Hydrolysis of Carboxylate and Phosphate Esters Using Monopyridinium Oximes in Cationic Micellar Media

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ABSTRACT: The reactions of *p*-nitrophenyl acetate (PNPA) with a series of monopyridinium oximes, viz. 2-PAM (2-hydroxyiminomethyl-1-methylpyridinium iodide), 3-PAM (3-hydroxyiminomethyl-1-methylpyridinium iodide), and 4-PAM (4-hydroxyiminomethyl-1-methylpyridinium iodide) have been studied in the presence of cationic surfactants of same hydrophobic chain length (C_{16}) within the concentration range of 0.5–6.0 mM at pH 8.0 under the pseudo-first-order condition. The observed rate constant (k_{obs}) increases with increasing surfactant concentration culminating into a maximum, and this has been analyzed in detail following the concepts of micellar catalysis. The structure–activity relationship of the investigated oximes has been discussed, and 2-PAM was found to be the most reactive among all the three investigated oximes for the cleavage of PNPA. Esterolytic decomposition of *p*-nitrophenyldiphenyl phosphate with oximate ions (—CH═NO^-) was followed in cetyltrimethylammonium bromide micelles at pH 9.0, and 4-PAM was the most reactive oxime for the micellar hydrolysis of phosphate ester. The apparent acid dissociation constants (pK_a) of the investigated oximes have been determined spectrophotometrically. © 2011 Wiley Periodicals, Inc. Int J Chem Kinet 43: 569–578, 2011

INTRODUCTION

Organophosphorous (OP) compounds are widely used as pesticides, insecticides, and chemical warfare agents [1,2] and have a widespread environmental concern. Although some very promising methods for the destruction of OP toxicants are available [3,4], none of them is suitable to all situations or classes of compounds, thus spurring research into alternative methods for their destruction. The inhibitory effect of these OP compounds is based on phosphorylation of a serine hydroxyl group located at the active site of acetylcholinesterase (AChE), an enzyme that plays an important role in modulating cholinergic neurotransmission [5,6]. Reactivation of inhibited AChE by nucleophiles such as oximes is an efficient way to attenuate toxicity; it plays a key role in the treatment of OP poisoning and has been a subject of extensive investigation for decades to find more effective reactivators for the

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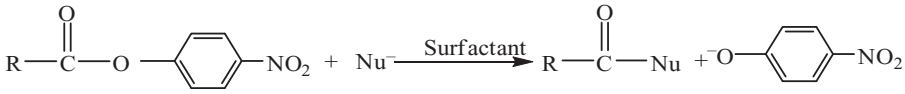
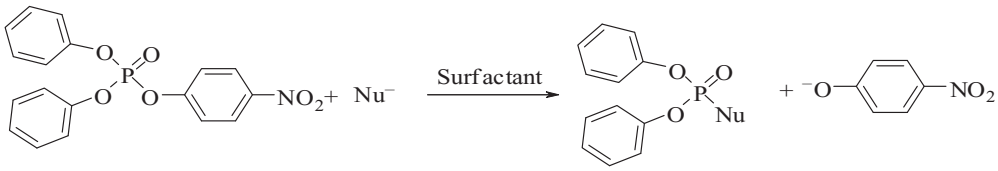


R = CH_3 *p*-nitrophenyl acetate (PNPA)



p-Nitrophenyldiphenyl phosphate (PNPDPP)

Scheme 1

treatment of OP pesticide and chemical warfare agent toxicity. Considerable attention has been directed toward detection and decomposition of organophosphates and other toxicants. Most of the cases of poisoning can be prevented by better administrative control, restricted access to OP pesticides, effective measures of personal protection, and education of OP pesticide applicators and medical personnel. One strategy to improve the efficacy of reactivators is to characterize their structural features that accelerate displacement of OP-bound moiety and introduce them into newly designed oximes [7].

