; $k_{OH^-}^w$ and α_{OH^-} correspond to the contributions of alkaline hydrolysis; K_a is rate constant for acid ionization of oxime; and a_{OH^-} is the hydrogen ion activity.

We estimated the alkaline hydrolysis route under reaction conditions. For mole fraction of 3-C$_{12}$ 0.8: $(1-\alpha) = 0.2$, $a_{OH^-} = 0.00001$ M, $K_s = 4000$ M^{-1}, $K_{OH} = 50$ M^{-1}, $k_{2,OH} = 0.003$ M$^{-1}\cdot$s^{-1}. Suggesting that the nucleophilicity is the same in the pseudophase as in the bulk phase ($k_{2,OH}^w \approx k_{2,OH}^m$), at $C = 0.005$ M we found $k_{obsd} < 5 \times 10^{-6}$ s^{-1} that is 1000 times lower than the observed rate. Thus, at the proposed condition it is the functionalized surfactant that provides cleavage of the substrate.

So we can simplify eq 7 to eq 8:

$$k_{obsd} = \frac{\alpha(k_{2,Oxime}^m/V_M)K_S C + k_{OH^-}^w a_{OH^-}}{1 + K_S C}\frac{K_{a,app}}{K_{a,app} + a_{H^+}} \quad (8)$$

The following results were obtained by the optimization: K_S is 2500 ± 900 M^{-1}, $k'_m = 0.007 \pm 0.0006$ s^{-1}. This k'_m is
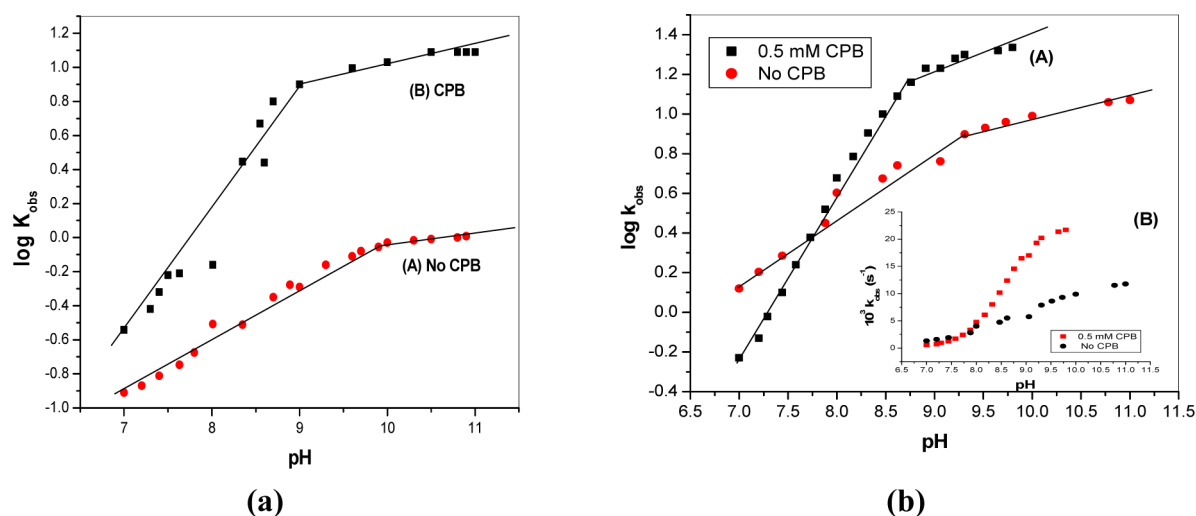
Figure 10. (a) log k_{obs} vs pH profile for the cleavage of BDNPP with 3-C$_{12}$ in the absence (A) and presence (B) of CPB. (b) pH profiles for the cleavage of BDNPP with 3-C$_{16}$. (A) log k_{obs} vs pH. Inset (B): k_{obs} vs pH. Reaction conditions: [BDNPP] = 0.5×10^{-4} M, [3-C$_n$] = 0.5×10^{-3} M, ionic strength, μ = 0.1 M KCl, [CPB] = 0.5×10^{-3} M, temperature = 300 K.

apparent constant because it has to be corrected by the portion of deprotonated species.

