Kinetic study of hydrolytic decomposition of organophosphates and thiophosphate by N-hydroxyamides in cationic micellar media

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The nucleophilic hydrolytic reactions of *p*-nitrophenyl diphenyl phosphate (PNPDPP), *p*-nitrophenyl diethyl phosphate (Paraoxon) and *p*-nitrophenyl diethyl phosphorothioate (Parathion) with N-hydroxyamides have been investigated at 27 °C. With cationic micelles, rate enhancement has been observed on the nucleophilic attack at P center. All the rate surfactant profiles show typical micelle assisted bimolecular reactions. The interfacial ion exchange, control of the interfacial nucleophile concentration and the reactivity at the micellar interface has been explained.

Keywords: Kinetic study, hydrolytic decomposition, organophosphates, thiophosphate, N-hydroxyamides, cationic micellar media

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Synthetic organophosphates (OPs) are among the most toxic substances known. These neurotoxic chemicals are used not only as pesticides and insecticides but also as chemical warfare agents. *p*-Nitrophenyldiphenyl substituted OPs (**Scheme I**), such as methyl parathion, parathion, and paraoxon *etc*. are some of the most widely used pesticides in agriculture. These esters are potent acetylcholinesterase (AChE) and butyrylcholinesterase inhibitors. Due to their biological and environmental significance, their degradation has been extensively investigated using different hydrolysing α-nucleophiles[1-20]. The active OPs function by blocking AChE at the synapses. The extensive usage of these pesticides generates large volumes of excess aqueous pesticide-containing waste.

Although some very effective methods are also available for the detoxification of organophosphates, none of them is well suited to all classes of these compounds. Due to their extreme toxicity, there are immediate needs for innovative analytical and environmental friendly methods to decompose neurotoxic phosphate esters. Nucleophilic hydrolysis and oxidation are the most preferred reactions to detoxify them. However, the high toxicity and licensing problems associated with such compounds mandates that most university research laboratories employ stimulants instead of the actual target compounds.
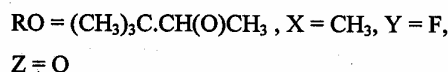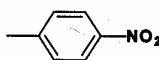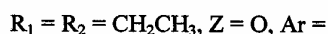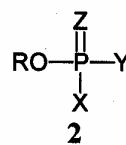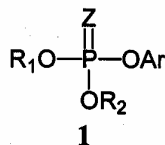
Organized assemblies and biomimetic models containing nucleophiles have been extensively employed as potent esterolytic agents. Micelles and other association colloids act as self-assembled microreactors − compartmentalizing, concentrating or separating and diluting reactants, thereby altering rate-equilibrium constants of chemical reactions. Most of these catalytic processes proceed with the attack of nucleophiles on the acyl carbonyl and phosphate groups. Consequently, such processes are potentiated by performing the reactions in aggregates such as cationic micelles or vesicles which assist in bringing together nucleophilic reagents and hydrophobic substrates. These aqueous surfactant dispersions such as micelles, microemulsions, vesicles, *etc*. alongwith their ability to support the rate enhancement of esterolytic reactions, also provide the best means for solubilization of hydrophobic compounds in aqueous media. Enhanced nucleophilic reactivity is generally governed by micellar effects and nature of the particular nucleophile. The nucleophiles exhibiting α-effect are oximate $(R_2C=NO^-)^2$, hydroxamate$(RC(O)NHO^-)^{6,16}$, peroxides $(ROO^-)^4$, hydroxylamine $(NH_2OH)^4$, hydrazine $(RNH-NH_2)^8$, hypochlorite[15], hydroxybenzotriazoles
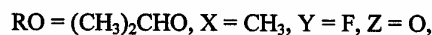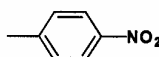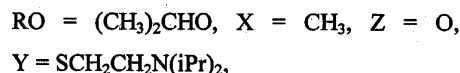
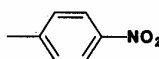**PESTICIDES**

CHEMICAL WARFARE AGENTS

$$R_1O-\overset{\overset{\displaystyle Z}{\|}}{\underset{\underset{\displaystyle OR_2}{|}}{P}}-OAr$$

1

$$RO-\overset{\overset{\displaystyle Z}{\|}}{\underset{\underset{\displaystyle X}{|}}{P}}-Y$$

2

$R_1 = R_2 = CH_2CH_3$, $Z = O$, Ar = ⟨benzene⟩—NO_2

Paraoxon

(*p*-nitrophenyl diethyl phosphate)

$RO = (CH_3)_3C.CH(O)CH_3$, $X = CH_3$, $Y = F$, $Z = O$

Soman

$R_1 = R_2 = CH_2CH_3$, $Z = S$, Ar = ⟨benzene⟩—NO_2

Parathion

(*p*-nitrophenyl diethyl phosphorothioate)

$RO = (CH_3)_2CHO$, $X = CH_3$, $Y = F$, $Z = O$,

Sarin

$R_1O = C_6H_5$, $R_2 = C_2H_5$, $Z = S$, Ar = ⟨benzene⟩—NO_2

EPN
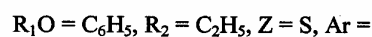
(*p*-nitrophenyl O-ethyl phenyl phosphonothioate)

$RO = (CH_3)_2CHO$, $X = CH_3$, $Z = O$, $Y = SCH_2CH_2N(iPr)_2$,

VX

Scheme I

/tetrazoles[11] and iodosylcarboxylates[17] *etc*. N-hydroxyamides are structural analogues of hydroxamic acids with N-OH functional group.