Oximes (especially oximate anions) are used as potential reactivators of OP-inhibited AChE due to their unique α-effect nucleophilic reactivity. They are an important group of drugs used as antidotes in the treatment of intoxications with highly toxic OP compounds such as pesticides (paraoxon, parathion, chlorpyrifos, etc.) and nerve agents (sarin, soman, tabun, etc.) [8–11]. Scientists worldwide are engaged in designing and developing some potential reactivators of toxic OP compounds. Kuca et al. [12–15] have made incessant effort in this field. They have synthesized many novel and powerful universal reactivators and performed their reactivation potential in vivo and in vitro studies. In spite of such efforts, a single reactivator that may be universally potent against all kinds of nerve agents and OPs is still lacking. For the past few years, our laboratory has aimed to study and develop some novel promising decontamination agents, which can detoxify nerve agents. In our recent papers, various oxime-based compounds were tested with very promising results [16–18].

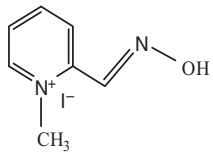
In the present investigation, micellar-mediated hydrolysis of *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyldiphenyl phosphate (PNPDPP) (Scheme 1) was studied in the presence of three monopyridinium oximes, viz. 2-hydroxyiminomethyl-1-methylpyridinium iodide (2-PAM), 3-hydroxyiminomethyl-1-methylpyridinium iodide (3-PAM), and 4-hydroxyiminomethyl-1-methylpyridinium iodide (4-PAM) (Scheme 2). The cleaving efficacy of all three oximes is compared and discussed. Since it is well known that reactivity of nucleophile increases in the presence of surfactants [19], the entire kinetic studies are performed in cationic micellar media with a common hydrophobic chain length, i.e., cetyl (C_{16}). The use of novel surfactants in assisting a variety of organic reactions is highly promising for basic and applied research [20–22].

The application of quantitative data to micellar-mediated reactions and the implications of different modes describing such reactions are also topic of continuing research. The majority of fundamental studies on micellar S_N2 reactions have been conducted in the presence of cationic micelles of quaternary ammonium surfactants such as those with trialkylammonium and quinolinium bromides and chlorides [23,24]. Scheme 1 shows the reaction for the nucleophlic attack of oximate ions on PNPA and PNPDPP in the presence of surfactants. The chemical structures of monopyridinium oximes and cationic surfactants used in the present investigation are shown in Scheme 2.

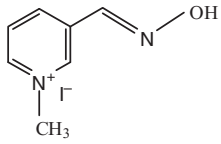
EXPERIMENTAL

Materials

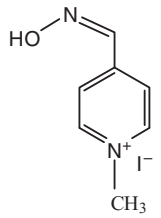
All the three pyridinium oximes (2-PAM, 3-PAM, and 4-PAM) were prepared in the laboratory of Dr. Kamil Kuca. PNPA was procured from Fluka (Buchs, Switzerland), and PNPDPP was prepared in the Vertox Laboratory of the Defence Research Development



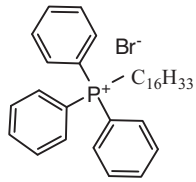
2-Hydroxyiminomethyl-
1-methylpyridinium iodide
(2-PAM)



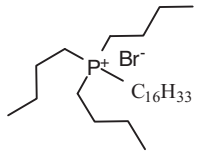
3-Hydroxyiminomethyl-
1-methylpyridinium iodide
(3-PAM)



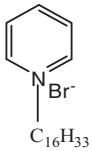
4-Hydroxyiminomethyl-
1-methylpyridinium iodide
(4-PAM)



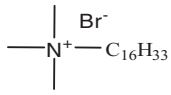
Cetyltriphenylphosphonium bromide
(CTPB)



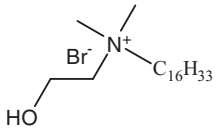
Cetyltributylphosphonium bromide
(CTBPB)



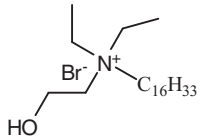
Cetylpyridinium bromide
(CPB)



Cetyltrimethylammonium bromide
(CTAB)



Cetyldimethylethanolammonium bromide
(CDMEAB)



Cetyldiethylethanolammonium bromide
(CDEEAB)

Scheme 2

Establishment (Gwalior, India). Cetyltriphenylphosphonium bromide (CTPB), cetyltributylphosphonium bromide (CTBPB), cetyldiethylethanolammonium bromide (CDEEAB), and cetyldimethylethanolammonium bromide (CDMEAB) were obtained from the laboratory of Prof. R. M. Palepu (St. Francis University, Antigonish, Canada). Surfactants such as cetyltrimethylammonium bromide (CTAB) and cetylpyridinium bromide (CPB) were purchased from Sigma (St. Louis, MO). All the solutions were prepared in triple-distilled water.

