CHAPTER III

α-EFFECTS IN THE ESTER CLEAVAGES BY
VARIOUS NUCLEOPHILES IN MICELLES*

The nucleophilic substitution reaction of p-nitrophenyl acetate, p-nitrophenyl diphenyl phosphinate, and parathion with different α-effect nucleophiles (I), i.e. N-phenylbenzo hydroxamate ion, o-iodosobenzoate, oximates, butane 2,3-dione monoximate and 1-hydroxybenzotriazole) have been investigated in the absence and presence of cationic surfactant. Kinetic measurements were performed for the hydrolysis of p-nitrophenyl acetate as a model compound in micellar media. This reaction was studied both in the presence and absence of various α-effect nucleophiles, and in depth analyses were performed using acetohydroxamic acid (AHA). Rate surfactant profiles were obtained in the absence and presence of the AHA nucleophile for the alkyl triphenylphosphonium bromides (C₅PPh₃Br) surfactant series. All rate surfactant profiles were analyzed using the pseudophase model and modified pseudophase model. Studies in the presence of acetohydroxamic acid and the alkyl triphenylphosphonium surfactants were also conducted as a function of pH to obtain the pKₐ value of the acetohydroxamic acid in the micellar media.

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CHAPTER III: \( \alpha \)-EFFECTS IN THE ESTER CLEAVAGES BY VARIOUS NUCLEOPHILES IN MICELLES

3.0 INTRODUCTION

The \( \alpha \)-effect has been reported in different types of reactions in solutions.\(^1\)\(^-\)\(^4\) Classical physical organic chemistry studies over the last twenty years have yielded some important clues about the nature of \( \alpha \)-effect.\(^5\)\(^-\)\(^15\) Although many attempts have been made to rationalize \( \alpha \)-effects in terms of physiochemical factors, (e.g., polarizability, hydrogen bonding, single electron transfer character, and other) mechanistic details have not been sufficiently clear. In the preceding chapter, the role of dihydroxamic acids on the hydrolysis of esters have been described. \( \alpha \)-Nucleophiles are also characterized by anomalously high reactivity with respect to electron deficient centers of various origins, e.g., carbon, sulfur and phosphorus. This fact attracts interest from the viewpoints of utilization of organophosphorus ecotoxicants and search for effective detoxicants and antidotes.

Some organophosphorus compounds are highly toxic species that directly affect the central nervous system (CNS) by acting, as powerful inhibitors of the enzyme acetylcholinesterase.\(^16\)\(^-\)\(^18\) The facile hydrolysis of toxic organophosphorus compounds is of theoretical and practical interest since these compounds appear in day-to-day applications as pesticides and have been used as potent chemical warfare agents.\(^22\)\(^-\)\(^23\) As such, there is an apparent need to develop safe, efficient and inexpensive methods to decontaminate these species.
The primary organophosphorus compounds that are of concern and in great abundance are sarin (o-isopropyl methyl phosponofluoridate) and soman (o-pinacolyl methylphosphonofluoridate), but due to extreme toxicity, testing cannot be performed on such chemicals. Instead, model compounds that behave in a similar manner under similar conditions must be used, and these include compounds such as the phosphorus ester, p-nitrophenyl diphenyl phosphinate (PNPDP) and carboxylate ester, p-nitrophenyl acetate (PNPA).

Various methods have been developed to enhance the hydrolysis of phosphorus and carboxylate esters, and these include the employment of metal ions which act as lewis acid catalysts, metallomicelles, enzymes, and reactive α-effect nucleophiles such as oximates, hydroxymates, hydrazines and hydroxylamine to name a few. It has also been recognized that cationic micelles serve to enhance the rate of hydrolysis of such compounds via micellar catalysis. Moss and others have studied extensively the catalytic cleavage of carboxylate and phosphate esters by a series of o-iodosobenzoic acid.

Changing the electrophilic center from a carbonyl to a sulfonyl or phosphonyl group would exert significant effect on their electrophilicity. However systematic studies on changing such electrophilic centers have been lacking. Only scattered information on the reactivity of carbonyl, sulfonyl and phosphonyl esters of similar structures is available.

Chemical means of achieving efficient degradation of organophosphate esters remains an active area of research, with attention focused recently on nucleophilic reagents such as peroxides, iodosarene carboxylates, 4-N,N-dialkyaminopyridines, and metallomicelles employed primarily in cetyltrimethylammonium (CTA+) micelles as media.
It is of interest to establish efficient and cost effective means of PNPA hydrolysis that can be extrapolated in industry and applied to the nucleophilic breakdown of organophosphorus compounds. It is thought that the micellar media works to increase the rates of PNPA hydrolysis by localizing the reactions such that for their interaction is maximized. The PNPA is partitioned into the micellar interface by coulombic and hydrophobic interactions. The deprotonation site of hydroxamic acids (RCONHO⁻) has provided a challenging example, due to its extreme sensitivity to structure and solvent.

3.1 REVIEW OF EARLIER WORK

Bagno et al.⁴⁴ proposed that O-ionization of CH₃CONHOH (AHA) give rise to an oxyanion with a localized charge (which is well stabilized in water). Similarly Exner and Bohm⁴⁵ also advocated O-anion form. Garcia et al.⁴⁶ performed ab initio calculations and different experimental (NMR and UV-vis) measurements of the isomers of AHA and their deprotonation processes. According to them anions are considered with O-deprotonation. This species is more nucleophilic towards the carbonyl carbon of ρ-nitrophenyl acetate.