Previously, we have investigated nucleophilic catalysis of carboxylic ester hydrolysis using N-hydroxyamides[21]. The present paper focuses on the nucleophilic decomposition of *p*-nitrophenyl diphenyl phosphate (PNPDPP) and *p*-nitrophenyl diethyl phosphate (Paraoxon) and *p*-nitrophenyl diethyl phosphorothioate (Parathion) by N-hydroxyamides (**Scheme II**) in cationic micellar media.

Results and Discussion

The rates of hydrolyses of PNPDPP, paraoxon and parathion were studied spectrophotometrically with varying concentrations of N-hydroxyamides in micellar and non-micellar media at 27°C under pseudo-first-order conditions. The first order rate constants, k_{obs} were reckoned from linear plots of log $(A_\infty - A_o)$ / $A_\infty - A_t$ *vs*. time. The p*H*-dependent pseudo-first-order rate constants for PNPDPP, paraoxon and parathion cleavages at 27 °C were determined at different p*H* values between 8.00-12.4 by following the release of *p*-nitrophenoxide ion at 400 nm spectrophotometrically. The p*H*- rate constant profiles data for all the three esters under CTAB micellar condition are shown in **Table I**. The observed first order rate constant increases with increasing p*H* values. At higher p*H*, the reaction is very fast and the rate of decomposition cannot be measured.

The decomposition reaction is nucleophile concentration dependent. The reaction rate increases with increasing concentration of N-hydroxyamide. The linear nature of plot (rate-nucleophile concentration) with small intercept value shows true catalysis by the N-hydroxyamides against the hydrolysis of phosphate esters (data not shown).

The rate of hydrolytic reactions in aqueous media can be shown as,
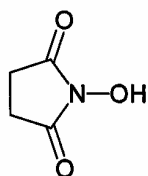
$$k_{obs} = k_o + k_{Nu} [Nu^-] \qquad \ldots (1)$$

$$k_o = k_{H_2O} + k_{OH^-}[OH] \qquad \ldots (2)$$
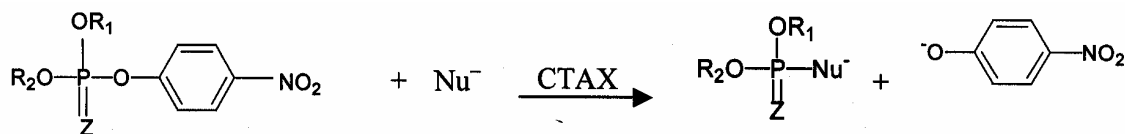
$R_1 = R_2 = C_6H_5$, Z = O, **PNPDPP**; $R_1 = R_2 = C_2H_5$, Z= O, **PARAOXON**

$R_1 = R_2 = C_2H_5$, Z = S, **PARATHION.**

Nu⁻ =
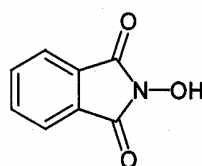
N-hydroxysuccinimide   N-hydroxyphthalimide

CTAX = Cetyltrimethylammonium halides, CTA⁺ = n-$C_{16}H_{33}N^+(Me)_3$, X⁻ = Br⁻, CTAB; X⁻ = Cl⁻, CTACl

Scheme II

Table I — pH-dependent pseudo-first order rate constants for the reactions of N-hydroxyamides with PNPDPP, Paraoxon and Parathion

$\mu = 0.1$ M KCl

pH	$k_{obs}10^4/s^{-1}$				
	Paraoxon		PNPDPP		Parathion
	NHS	NHP	NHS	NHP	NHP
8.00	a	a	2.30	2.12	1.83
9.00	a	a	2.61	2.64	5.26
10.0	0.34	0.46	5.47	8.62	21.9
10.5	0.51	1.07			
11.0	1.22	1.56	14.3	24.8	b
11.5	2.11	2.35	b	b	b
12.0	7.51	3.60	b	b	b
12.4	13.3	15.6	b	b	b

Temp.27°C [Substrate] = 1.0×10^{-4} M;
a = reaction is very slow
[Nu] = 1.0×10^{-3} M [Surfactant] = 1.0×10^{-3} M;
b = reaction is very fast

N-Hydroxyamides are strong α-nucleophiles, so that competition with other nucleophiles, in particular, H_2O and OH⁻ is not expected.