General Synthetic Procedure of Monopyridinium Oximes

In a typical synthetic procedure, pyridine aldoxime was dissolved in acetone and to this methyl iodide was added. The mixture was refluxed for 4 h. The crystals were filtered and left to dry. The crude product was dissolved in a small amount of distilled water, and acetone was added to form the crystals. The solid phase was filtered and dried to obtain a pure compound.

Kinetic Measurements

The reactions were studied spectrophotometrically with a Varian Cary 50 spectrophotometer and Systronics type-118 UV–vis spectrophotometer by monitoring the appearance of the leaving *p*-nitrophenoxide ion at 400 nm at 27 ± 0.2°C. All the kinetic experiments were performed at an ionic strength of 0.1 M KCl. Phosphate buffer was employed to control the pH of the media. All the pH measurements were obtained using a Systronics pH meter (type 362). All reactions were conducted under pseudo-first-order conditions, i.e., large excess of oximate anions over the substrate (1:10). For all the kinetic runs, the absorbance/time result fits very well with the first-order rate equation. The pseudo-first-order rate constants (k_{obs}) were determined from the plots of $\log(A_0 - A_t/A_\infty - A_t)$ versus time with A_0, A_t, and A_∞ being the absorbance values at zero, time, and infinite time, respectively. The substrate (PNPA) concentration was kept the same for all the reactions. The kinetic study was performed at various concentrations of surfactant so as to investigate the effect of surfactant on the cleaving efficiency of oximes.

Electrical Conductivity Measurements

The critical micelle concentration (cmc) of the cationic surfactants was determined by conductance measurements using a Systronics direct reading digital conductivity meter (types 304 and 306). The conductivity cell was calibrated with KCl solutions in an appropriate concentration range. A concentrated surfactant solution (∼10–20 times the cmc) was progressively added to a 10-mL medium in a thermostat container (having a temperature accuracy of ±0.01°C) using a micropipette. After thorough mixing, the specific conductance was measured. The accuracy of conductivity measurements was within ±0.5%.

Determination of Acid Dissociation Constant (pK_a)

The acid dissociation constant (pK_a) values of all the monopyridinium oximes were determined spectrophotometrically by using the method of Albert and Sergeant [25]. 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 a 25-mL phosphate buffer solution. Different pH values ranging from 6.12 to 9.92 were selected to determine the pK_a values of oximes. The pH of the solution was measured using Systronics (type-362) pH meter, and the spectrum was recorded using a buffer solution as a blank. The absorption spectrum was recorded using a Varian Cary 50 UV–vis spectrophotometer in the range of 200–400 nm and at different pH values. 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 oxime 4-PAM is shown in Fig. 1 at the temperature 27°C. The calculations of pK_a were made around half neutralization using the following equation:

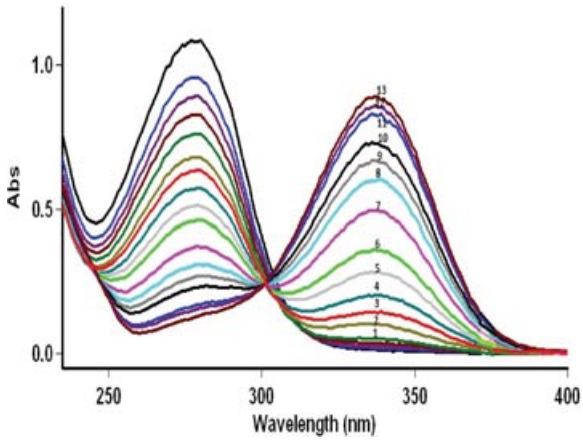


Figure 1 Absorbance spectra of 4-PAM at different pH values. [4-PAM] = 5.3×10^{-5} M at 27°C. Run and pH: (1) 7.0, (2) 7.3, (3) 7.5, (4) 7.7, (5) 7.9, (6) 8.1, (7) 8.3, (8) 8.5, (9) 8.7, (10) 8.9, (11) 9.2, (12) 9.4, (13) 9.7. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