Among the many reagents, the iodosocarboxylates (iodosobenzoate and iodosonaphthoate) and certain metallomicelles stand out as characterized by rapid cleavage of ρ-nitrophenyl diphenyl phosphate and catalytic turnover⁵².

In 1991, Bunton et al.⁴⁷ studied hydrolysis of phosphinate and thiophosphinate esters including parathion with hydroxide ion in aqueous and CTAB micellar solution. The reactions were explained on the basis of
pseudophase model considering distribution of reactants in both aqueous and micellar phases.

Moss et al.\textsuperscript{33-37} performed kinetic studies on parathion with \( \alpha \)-iodosobenzoate (IBA) (V) as catalyst in CTACI and CTAB micellar media. In another experiment they extended the studies in functionalized IBA surfactant (VI), which showed best results for the parathion catalysis\textsuperscript{17}.

Um et al.\textsuperscript{39} reported alkaline hydrolyses of parathion and paraoxon in dimethyl sulfoxide (DMSO-H\textsubscript{2}O) mixtures at varying compositions.

3.2 \textit{PRESENT INVESTIGATION}

This chapter is divided into three sections:

[A] Comparative Nucleophilic Reactivities of Some \( \alpha \)-Nucleophiles in Carboxylate, Phosphinate and Thiophosphate Esters Cleavage.


[C] Bronsted Relationship

In Section-A, the nucleophilic substitution reaction of \( p \)-nitrophenyl acetate, \( p \)-nitrophenyl diphenyl phosphinate, and parathion (\( p \)-nitrophenyl diethyl phosphorothioate) with different \( \alpha \)-effect nucleophiles (I), \( N \)-phenylbenzohydroxamic acid (PBHA) i.e \( \alpha \)-iodosobenzoate (IBA), \( 1 \)-hydroxybenzotriazole (HOBT) and oximates (butane 2,3-dione monoxime) have been investigated in the absence and presence of cationic surfactant (Scheme 3.1).
α-Effect in the ester cleavages by various nucleophiles in micelles

\[ CH_3-CO-O-C_6H_4-NO_2 \]
\[ p-Nitrophenyl acetate (PNPA) \]

\[ C_6H_4-CO-O-C_6H_4-NO_2 \]
\[ p-Nitrophenyl diphenyl phosphinate (PNPDP) \]

\[ C_2H_5O-P-O-C_6H_4-NO_2 \]
\[ p-Nitrophenyl diethyl phosphorothioate (PARATHION) \]

\[ C_6H_4-N-OH \]
\[ C_6H_5-C=O \]
\[ N-phenylbenzhydroxamic acid \ (PBHA) \]

\[ C_6H_5-CO-O-C_6H_4-CH_3 \]
\[ o-Iodosobenzoic acid \ (IBA) \]

\[ CH_3-C=O \]
\[ Butane 2,3-dione monoxime \ (Oxime) \]

\[ HN-C=O \]
\[ 1-Hydroxybenzotriazole \ (HOBT) \]

α: Nucleophiles

**Scheme 3.1**
In Section-B, detailed kinetic measurements were performed for the hydrolysis of p-nitrophenyl acetate as a model compound in micellar media. The surfactants that have been employed for use in micellar catalysis include the alkyl triphenylphosphonium bromide series (CnPPh3Br, where n = 10, 12, 14, 16). Comparative studies have also been performed on cetyl pyridinium bromide (CPBr), and cetyltrimethylammonium bromide (CTAB) to demonstrate the effectiveness of the CnPPh3Br surfactants. The use of acetohydroxamic acid (CH3CONHOH) as a catalytic α-nucleophile in the system was employed as a means to improve the rates of PNPA hydrolysis.

In Section C, the reactions of PNPA with a series of α-nucleophiles i.e., hydroxamic acid [RCONOHR'; R= C6H5, R' = H; R=CH3, R'= H; R=2-OHC6H5, R'= H; R= C6H5, R'= C6H5, R'=2-Cl C6H5, R'= CH3 ], oximates (Butane 2,3-dione monoxime, Acetaldoxime) and other nucleophiles having pKₐ values in the range of 6.5-11.8 were studied at 27°C.

3.3 EXPERIMENTAL

Materials:

p-Nitrophenyl acetate (PNPA) was purchased from Sigma/Aldrich and was used as received. p-Nitrophenyl diphenyl phosphinate (PNPDP) and Parathion were prepared by literature method at the Vertox laboratory of Defence Research Development Establishment, Gwalior. N-phenylbenzohydroxamic acid, were synthetically prepared as described in the literature48. Other hydroxamic acids were procured from Sigma/Aldrich. Butane 2,3-dione monoxime, α-iodosobenzoic acid, and 1-hydroxybenzotriazole were purchased from Sigma. Alkyl triphenylphosphonium bromide surfactants were obtained (Lancaster Synthesis), from Prof. R. M. Palepu, St. Francis Xavier University, Antigonish, Canada. (>97-
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98% purity) The sodium dihydrogen phosphate (NaH₂PO₄) was purchased from Fisher, and the disodium hydrogen phosphate (Na₂HPO₄) was purchased from BDH Chemicals.

To control the degree of ionization of the hydroxamic acids, it was necessary to prepare solutions in a buffer mixture of pH 8.0, which consisted of H₂PO₄⁻ and HPO₄²⁻ (in a 0.5:9.5 mole ratio of H₂PO₄⁻:HPO₄²⁻) dissolved in triply deionized water. Buffers of higher pH (between 8.0 and 9.0) were prepared by the addition of sufficient 0.1 M NaOH solution to the pH 8.0 buffer. All buffers higher than pH 9.0 were prepared using 0.01 M borax and 0.1 M NaOH solutions. Mother solutions of the PNPA and the hydroxamic acids (AHA and oximate) were prepared at 0.0015 M and 0.01 M respectively.