$$k_m = k'_m \frac{K_{a,app}}{K_{a,app} + a_{H^+}} \qquad (9)$$

Effect of pH. The effect of pH was studied on BDNPP hydrolysis with 0.5×10^{-3} M of 3-C$_n$ (n = 12, 14, 16) in the presence and absence of CPB (1:1) by employing different buffers (0.1 M) ranging from pH 7 to 11 as added to the reaction medium. Studying pH effect allows us to estimate the pK_a and therefore provide control on the rate of reaction at preferable reaction conditions. In support of the above-mentioned investigations regarding reactivity order of the alkyl chain length, pH study also demonstrates hexadecyl (3-C$_{16}$) to be the most reactive. Log k_{obs} vs pH plots for 3-C$_{12}$ and 3-C$_{16}$ reveal that oxime ions from functional micelles in comicellar CPB are more reactive and reduction in pK_a values may be observed in the presence of CPB (Figure 10). 3-C$_{16}$ + CPB proved to be the most efficient system for ester cleavage and this has been proved by the strong synergistic interactions obtained by conductometric and surface tension measurements. There was noticeable effect of pH on reaction rates. At pH > pK_a sufficient kinetic advantage may be observed due to the presence of oxime functionality into the completely dissociated form (−CH=NO$^-$). The most important indications arising from these experiments is the behavior of oximes as zwitterionic species by complete deprotonation above their acid dissociation constant in the solution and this provides surprising kinetic benefits. Effect of pH on the hydrolysis of BDNPP at different nucleophilic concentrations of 4-C$_{10}$ and 4-C$_{12}$ in the absence of CPB comicelles is shown in Table S3 in the Supporting Information. It may be clearly predicted from the table that, even in the absence of comicelles, BDNPP may be easily hydrolyzed at pH near to the pK_a of 4-C$_n$ functionalized surfactants.

Nucleophilic attack of an oxime on the unsaturated (electrophilic) center of phosphorus (carbon, sulfur) is well-known and discussed extensively since the past few decades.[30,54] The kinetic results reported in the present study indicate oxime phosphorylation in the presence of functional

zwitterionic aggregates. There is ample evidence for the nucleophilic deacylation and dephosphorylation[55] reactions. Bhattacharya et al.[56] documented evidence of acylated and phosphorylated monoperoxypthalates formation in three different solutions composed of cationic surfactant, microemulsion, and vesicular medium with the help of ^{1}H NMR and ^{31}P NMR spectrometry. They successfully reported turnover behavior of all the systems in excess substrates. Regarding oxime phosphorylation, worth mentioning are the efforts of Anslyn et al.[57] to study the effect of oxime and hydrazone (as chromogenic indicators) upon dephosphorylation of CWA simulants. With the help of ^{1}H NMR, ^{31}P NMR, and mass spectroscopy, they proved the attack of oximate anion on phosphorus center of diethyl chlorophosphate (DCP) and formation of oximate−DCP complex. Similar evidence was observed for the formation of oximate−DFP (diisopropyl fluorophosphate) complex.

■ CONCLUSIONS

The present investigation was aimed at the determination of nucleophilic efficiency of functionalized surfactants for the cleavage of phosphate triester and diester (simulants of toxic organophosphates) in the presence of CPB comicelles. To gain insight into the reaction mechanism, the physicochemical parameters of mixed micellar systems were thoroughly investigated. 3-C$_{16}$ + CPB and 3-C$_{18}$ + CPB mixed systems showed synergistic interactions. It was of much interest to note that the kinetic rate constants with functionalized surfactants were enhanced for the cleavage at P=O centers of phosphate ester in CPB comicelles. At any rate, it was worth noticing that in the presence of CPB comicelles the reactions were faster than in the absence. Functionalized surfactants with chain length C$_{16}$ (hexadecyl) showed maximum reactivity due to its low cmc value and lower acid dissociation constant. Moreover, the main source of kinetic rates observed is the high concentration of the reactants in the reaction core. Kinetic studies reported in the present investigation may be relevant to organophosphate decontamination purposes. These systems are very efficient to promote phosphate esterolysis. Functionalized aggregates in comicelles can reveal interesting applications in designing of potential catalytic systems. The present inves-

tigation was designed to overcome a few of the unavoidable limitations of kinetics in aqueous medium such as limited solubility of substrates. With a view to designing efficient micellar reactivators of OPC-deactivated AChEs, the present work delineates an in-depth structure−function studies on some oxime-based functionalized surfactants and their role as micellar catalysts.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

Surface properties and thermodynamic parameters of 3-series functionalized surfactants in the presence and absence of CPB in aqueous medium at 300 K; effect of CPB as comicelles on the hydrolysis of BDNPP with 3-hydroxyiminomethyl-1-alkylpyridinium bromide; plots for the surface tension versus concentration of CPB + 3-C_{16} and CPB + 3-C_{18} mixed systems (1:1) at pH at 300 K (pH 7.1); rate profiles for the effect of CPB on nucleophilic cleavage of BDNPP with 4-C_{10} and 4-C_{12}; effect of pH on the cleavage of BDNPP at various nucleophilic concentrations of 4-C_{10} and 4-C_{12} in the absence of CPB comicelles. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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