$$pK_a = pH_{exp} - \log \frac{Abs_\psi - Abs_{Hox}}{Abs_{ox} - Abs_\psi} \qquad (1)$$

where Abs_{Hox} is the absorbance of unionized form of compound, Abs_ψ is the absorbance of partially ionized form of compound, and Abs_{ox} is the absorbance of completely ionized form of compound. The absorption spectrum of 4-PAM is represented in Fig. 1 showing two characteristic maxima obtained in UV in the region 200–400 nm. The first absorption maxima for 4-PAM around 341 nm was as a result of absorption of the nondissociated oxime group (Fig. 1, peak 1), and all the above peaks were as a result of absorption of the dissociated oxime group. The sharp isobestic point at 310–312 nm indicates an acid–base equilibrium.

RESULTS AND DISCUSSION

First-order rate constants for the nucleophilic substitution reaction of PNPA with monopyridinium oximes (2-PAM, 3-PAM, and 4-PAM) were determined under pseudo-first-order condition, i.e., nucleophiles were

in large excess over the substrates in the presence and absence of surfactants with the same hydrophobic chain length (C_{16}) and varying hydrophilic head groups. Cationic micelles bring reactants closer by hydrophobically binding of substrate and coulombically attracting negatively charged nucleophile. Maximum rate constants were observed with surfactants having phosphonium head groups. Since the deprotonated oxime was involved in the nucleophilic attack during the hydrolytic reactions, it is therefore essential that pK_a values be taken into account while studying their reactivity.

Structure and Properties of Oximes

Figure 2 shows the comparison between the reactivity of different oximes in CTBPB micelles. It can be inferred from the figure that 2-PAM is far more reactive than 3-PAM and 4-PAM. Similar trends can be observed for other surfactants (Tables I–III). There are some significant structural factors regarding the activity of monopyridinium oximes, which influence their affinity toward inhibited AChE and subsequent reactivity. The presence of quaternary nitrogen in the molecule, position of the oxime group in the pyridinium ring, and the number of pyridinium rings in the structure of the reactivator basically determine the reactivation potency of the pyridinium-based oximes.

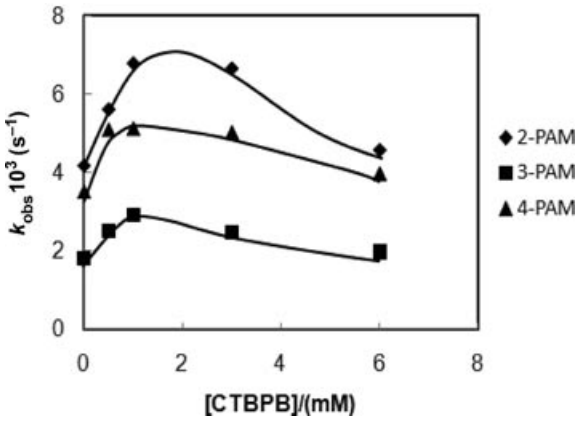


Figure 2 Rate surfactant profile for the reaction of PNPA with 2-PAM, 3-PAM, and 4-PAM in CTBPB micellar solutions at 27°C and pH 8.0.

Structure–activity relationships for oxime efficacy are poorly understood because oxime reactivation has a complex dependency on the nucleophilicity and orientation of the oxime.