Methods:

To measure reaction rate, a Hewlett Packard 8452A diode array single beam and Varian Cary-50 Spectrophotometers were used to follow the reaction as it proceeded spectrophotometrically. When used in the reaction conditions, AHA and surfactant were added to the system contained in a cuvette in sufficient quantities using Labsystems micropipette. The system was stirred promptly after the addition of substrate to allow for thorough mixing, and the measurement of reaction rates was then started, and the time of addition was taken to be time zero. In reaction conditions where substrate concentration was not varied, the PNPA concentration was made to be 1.5 x 10⁻⁴ M. The total volume of the system present in the cuvette was 3 ml.
Figure 3.1: Repeat scans in every one minute showing the increasing absorbance at 400 nm. [MCBHA] = 1.0 mM, [PNPA] = 0.1 mM, [C_{16}PPh_{3}Br] = 5mM pH = 8.0

Absorption spectra were measured from 300 to 500 nm, and rates of reactions were measured at 400 nm, which is the point of maximum absorption of the products formed. Temperature was maintained using a Haake DC-3 water bath and water-jacketed cell compartment.

The pseudo-first-order rate constants can be determined by least squares fits. Each experiment was repeated at least twice, and the observed rate constant was found to be reproducible within a precision of about 3% or better. Figure 3.1 shows the absorption spectra of the product (p-nitrophenoxide ion) PNPA in the presence of MCBHA and C_{16}PPh_{3}Br at pH 8.0. The absorption band centered at...
400 nm, corresponding to the $p$-nitrophenoxide ions increases with time. The breakdown of PNPA was confirmed by the appearance of peak at 400 nm, when nucleophiles were added to the reaction medium. The spectrum exhibits an increase in absorbance at 400 nm with the formation of $p$-nitrophenoxide ion during the course of reaction.

3.4 RESULTS AND DISCUSSION

[A] Comparative Nucleophilic Reactivities of Some $\alpha$-Nucleophile In Carboxylate, Phosphinate And Thiophosphate Esters Cleavage

3.41 pH-Dependent Reaction

Pseudo-first order rate constants for the reaction of $p$-nitrophenyl diphenyl phosphinate with a series of $\alpha$-nucleophiles i.e., o-iodosobenzoic acid (IBA), Butane 2,3-dione monoxime, (oxime) and N-phenylbenoylhydroxamic acid (PBHA) at different pH are summarized in Table-3.1.

The rate data indicates that the rate of reaction increase with increasing pH values. Plot of log $k_{obs}$ versus pH (Figure-3.2) gave discontinuity at definite pH values for IBA, oxime and PBHA. These break points were taken as apparent $pK_a$ of these nucleophiles (IBA=7.45, Oxime=9.0, PBHA=8.9.)
**TABLE-3.1**

pH-dependent pseudo-first order rate constants for the reaction of p-nitrophenyl diphenyl phosphinate with IBA, Oxime and PBHA at 27°C

<table>
<thead>
<tr>
<th>pH</th>
<th>10^3 k_{obs.}/s⁻¹</th>
<th>IBA</th>
<th>Oxime</th>
<th>PBHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>1.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7.2</td>
<td>5.3</td>
<td>0.14</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>8.0</td>
<td>8.3</td>
<td>0.46</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>9.01</td>
<td>11.5</td>
<td>3.96</td>
<td>2.07</td>
<td></td>
</tr>
<tr>
<td>9.58</td>
<td>16.6</td>
<td>6.01</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>10.1</td>
<td>25.6</td>
<td>12.4</td>
<td>3.46</td>
<td></td>
</tr>
<tr>
<td>11.1</td>
<td>32.6</td>
<td>27.6</td>
<td>17.0</td>
<td></td>
</tr>
</tbody>
</table>

[Phosphinate] = 1.0 X 10⁻⁴ M,  [Nu] = 1.0 X 10⁻³ M, KCl = 0.1 M
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**Graphs:***

1. **(IBA)***
   - Y-axis: $\log k_{\text{cat}}$ / s$^{-1}$
   - X-axis: pH
   - Data points and lines indicating trends with pH.

2. **(Oxime)***
   - Y-axis: $10^3 k_{\text{cat}}$ / s$^{-1}$
   - X-axis: pH
   - Data points and lines indicating trends with pH.
Figure-3.2 Plots of observed rate constant vs. pH and log of observed rate constant vs. pH for the hydrolysis of p-nitrophenyl diphenyl phosphinate by o-iodosobenzoic acid (IBA), Butane 2,3-dione monoxime (oxime) and N-phenylbenzohydroxamic acid (PBHA) at 27° C.
Aqueous cationic surfactant solutions are known to accelerate the spontaneous hydrolysis of carboxylic and phosphate esters. The ability of micellized surfactants to control rates of moderately slower reactions is well established.\textsuperscript{49-54} Cationic micelles bring reactants closer by hydrophobically binding of substrate and coulombically attracting the negatively charged nucleophile.

The effects of cetyl triphenylphosphonium bromide (C\textsubscript{16}PPh\textsubscript{3}Br) (I) on the hydrolysis of PNPA, PNPDP and parathion using different $\alpha$-nucleophiles are given in Table 3.2.