Effect of Cationic Surfactant

Aqueous cationic surfactant solutions are known to accelerate the spontaneous hydrolysis of carboxylic and phosphate esters. The reactivity depends upon nature of the substrate, pH and type of nucleophile. The kinetic results of all the three substrates in different concentrations of CTAB and CTACl are shown in **Table II**. Reactivities in surfactant micro-organized media is illustrated by results on micellar catalysis in micelles. Degradation of Paraoxon and Parathion by N-hydroxyamides, in presence of cationic surfactants, cetyltrimethylammonium salts, CTAX is given in **Table II**. As is apparent from **Table II**, degradation of substrates is accelerated by the presence of CTA surfactant in case of both nucleophiles, N-hydroxysuccinimide and N-hydroxyphthalimide. The rate constants increase with increase in surfactant concentration culminating in a maximum above the cmc value. It has been amply demonstrated in a number of studies[21] that at concentrations below the cmc, hydrophobic substrates induce the formation of submicellar aggregates where the reaction takes place. Above the cmc, rate of decomposition of Paraoxon becomes double in case of N-hydroxysuccinimide and three times in case of N-hydroxyphthalimide at the rate maxima. The degradation of PNPDPP in the presence of NHS and NHP is not very significant whereas in the case of paraoxon and parathion the observed first order rate constant increases with surfactant concentration.

The rate of reaction of paraoxon with N-hydroxyamide increases with increasing surfactant concentration, thus no rate maxima is observed. The rate of reaction for PNPDPP increases with increasing surfactant concentration up to maximum and then decreases (**Table II**). Paraoxon is much more hydrophilic in nature as compared to p-nitro-phenyldiphenyl phosphate (PNPDPP). Rate data shows that the nucleophilic reaction of paraoxon is

Table II — Kinetic rate data for the reaction of PNPDPP, Paraoxon and Parathion with N-hydroxyamides in cationic micellar media at 27°C

$\mu = 0.1\ M$ KCl

[surfactant] $10^{-3}\ M$	$k_{obs}\ 10^4/s^{-1}$								
	PNPDPP				Paraoxon[b]				Parathion[a]
	NHS		NHP		NHS		NHP		NHP
	CTAB	CTACl	CTAB	CTACl	CTAB	CTACl	CTAB	CTACl	CTAB
0.0					7.51	7.51	3.6	3.6	
0.9	1.78	1.90	1.80	1.96	7.62	7.30	5.60	5.40	4.99
1.8	2.61	2.68	2.64	2.64	7.69	8.50	6.80	6.75	5.26
3.6	1.09	1.59	1.92	2.48	7.78	9.49	8.54	8.71	11.7
9.1	0.94	1.48	1.76	2.36	8.56	10.7	10.8	12.6	12.5
18.2	0.85	1.41	1.68	1.87	10.0	14.2	12.1		14.3

a = *p*H 9.1
b = *p*H 12.0

more significant with N-hydroxysuccinimide in aqueous media. But in micellar solution, the reaction is not as significant as compared to N-hydroxyphthalimide. The nucleophilic reactivity in micelle depends upon the binding of substrate and interaction with anionic nucleophiles[22]. These reactions have an advantage in micellar media for solubility reasons since, the substrate, PNPDPP is highly hydrophobic.

The kinetic counterion effect is quite significant since the overall micellar effect, k_{max}/k_{Nu} is higher on changing over from bromide to chloride for the reaction of paraoxon and PNPDPP. High concentration of anionic nucleophiles in the Stern layer of a cationic micelle implies that the surfactant counterion is readily transferred to the aqueous phase since the reaction must occur at this interface and the micellar surface cannot be oversaturated by anions[23]. The reactivity of N-hydroxyamides with Paraoxon and PNPDPP is higher in CTACl micelle because Cl^- counterion is readily exchangeable as compared to Br^- ion.

Experimental Section

Paraoxon and parathion were prepared by literature method at the Vertox laboratory, Defence Research Development Establishment, Gwalior. All the esters were characterized by spectroscopic techniques. All other reactants (nucleophiles) and surfactants used were obtained from Sigma / Aldrich and are of the highest purity available commercially and were used as such without further purification. The concentration of nucleophiles used were in the concentration range of $0.5 - 1.83 \times 10^{-3}$M. Due to the low solubility of PNPDPP in water, its solution was prepared in acetonitrile.

Kinetic experiments were monitored by observing the rate of formation of *p*-nitrophenoxide ion at 400 nm using Unicam 2 300 UV-Vis Spectrophotometer. All the experiments were performed at an ionic strength (μ) of 0.1M KCl. The values of rate constants were reproducible to within 3%. The phosphate and borate buffers were employed.

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