The pyridinium oximes are claimed to react so effectively with the carboxylate and phosphate esters because of their relatively low pK_a (in the physiological pH range) that ensures, in neutral aqueous solutions, a substantial dissociation to oximate anions, which are powerful α-nucleophiles. The presence of positively

Table I Kinetic Rate Data for the Reaction of PNPA with 2-PAM in the Presence of Different Surfactants

	$k_{obs}\ 10^3\ (s^{-1})$					
[Surfactant] (mM)	CTAB	CTPB	CPB	CTBPB	CDMEAB	CDEEAB
0.0	4.16	4.16	4.16	4.16	4.16	4.16
0.5	–	5.60	5.66	6.02	5.20	5.15
1.0	6.88	6.78	6.91	8.05	7.76	2.53
3.0	6.22	6.65	6.01	6.41	4.18	1.87
6.0	5.20	4.56	–	–	–	

Experimental conditions: Temperature = 27°C; pH 8.0; [PNPA] = 0.5×10^{-4} M; [2-PAM] = 0.5×10^{-3} M; ionic strength, μ = 0.1 M KCl.

Table II Kinetic Rate Data for the Reaction of PNPA with 3-PAM in the Presence of Different Surfactants

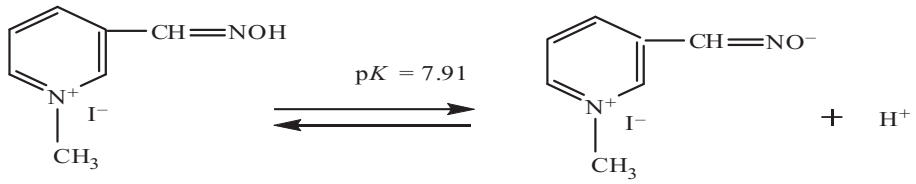
	$k_{obs}\ 10^3(s^{-1})$					
[Surfactant] (mM)	CTAB	CTPB	CPB	CTBPB	CDMEAB	CDEEAB
0.0	1.80	1.80	1.80	1.80	1.80	1.80
0.5	–	2.50	2.48	2.20	4.00	3.61
1.0	2.16	2.91	2.63	2.38	4.50	4.24
3.0	1.65	2.46	3.58	1.50	3.50	3.70
6.0	–	1.96	3.23	–	–	–

Experimental conditions: Temperature = 27°C; pH 8.0; [PNPA] = 0.5×10^{-4} M; [3-PAM] = 0.5×10^{-3} M; ionic strength, μ = 0.1 M KCl.

Table III Kinetic Rate Data for the Reaction of PNPA with 4-PAM in the Presence of Different Surfactants

	k_{obs} 10^3 (s^{-1})					
[Surfactant] (mM)	CTAB	CTPB	CPB	CTBPB	CDMEAB	CDEEAB
0.0	3.50	3.50	3.50	3.50	3.50	3.50
0.5	–	5.08	4.30	5.86	3.80	4.40
1.0	4.33	5.11	4.83	7.48	3.73	5.49
3.0	4.01	5.01	4.20	4.96	2.61	4.35
6.0	–	3.96	–	–	–	–

Experimental conditions: Temperature = 27°C, pH 8.0, [PNPA] = 0.5×10^{-4} M, [4-PAM] = 0.5×10^{-3} M, ionic strength, μ = 0.1 M KCl.



2-PAM Active species

Scheme 3

charged quaternary nitrogen in the pyridinium ring substantially decreases the pK_a value of the oxime. The electron-withdrawing effect of quaternary nitrogen in the pyridinium oximes increases the acidity of the hydroxyimino group, which is relatively low in nonsubstituted aromatic or aliphatic oximes (p$K_a \approx$ 12–13). The increased acidity of pyridinium aldoximes and ketoximes (p$K_a \approx$ 8–10) provides a sufficient concentration of the nucleophilic oximate anion even in neutral solutions.