It has been shown that observed first-order rate constant increases with the increasing concentrations of the surfactants. In the present case, no rate maxima have been observed (Figure 3.3) (a, b). The rate-surfactant concentration profiles obtained with various surfactants / catalysts are characteristic of micelle catalyzed reaction.\textsuperscript{52} The reactivity of these $\alpha$-nucleophiles i.e. IBA, oxime and PBHA have been observed to be more significant for the hydrolysis of PNPA. Under comparable conditions, the $k_{obs}$ values for hydrolysis of PNPA in IBA was found to be greater than PBHA, which in turn was more reactive than oxime and HOBT.
The hydrolysis of parathion in the presence of α-nucleophiles is not very significant whereas in the case of PNPA and PNPDP the observed first order rate constant increases with surfactant concentration. The nucleophilic reactivity of micelle depends upon the binding of substrate and interaction with anionic nucleophiles. In case of PNPDP, in comparison to other α-nucleophiles, IBA was found to be most reactive and HOBT is least reactive. At all concentration of surfactants, the reaction was fast in case of IBA-PNPDP to be interpreted. In case of parathion, irrespective of concentration of surfactants, IBA show the maximum rate as compared to oxime, PBHA and HOBT. PBHA and oxime exhibited comparable reactivity. The reactivity order for all the nucleophiles was IBA > PBHA > Oxime > HOBT. In case of all the substrates studied, IBA showed the highest reactivity compared to PBHA. PBHA showed higher reactivity relative to other nucleophiles.

As shown in Table 3.2, the reactivity of PNPA, PNPDP and Parathion toward these α-nucleophiles is PNPA (C=O) > PNPDP (P=O) > Parathion (P=S). The nucleophilic reactivity of these α-nucleophiles toward P=S centre is less than P=O center due to strong pπ−dπ interaction in P=O than in P=S center. Electrophilicity of central atom in P=O and P=S esters reduce in same order due to pπ−dπ bonding, which hinders the attack of α-nucleophile in the rate determining step. On the contrary, the non-existence of pπ−dπ bonding manifested to highest reactivity of C=O ester.
<table>
<thead>
<tr>
<th>[Substrate]=[1.0 X 10^{-4} M]</th>
<th>[Nu]=1mM, [H_2]=0.1 M KCl, pH=8.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>[PARATHION]=</td>
<td>[PNPDP]=</td>
</tr>
<tr>
<td>0.91</td>
<td>0.26</td>
</tr>
<tr>
<td>1.46</td>
<td>0.64</td>
</tr>
<tr>
<td>1.07</td>
<td>0.46</td>
</tr>
<tr>
<td>3.94</td>
<td>1.09</td>
</tr>
<tr>
<td>4.78</td>
<td>1.12</td>
</tr>
</tbody>
</table>

Summary of Kinetic Rate Data for the Reaction of PNP, PNPDP and PARATHION in Micellar Media.

**TABLE 3.2**
Figure 3.3 (a) Plots of $k_{obs}$ vs. [surfactant] for the hydrolysis of PNPA and PNPDP using IBA.

Figure 3.3 (b) Plots of $k_{obs}$ vs. [surfactant] for the hydrolysis of PNPA, PNPDP and Parathion using PBHA.

It is of interest to establish efficient and cost effective means of PNPA hydrolysis that can be extrapolated in industry and applied to the nucleophilic breakdown of organophosphorus compounds. Comparative studies have also been performed on cetyl pyridinium bromide (CPBr), and cetyltrimethylammonium bromide (CTAB) to demonstrate the effectiveness of the CnPPh₃Br surfactants. The use of acetohydroxamic acid (∆H₂CONHOH) as a catalytic α-nucleophile in the system was employed as a means to improve the rates of PNPA hydrolysis. The hydrolysis itself is believed to be of an \( S_N2 \) mechanism, whereby the hydroxide in the water media is attaches to the slightly positive carbonyl centre of the PNPA. The hydrolysis of this compound has been previously studied in micellar media consisting of the cetyltrimethylammonium bromide surfactant (CTAB) and various hydroxamate ions. However, the reaction has yet to be studied in the novel surfactant systems of the alkyl triphenylphosphonium bromide series. These surfactants especially are of interest to study as they have previously been shown to enhance the rates of \( S_N2 \) reactions.\(^{55-56}\) It is thought that the micellar media works to increase the rates of PNPA hydrolysis by localizing the reactions such that for their interaction is maximized. The PNPA is partitioned into the micellar interface by coulombic and hydrophobic interactions. The reaction in the absence and presence of α-effect nucleophile acetohydroxamic acid is depicted in Scheme-3.2. The deprotonation site of hydroxamic acids (RCONHO⁻) has provided a challenging example, due to its extreme sensitivity to structure and solvent. This species is more nucleophilic towards the carbonyl carbon of \( p \)-nitrophenyl acetate.
Scheme 3.2 Cleavage of PNPA both i) in the presence and ii) in the absence of the hydroxamate anion nucleophile, (CH$_3$CONO$^-$).
3.43 Kinetic Studies in Micelles

The reaction kinetics of hydrolysis of PNPA were measured in the presence of various C_{16} surfactants at a concentration of 6 mM with and without acetohydroxamic acid, and the resulting $k_{obs}$ values are shown in Table 3.3. Upon comparison of the resulting rates for each surfactant, it is apparent that the C_{11} PPh_{3}Br showed promising results. These surfactants, which have previously been well-characterized^{57-58} are novel in their use in micellar catalysis. The reaction kinetics was studied as a function of surfactant concentration for each alkyl chain length to generate a rate surfactant profile.

Reaction kinetics with hydroxyl ion as a nucleophile in the micellar media was analyzed with the pseudophase model (PPM) and is depicted by the model^{33} in Scheme 3.3.

\[ S_{w} + D_{n} \xrightarrow{K_{m}^{PNPA}} SD_{n} \]

\[ k_{w} \quad k_{m} \quad Products \]

**Scheme 3.3**: Pseudophase Model

The PPM is based on the main premise that the $k_{obs}$ is thought to be affected by reactant distribution in the micelle. Scheme 3.3 is a representation of the pseudophase model, whereby $S_{w}$ is the substrate in the aqueous phase, $D_{n}$ is the micellized surfactant, $SD_{n}$ is the substrate-micelle complex, $K_{m}^{PNPA}$ is the binding constant for substrate-micelle binding, and $k_{w}$ and $k_{m}$ are the first order rate constants in the aqueous and micellar pseudophases respectively^{15-16}. 

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**TABLE 3.3**

Comparative Reactivities of PNPA (0.00015 M) in Different Cationic Surfactants at pH 7.9,

<table>
<thead>
<tr>
<th>Surfactant</th>
<th>$10^3 k_{obs}^o$ (s$^{-1}$)</th>
<th>$10^3 k_{obs}^{AHA}$ (s$^{-1}$)</th>
<th>$k_{obs}^o/k_w$</th>
<th>$k_{obs}^{AHA}/k_w$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_{16}$PPh$_3$Br</td>
<td>0.17</td>
<td>4.02</td>
<td>6.93</td>
<td>164</td>
</tr>
<tr>
<td>CTAB</td>
<td>0.13</td>
<td>2.61</td>
<td>5.30</td>
<td>107</td>
</tr>
<tr>
<td>CPBr</td>
<td>0.16</td>
<td>2.82</td>
<td>6.53</td>
<td>115</td>
</tr>
</tbody>
</table>

[Surfactant] = 0.006 M, $k_w$ = 2.45 x 10$^{-5}$ s$^{-1}$

**Figure 3.4:** Plots of $k_{obs}$ for the hydrolysis of PNPA (0.00015 M) vs. different RPh$_3$Br surfactant concentrations in pH 7.9 at 25°C.
The observed rate constants according to scheme 3.4 can be represented as follows:

\[ k_{\text{obs}} = \frac{k_w + k_m K_m^{\text{PNPA}} [D_n]}{1 + K_m^{\text{PNPA}} [D_n]} \] (2)

The rate surfactant profiles in the presence of the Cₙ PPh₃Br surfactants are given in Figure 3.2. The solid lines for each chain length generated from the analysis from the regression describing the pseudo phase model (PPM) shown in Equation 2.34. A common and expected trend for these series is that the observed rates approach a limiting value with an increase in surfactant concentration as the substrate is hydrolyzed. Another expected and apparent trend for these profiles is the direct relationship between the observed rates and the alkyl chain lengths for each series. That is, as the alkyl chain lengths increase, the observed rates tend to increase since the longer chain lengths result in a larger micellar interface surface area, allowing for more accommodation of the substrate and therefore faster hydrolysis. Increasing the surfactant chain length increases the hydrophobicity of surfactant and the substrate binding.

By fitting curves to the rate surfactant profiles, theoretical regression parameters were obtained and are presented in Table 3.4. For the Cₙ PPh₃Br series, it is apparent that both the substrate binding constant, \( K_m^{\text{PNPA}} \), and the first order rate constant at the micellar interface, \( k_m \), increase with increasing alkyl chain length within experimental error.
The C₆ PPh₃Br systems were also studied in the presence of certain hydroxamic acids which have been shown to be excellent α-effect nucleophiles[7]. The α-effect is defined as the unexpected enhancement of nucleophilic reactivity due to the adjacent unpaired electrons pair. Buncel et al. and Fountain et al. have established that the degree of the α-effect is largely dependent on the electrophilic centre of the system, that is, a decrease in π-character of the electrophilic carbon centre reflects an increase in the α-effect (sp³ < sp² < sp).

**TABLE 3.4**

Fitting parameters for the hydrolysis of PNPA (pH = 7.9, 25°C) in the absence of AHA

<table>
<thead>
<tr>
<th>Surfactant</th>
<th>(K_m^{PNPA} \text{(M}^{-1}\text{)})</th>
<th>(10^4K_m^2\text{(s}^{-1}\text{)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₁₆ PPh₃Br</td>
<td>620</td>
<td>2.31</td>
</tr>
<tr>
<td>C₁₄ PPh₃Br</td>
<td>390</td>
<td>2.05</td>
</tr>
<tr>
<td>C₁₂ PPh₃Br</td>
<td>160</td>
<td>1.77</td>
</tr>
</tbody>
</table>

It is believed that the increase in reactivity of the α-nucleophile occurs due to a stabilization of the transition state. Mechanistic details have not yet been sufficiently clear to rationalize α-effects in terms of various factors. Various hydroxamic acids present in their ionic form in the system have been used in the PNPA hydrolysis system and their observed rates were measured to compare the reactivity of such α-nucleophiles. These results are given in Table 3.5. We have employed acetohydroxamic acid (AHA) as a α-nucleophile for detailed study of hydrolysis of PNPA.
The employment of such α-nucleophiles into the system allows for improved rate enhancements. Previous investigations in literature have shown that these hydroxamic acids which act as α-nucleophiles are characterized by having a catalytic nature\(^{13}\). By measuring the observed rates for the hydrolysis as a function of AHA concentration, a straight line, which passed through the origin, was obtained which could be fitted to the following equation:

\[
\kappa_{\text{HA}}^{\text{obs}} = \kappa_{\text{obs}}^{0} + \kappa_{\text{Nu}} \left[ \text{Nu} \right]
\]  