The oxime group (—CH=NOH) dissociates and forms oximate anion (—CH=NO), which now acts as an α-nucleophile and cleaves the bond at the carbon center. Furthermore, the position of the oxime group is one of the most important structural factors responsible for the activity of oximes. 2-PAM is a well-known antidote for the reactivation of inhibited AChE in organophosphate poisoning [26,27]. The position of the oxime group can affect the dissociation constant lowering the pK_a. 2-PAM is the most reactive among all the oximes (Fig. 2) due to the presence of the oxime group at second position, where as 3-PAM is the least reactive oxime for the hydrolysis of PNPA. This can be accounted for by the fact that the acid dissociation constant (pK_a) of 2-PAM is less than the oximes substituted at 3- and 4-positions. (The pK_a values of 2-PAM, 3-PAM, and 4-PAM were calculated as 7.91, 9.53, and 8.36, respectively.) Dissociation of 2-PAM into active species is depicted in Scheme 3.

To study the effect of investigated oximes on the hydrolysis of phosphate ester, first-order rate constants for the reaction of PNPDPP with 2-PAM, 3-PAM, and 4-PAM in CTAB at pH 9.0 were determined. The results are summarized in Table IV. The same trend was not obtained when the substrate was changed. For the hydrolysis of PNPDPP, 4-PAM was found to be the most reactive and the reactivity order of oximes can be presented as 4-PAM > 3-PAM > 2-PAM. The reactivity order of oximes may be explained on the basis of steric hindrance for the cleavage of bond at phosphorus center. 4-PAM possesses the least steric hindrance and for this reason it is most reactive for the hydrolysis of PNPDPP. However, the position of the oxime

Table IV Kinetic Rate Data for the Reaction of PNPDPP with 2-PAM, 3-PAM, and 4-PAM in the Presence of CTAB

	k_{obs} 10^3 (s^{-1})		
[CTAB] (mM)	2-PAM	3-PAM	4-PAM
0.0	0.40	0.48	0.43
0.5	0.53	0.56	0.76
1.0	0.43	0.53	0.65
3.0	0.40	0.50	0.60

Experimental conditions: Temperature = 27°C; pH 9.0; [PNPDPP] = 0.5×10^{-4} M; [PAM] = 0.5×10^{-3} M; ionic strength, μ = 0.1 M KCl.

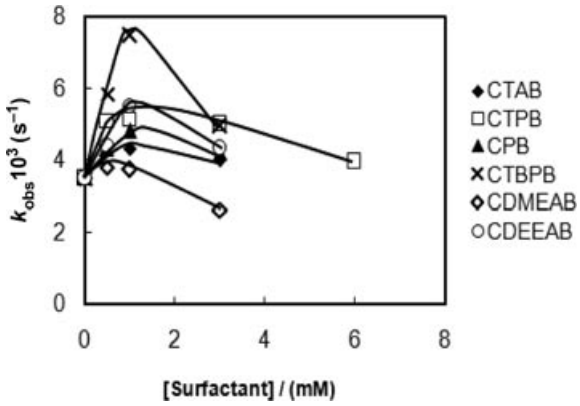


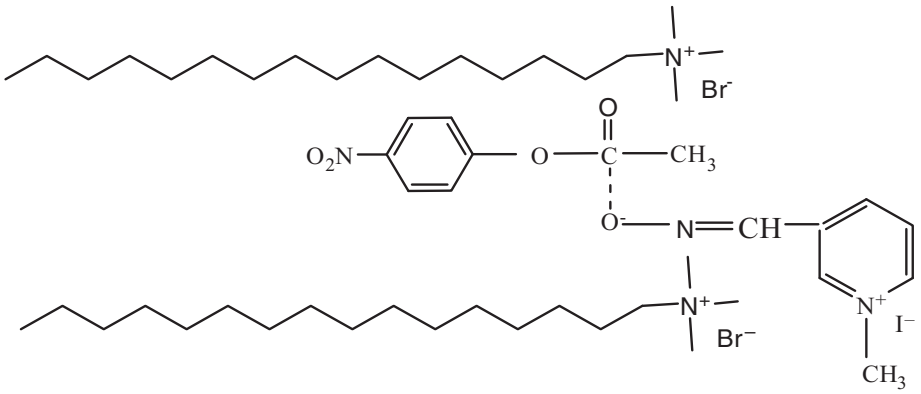
Figure 3 Rate surfactant profile for the reaction of PNPA with 4-PAM in various concentrations of different cationic surfactants at 27°C and pH 8.0.

group and the ability to reactivate to some extent also depends on the type of the substrate used [28].