In the above equation, \(\kappa_{\text{HA}}^{\text{obs}}\) corresponds to the observed rate in the presence of the AHA, \(\kappa_{\text{obs}}^{0}\) corresponds to the observed rate in water, \(\kappa_{\text{Nu}}\) corresponds to the rate contribution due to the AHA alone, and \([\text{Nu}]\) corresponds to the concentration of the AHA in the system. A plot of \(\kappa_{\text{HA}}^{\text{obs}}\) vs. [AHA\(^{-}\)] is shown in Figure 3.5. The slope of the straight line obtained corresponds to the \(\kappa_{\text{Nu}}\) value, which was found to be around 45 s\(^{-1}\)M\(^{-1}\), and the intercept corresponds to the \(\kappa_{\text{obs}}^{0}\) value, which is very close to zero. Due to the large deviation in magnitudes of the rate enhancements from the water and the AHA respectively, it is clear that competition between the OH\(^{-}\) and the AHA\(^{-}\) ions is not expected, and the ability of the AHA\(^{-}\) to act as a nucleophile is very strong. As such, the AHA is considered to be a type of true catalytic nucleophile in the system\(^{4}\).

The PNPA hydrolysis was investigated in the presence of AHA at various C\(_n\) PPh\(_3\)Br concentrations to obtain rate-surfactant profiles. These studies were carried out for the C\(_{12}\)–C\(_{16}\) alkyl chain lengths, and are depicted in Figure 3.4 (Table-3.5). The plateau observed is a consequence of incorporation of the substrate to the micellar pseudophase.
Figure 3.5. \( k_{\text{obs}} \) vs. [AHA'] at 25°C demonstrating the nucleophilic nature of AHA.
The results were analyzed with modified PPM model as depicted in scheme 3.4 resulting in equation 5

\[
\begin{align*}
\text{PNPA}_w + D_n & \xrightleftharpoons{K_{m,\text{PNPA}}} \text{PNPA}_m + D_n \\
\text{AHA}_w + D_n & \xrightleftharpoons{K_{m,\text{AHA}}} \text{AHA}^- + D_n
\end{align*}
\]

Scheme 3.4: The distribution of both the PNPA (substrate) and AHA (α-nucleophile) in the micellar and bulk water pseudophases

\[
k_{\text{obs}} = \frac{k^w_2 + \frac{k^m_2}{V} K_{m,\text{PNPA}} K_{m,\text{AHA}} [D_n]}{(1 + K_{m,\text{PNPA}} [D_n]) (1 + K_{m,\text{AHA}} [D_n])} [\text{AHA}]_T \tag{5}
\]

In the above expression for the modified PPM, \(k_{\text{obs}}\) is the overall rate constant for the reaction, \(k^w_2\) is the second order rate constant in the bulk water phase. \(k^m_2\) is the second order rate constant in the micellar pseudophase. \(V_m\) is the molar reaction volume previously determined to be 0.14 L mol\(^{-1}\). \(K_{m,\text{PNPA}}\) is the equilibrium constant describing the binding of the substrate (PNPA) to the micellar surface.
Figure 3.6 Plots of $k_{obs}$ for the hydrolysis of PNPA (0.00015 M) vs. different RPPh$_3$Br surfactant concentrations in pH 7.9 at 25°C in the presence of AHA (0.0005 M).
α- Effect in the ester cleavages by various nucleophiles in micelles

**TABLE 3.5**

Comparative Reactivities of Various α-Nucleophiles in the Presence of 6 mM C$_{16}$PPh$_3$Br and pH = 7.9, 25°C.

<table>
<thead>
<tr>
<th>α-Nucleophile</th>
<th>$k_{obs} \times 10^{-3}$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHA</td>
<td>4.02</td>
</tr>
<tr>
<td>PBHA</td>
<td>0.18</td>
</tr>
<tr>
<td>SHA</td>
<td>32.0</td>
</tr>
<tr>
<td>ODHA</td>
<td>47.8</td>
</tr>
<tr>
<td>Oxime</td>
<td>0.95</td>
</tr>
</tbody>
</table>

**TABLE 3.6**

Fitting parameters for the hydrolysis of PNPA (pH = 7.9, 25°C) in the presence of AHA, 0.0005 M.

<table>
<thead>
<tr>
<th>Surfactant</th>
<th>$k_2^m$ (M$^{-1}$s$^{-1}$)</th>
<th>$K_m^{PNPA}$ (M$^{-1}$)</th>
<th>$K_m^{AHA}$ (M$^{-1}$)</th>
<th>$k_2^m$ (M$^{-1}$s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_{12}$ PPh$_3$Br</td>
<td>16.7</td>
<td>160</td>
<td>23.8</td>
<td>0.214</td>
</tr>
<tr>
<td>C$_{14}$ PPh$_3$Br</td>
<td>16.7</td>
<td>390</td>
<td>10.9</td>
<td>0.471</td>
</tr>
<tr>
<td>C$_{16}$ PPh$_3$Br</td>
<td>16.7</td>
<td>620</td>
<td>11.0</td>
<td>0.520</td>
</tr>
</tbody>
</table>
The expected trends of increasing rates with alkyl chain length and the rates approaching a limiting value were again observed. Instead, the effects of the AHA⁻ exchange with counterions at the surfactant head groups due to the strong nucleophilic nature of the AHA had to be considered. In these values, it is obvious that the substrate binding constants increase with an increase in the chain length of the surfactant. This result is quite reasonable since the increase in micellar surface area due to an increase chain length would allow for a greater amount of the PNPA to bind to the micellar surface. However, an unexpected result appears to have arisen in this analysis in that the nucleophile binding constants do not appear to increase, but rather decrease with increasing alkyl chain length. This is accompanied by an increase in the second order rate constant with an increase in alkyl chain length for the reaction partitioned into the micellar media. Therefore, although the degree of substrate binding to the micelle increases and results in faster rates of reactions, the degree of nucleophile binding does not. Hydrolysis rate constant in the water pseudophase is constant. The increase on the observed rate constant is due to changes in the local concentration at micellar pseudophase. The result eliciting the decreased ability for larger chain length micelles to bind AHA is unexpected, albeit explainable with some knowledge of the micelle’s physical properties. It is known that degree of counterion binding at the micellar surface decreases as the hydrophobic chain length becomes smaller in size. This phenomenon is due to the higher apparent charge of the cationic head group, thus
Figure 3.7: Plot of observed rate constant vs. pH and log of observed rate constant vs. pH for the hydrolysis of PNPA in the presence of CnPh₃Br = [0.006]; [AHA] = 0.0005 M; [PNPA] = 0.00005 M for C₆ (A), C₁₄ (B), C₁₂ (C).
resulting in a greater electrostatic attraction between it and the oppositely charged counterion. Since the AHA ion nucleophile also exhibits an opposite charge to that of the cationic headgroup, it would experience a greater attraction to the micellar surface of smaller cationic surfactants.

Having acidic properties, the rates at which AHA enables hydrolysis is highly dependent on pH. By employing various buffers, the PNPA hydrolysis reaction in the presence of AHA was carried out as a function of pH. The values of the observed pseudo-first order rate constants for PNPA hydrolysis both in the absence and presence of AHA are presented in Table 3.7. In each case, the alkyl triphenylphosphonium bromide surfactants were present as the micellar media at a fixed concentration.

By comparing the $k_{obs}^{AHA}$ values to the $k_{obs}^{0}$ values, it is apparent that overall, there is a 10-fold increase in the rates of hydrolysis when AHA is included as the nucleophilic species in the system. The employment of AHA as a nucleophile, therefore, is potentially a very effective method in the breakdown of harmful ecotoxic substances.

To acknowledge the effects of the AHA ionization, the following equation can be considered[6]:

$$k_{obs}^{AHA} = k_{obs}^{0} + k_{AHA}^{AHA}[AHA]_{T} \cdot \alpha_{AHA}$$ (6)
TABLE 4.7

<table>
<thead>
<tr>
<th>pH</th>
<th><strong>k_{obs}^0 (s^{-1})</strong></th>
<th><strong>k_{obs}^{HA} (s^{-1})</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>7.9</td>
<td>4.02 0.21</td>
<td>3.63 0.15</td>
</tr>
<tr>
<td>8.4</td>
<td>9.20 0.34</td>
<td>8.43 0.24</td>
</tr>
<tr>
<td>8.7</td>
<td>30.4 1.21 9.66 1.51</td>
<td>18.3 1.07</td>
</tr>
<tr>
<td>9.2</td>
<td>43.2 4.26 37.7 3.07</td>
<td>22.3 2.19</td>
</tr>
<tr>
<td>9.5</td>
<td>- - 43.7 4.63</td>
<td>-</td>
</tr>
<tr>
<td>9.8</td>
<td>- - 45.2 4.67</td>
<td>-</td>
</tr>
</tbody>
</table>

Pseudo-first order rate constants for the hydrolysis of PNPA (0.0005 M) in the presence and absence of AHA.
where \([\text{AHA}]_T\) is the analytical concentration of AHA, and \(\alpha_{\text{AHA}}\) is the fraction of \([\text{AHA}]\) ionized. If \(K_a\) is taken to be the dissociation constant of AHA, the value of \(\alpha_{\text{AHA}}\) will be equal to \(K_a/(K_a + [H^+])\).

By using this relationship, Equation 6 can be rearranged to give Equation 7:

\[
\log(k_{\text{obs}}^{\text{AHA}} - k_{\text{obs}}^a) = \log(k_{\text{HA}}[\text{AHA}]_T + \log\left(\frac{K_a}{K_a + [H^+]}\right))
\]  

(7)

The apparent pK\(_a\) value of the AHA bound to the micellar surface is determined by plotting both the log\((k_{\text{obs}})\) and \(k_{\text{obs}}\) values as a function of pH. Whereas the latter plots will yield a sigmoidal relationship, the log plots will show discontinuities at specific pH values (Fig 3.7). By employing these plots, the pK\(_a\) is determined from the break point in the straight lines and was found to be approximately 8.6. The pK\(_a\) of AHA in aqueous medium is 9.2. It was observed that the pK\(_a\) values of AHA slightly decrease in the presence of alkyltriphenyl phosphonium bromides surfactants, however, the deviation is not considered to be significant. This decrease in pK\(_a\) is due to an enhanced local pH at the cationic surface and an ion-pair interactions.

[C] Bronsted Relationship

The reactions of PNP A with a series of \(\alpha\)-nucleophiles having pK\(_a\) values in the range of 6.5-11.8. have been studied at 27\(^\circ\)C. In order to investigate the effect of the basicity of \(\alpha\)-nucleophiles on the reactivity for the present hydrolysis, Bronsted-type plot has been constructed. The first order and second order rate constants for these reactions are given in Table 3.8. A Bronsted-type plot of log \(k_2\) vs. pK\(_a\) of the nucleophile is displayed in Figure 3.8. \(\beta_{\text{nuc}}\) value of 0.60 is
obtained. This indicates that within a given reaction series, basicity is of great importance in nucleophilic reactivity towards PNPA.