Effect of Cationic Surfactants

Table I shows the kinetic rate data for the hydrolysis of PNPA with 2-PAM in the presence of different cationic surfactants at pH 8.0 and temperature 27°C. It is clearly depicted that as the surfactant concentration increases, the observed rate constant first increases and reaches maximum and then decreases at a higher concentration of surfactants. Similar trends are observed for the kinetic study with 3-PAM and 4-PAM, as presented in Tables II and III. The efficacy of 4-PAM toward the hydrolysis of ester in cationic micellar media is also depicted in Fig. 3, which shows the observed rate constants for the cleavage of PNPA with 4-PAM in the presence of surfactants. Micelles are known to amplify the kinetic benefits by bringing together a small volume of the reactant species, and this is particularly relevant when they are marked lipophilic and hence sparingly soluble in a bulk solution. In the present investigation, cationic micelles are used because they are known to lower the pK_a values of acidic functions (oximate nucleophiles). Furthermore, hexadecyl chain length provides a lower critical micelle concentration to the surfactants and thus a kinetic study becomes easier under such conditions. The kinetic runs were performed at different surfactant concentrations within the range of 0.5–6.0 mM, i.e., well above and below the cmc of the surfactants used, and the rate enhancement of ester cleavage in micelles was compared with that of only buffer systems (the absence of surfactant). For the reaction of 2-PAM with PNPA at 1.0 mM of CTBPB, the rate acceleration was 1.93 folds with respect to only buffer system (Table I). It was observed that first-order rate constant increases sharply with increasing the concentration of the surfactant in the reaction medium, reaches a maximum, and then decreases smoothly upon further addition of the surfactant in the presence of nucleophiles for most of the kinetic runs. The rate–surfactant concentration profiles obtained with surfactants are characteristic of the micelle-catalyzed reaction.

However, in a few cases, this trend was not found and a rate maximum was observed even below the expected cmc in water. The rate constant increases with an increase in the [surfactant] below the cmc, and it has been already established [29–31] that at the concentrations below the cmc hydrophobic substrates induce the formation of submicellar aggregates where the reaction takes place. One consequence of such aggregation of cationic surfactants is the generally observed rate acceleration of nucleophilic processes in this region. Savelli et al. also encountered similar rate maxima below the cmc of surfactant for the hydrolysis of methylnaphthalene-2-sulfonate, and they termed it as substrate-induced premicellization [32]. In a few of the cases, especially for the esterolytic cleavage of PNPDPP at the fixed concentration of $-CH{=}NO^-$ ions of 2-PAM, 3-PAM, and 4-PAM, the rate maximum was achieved even before the cmc in water of the CTAB. The variation of rate constants below the cmc is difficult to quantify due to reactant-induced micellization and the interaction with micellized surfactants. The maxima below the cmc in water can be attributed to the highly hydrophobic character of PNPDPP. Rate maxima below the cmc for the degradation of PNPA were observed in two systems: PNPA-2-PAM at 0.5 mM of CDEEAB (Table I) and PNPA-4-PAM at 0.5 mM of CDMEAB (Table III). This may be accounted for on the basis of *kinetic cmc*, i.e., deviation in cmc of the surfactant from aqueous medium to the reaction medium. To support this conclusion, cmc of the investigated surfactants was also determined conductometrically in a buffer medium of pH 8.0 in the presence of nucleophile, [2-PAM] $= 1 \times 10^{-3}$ M. As depicted in Table V, a reduction in cmc values was observed for all the cationic surfactants and thus the formation of micelles or premicellar aggregates in the reaction medium can be assumed [33]. Also, it has been documented that with a rise in pH, cmc of surfactants generally decreases [34,35]. However, it is likely that the extent of attack of oximate ions at the carbon center (C=O) is influenced by a number of factors apart from lipophilicity, including the nucleophilicity of the α-effect nucleophile, structure of the surfactant, and polarity of the medium [36]. Cationic micelles speed up the reaction providing a reaction environment that is less polar than water.



Scheme 4 Orientation of PNPA in CTAB for nucleophilic attack at C [38].

Kinetic Rate Constants above the cmc

According to the previous discussion, rate maxima for PNPA hydrolysis with oximate ions in micelles were obtained above the cmc of surfactants and this was due to the micelle-catalyzed reactions. Initially, an increase in the surfactant concentration generates more cationic micelles and an increase in the reaction rate occurs. With increasing micelles in the solution, a stage appears where all the substrates are almost entrapped in the micellar phase. Further addition of surfactant increases the number of micelles to such an extent that the oximate anions are bound in the "Stern layer"; thus the rate of reaction falls since the substrate in one micelle cannot react with nucleophile in another [37]. The reactants are microcompartmentalized in the micelles by electrostatic and hydrophobic interactions; the catalytic enhancement results from both the localized concentration of the reactants and the physicochemical properties of the micellar environment, which is quite different from those of the bulk solvent.

According to Buncel et al. [38], micellar kinetics is governed by the electrostatic attraction of the cationic head groups of the surfactants at the micellar surface and the increase in the concentration of the nucleophilic anions. This enhanced concentration of the reactants accounts for the higher rate of reaction (Scheme 4). Subsequent addition of the cationic surfactant after cmc caused a gradual decrease in the reaction rate, and this may be due to the decrease in the catalyst concentration in the micellar pseudophase. The excess of unreactive counterions competes with oximate ions for available sites in the Stern layer. Decrease in the observed reaction rates after maxima is due to the dilution of catalysts in the Stern layer of micelles [39]. The rate enhancement in the phosponium- and pyridinium-based cationic surfactants is greater than in alkyl ammonium head groups due to their bulky head group [22,40]. The effect would correspond to a general decrease in the polarity of the head group region that would therefore increase the rate of the nucleophilic substitution [16,41]. Another possible explanation is the steric effects by the phenyl rings in the head group region that would activate the bound substrate toward substitution [33]. The rate enhancement for the hydrolytic reactions in cationic micelles may also be explained on the basis of reduction in the acid dissociation constants (pK_a) of monopyridinium oximes due to the micellar environment. It has been well proved that cationic micelles are very often responsible for lowering of the pK_a values of different nucleophilic species and thus may be used as efficient decontaminating systems for toxic esters [42–44].

Table V Cmc of the Cationic Surfactants in Aqueous and Buffer Medium (pH 8.0) at Temperature 27°C

	cmc (mM)	
Surfactant	Aqueous	Buffer[a]
CTAB	0.90	0.55
CTPB	0.16	0.09
CPB	0.95	0.70
CTBPB	0.20	0.15
CDMEAB	0.84	0.50
CDEEAB	0.87	0.45

[a]Experimental conditions: pH 8.0 (phosphate buffer); [2-PAM] $= 0.5 \times 10^{-3}$; KCl = 0.1 M KCl; temperature = 27°C.

CONCLUSIONS

A significant objective of the present investigation was to study in detail the structure–activity relationship of monopyridinium oximes and their role in hydrolysis of model substrates of OP compounds and nerve agents in

the micellar medium. It can be concluded that the reactivation potency of oxime depends not only on its structure but also on the kind of substrate used. Cationic micelles showed a tremendous enhancement in the rate of spontaneous hydrolysis of esters and assisted the rate of reaction. The observed rate constants were found to increase with increasing surfactant concentration, which further decreases at a higher surfactant concentration, showing the nature of micellar-catalyzed reactions. 2-PAM was found to be the most reactive among all the investigated oximes for the hydrolysis at C═O, whereas 4-PAM was most effective oxime for the hydrolysis at the P═O center. Monopyridinium oximes are a particularly appealing class of α-nucleophiles to examine since they have pK_a values in the range 7–10, which makes them ideal candidates for decontamination in the environment, but their structural requirements still need to be explored. Results of this investigation will enrich our understanding about reactivators of AChE and their action and a promising role in detoxification purposes. Most significantly, results of this investigation are useful in developing an effective mechanism for the degradation of chemical and biological warfare agents under mild conditions.

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