In Bronsted equation log $k_2$ represents nucleophilic attack rather than proton-transfer reaction (Equation 8). This correlation has been widely employed in studies of nucleophilic reactions. The usual and, up to now, probably the only way by which the pK$_a$ of the nucleophile was varied for the purpose of construction of Bronsted type plots was by varying

$$\log k_2 = \beta_{\text{nuc}} pK_a + C$$  \hspace{1cm} (8)

substituents on the nucleophile at a position remote from the attacking atom. Figure 3.8 shows Bronsted plot (plot of log$k_2$ vs. pK$_a$) for the reaction of p-nitrophenyl acetate with hydroxamate ions. The second order rate constant $k_2$ can be determined by equation 9.

$$k_2 = \frac{k_{\text{obs.}}}{[HA]_T \cdot \alpha_{HA}}$$  \hspace{1cm} (9)

where $[HA]_T$ is the analytical concentration of hydroxamic acid, and $\alpha_{HA}$ is the fraction of $[HA]_T$ ionized. \{ $\alpha_{HA} = \frac{K_a}{K_a + [H^+]}$ \}

The slope of the plot ($\beta_{\text{nuc}}$) is generally believed to the measure of the bond formation and the extent of nucleophilicity(Figure 3.8).

has been long known that the reactivity of the nucleophiles depends upon the nature of electrophilic center and the nature of leaving group. Bruice et al.$^{24}$ reported that the nucleophiles with higher value of $\beta_{\text{nuc}}$ are more reactive than the nucleophile of low $\beta_{\text{nuc}}$ values. They documented significant rate acceleration effect of the peroxide ions for the reaction of toluene sulfonate.
\(\alpha\) - Effect in the ester cleavages by various nucleophiles in micelles

**TABLE 3.8**

First and Second-orders rate constants for the reaction of \(p\)-nitrophenyl acetate with some \(\alpha\)- nucleophiles at 27 °C.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Nucleophile</th>
<th>(pK_a)</th>
<th>(10^3 k_{obs}$/s$</th>
<th>(k_2) M$^{-1}$s$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Salicylhydroxamic acid (SHA)</td>
<td>7.2</td>
<td>8.82</td>
<td>10.6</td>
</tr>
<tr>
<td>2.</td>
<td>Benzohydroxamic acid (BHA)</td>
<td>8.6</td>
<td>9.32</td>
<td>56.1</td>
</tr>
<tr>
<td>3.</td>
<td>Acetohydroxamic acid (AHA)</td>
<td>9.2</td>
<td>4.81</td>
<td>49.2</td>
</tr>
<tr>
<td>4.</td>
<td>(N)-methyl2-chlorobenzohydroxamic acid (MCBHA)</td>
<td>7.65</td>
<td>3.02</td>
<td>4.71</td>
</tr>
<tr>
<td>5.</td>
<td>(N)-Phenylbenzohydroxamic acid (b) (PBHA)</td>
<td>8.9</td>
<td>3.88</td>
<td>42.7</td>
</tr>
<tr>
<td>6.</td>
<td>(N)Hydroxysucciniamide (NHS)</td>
<td>6.6</td>
<td>0.16</td>
<td>0.17</td>
</tr>
<tr>
<td>7.</td>
<td>(N)-Hydroxyptalimide (NHP)</td>
<td>6.5</td>
<td>0.72</td>
<td>0.75</td>
</tr>
<tr>
<td>8.</td>
<td>Hydroxylamine (HAH)</td>
<td>5.9</td>
<td>2.79</td>
<td>2.81</td>
</tr>
<tr>
<td>9.</td>
<td>Butane 2,3-dione monoxime (Oxime)</td>
<td>9.3</td>
<td>3.32</td>
<td>86.2</td>
</tr>
<tr>
<td>10.</td>
<td>Acetaldoxime</td>
<td>11.8</td>
<td>0.18</td>
<td>1424.2</td>
</tr>
</tbody>
</table>

\([\text{PNPA}] = 1.0 \times 10^{-4} \text{ M}, \ [\text{HA}] = 1.0 \times 10^{-3} \text{ M}, \ \text{pH} = 8.0\)
Figure 3.8 Bronsted plot for the reaction of p-nitrophenyl acetate with some α-nucleophiles.
3.5 CONCLUSIONS

Reactions occur in an interfacial region, which for ionic micelles, is often identified with the Stern layer, and with dilute surfactant its volume is small relative to that of the total solution. In case of all the surfactants studied, IBA was found to be most reactive, and HOBT least reactive. Like oximates, hydroxamates are strong α-nucleophiles. The order of cleavage by α-nucleophiles ions–cationic surfactant hydrolyzing nucleophile is in the order of C=O > P=O > P=S.

The hydrolysis of PNPA was studied as a model for the hydrolysis of other harmful organophosphorus compounds. The hydrolysis was catalyzed via micellar catalysis using the Cₙ PPh₃Br surfactant series at various concentrations in both the presence and absence of the hydroxamic acid AHA. The Cₙ PPh₃Br series does improve hydrolysis perhaps by stabilizing the PNPA-micelle binding via π-π interactions, the lack of –OH groups in the head group region would eliminate the possibility for hydrogen bonding. The trends in the regression parameters were found for each system and appear to support the expected trends observed in the rate surfactant profiles. The hydrolysis was studied in micellar media to obtain the pKₐ value of AHA, which was found to be approximately 8.6.
REFERENCES

α–Effect in the ester cleavages by various nucleophiles in micelles


