CHAPTER IV

MEDIUM EFFECT ON THE NUCLEOPHILIC SUBSTITUTION REACTIONS OF CARBOXYLIC AND PHOSPHORUS ESTER WITH HYDROXAMATES IONS°

SUMMARY

The pseudo-first order rate constant for the hydrolysis of p-nitrophenyl acetate (PNPA) by benzohydroxamate ion was determined in water ethylene glycol mixtures using cationic micellar solutions of alkylidimethyl and diethyl ethanol ammonium bromides. From the conductivity data of these two surfactants in ethylene glycol, the critical micelle concentration (cmc) the degree of counter ion dissociation, (α) and Gibbs free energy of the micellization, (ΔG°ₘ) have also been determined. Addition of ethylene glycol in the micellar solutions results in an increase in the CMC and in an increase in micellar dissociation degree. The kinetic micellar effects was quantitatively explained by using pseudophase model.

A systematic study for the reaction of p-nitrophenyl diphenyl phosphinate (PNPDP) with acetohydroxamate ions in DMSO-H₂O mixture systems is also initiated.

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CHAPTER IV: MEDIUM EFFECT ON THE NUCLEOPHILIC SUBSTITUTION REACTIONS OF CARBOXYLIC AND PHOSPHORUS ESTERS WITH HYDROXAMATE IONS

4.0 INTRODUCTION

In recent years, there has been an upsurge of interest in studies of solvent effects preferential on reaction kinetics and equilibria. The importance of hydrophobic effects, solvation and solvent structural effects on kinetics of nucleophilic substitution reactions has been emphasized in several recent studies. It has been known that a change of medium can considerably influence the reactivity of homogenous chemical reactions.

In the preceding chapters the hydrolysis of carboxylate and phosphorus esters using hydroxamate ions (α-effect) have been described. Hydroxamate ions possessing nonbonding electron pairs at the position α to the nucleophilic center exhibit enhanced reactivity compared with reference nucleophiles of similar basicity. Among the possible causes of the α-effect, the effect of solvents has been particularly important. Solvent plays an important role in controlling the dynamics of the chemical reactions. Solvent effects refer to all different types of interaction between solvent and solute molecules that is, reactants, transition states and products-hydrogen bonding, ion-dipole, dipole-dipole, etc. DMSO is known to be one of the most useful dipolar aprotic solvents in investigations of reactivity and reaction mechanism.
It has been generally reported that reactions with anionic nucleophiles cause significant rate acceleration, while the ones between neutral molecules passing through a partially charged transition state structure exhibit rate retardation upon solvent change from \( \text{H}_2\text{O} \) to \( \text{DMSO} \).^10-11

Over the last few years, we have developed a research programme investigating the use of novel micellar media for the hydrolysis of carboxylate and phosphorus esters using hydroxamate ions.\(^{12-16}\) Considerable research efforts were focused recently in the synthesis, characterization of several cationic surfactants with a variety of head groups etc. The effect of solvent on reaction rates has been intensively studied\(^{17-21}\). Surprisingly, mechanistic details of hydrolysis of \( p \)-nitrophenyl acetate and the effect of solvents in the presence of novel surfactants like alkanol amine based surfactants have not yet been explored. Alkanol amine surfactants combine the characteristics of the amine and hydroxyl groups in terms of reactivity patterns and make them very versatile intermediate for industrial applications. Recently, Palepu et al.\(^{22}\) studied thermodynamic and related properties of alkyl cationic surfactants based on dimethyl and diethyl ethanol amines.

Currently, there is a lot of interest in the nature of micellization behaviour of surfactants in binary mixtures of organic solvents such as formamide, \( N, N\) -dimethyl formamide, dimethyl sulfoxide, dimethyl acetamide, \( N\)-methyl acetamide, glycerol and ethylene glycol (EG).\(^{23-46}\) All of these solvents have high dielectric constants and considerable hydrogen bonding ability.\(^{30}\) Evans et al.\(^{47}\) have suggested that the hydrogen bond ability is a prerequisite for micellization process. Among these solvents one of the most widely studied is ethylene glycol, since it has many characteristics similar to those of water.\(^{34,48-50}\) The molecule is small and can form hydrogen bond network. It also possesses a high cohesive energy and a fairly high dielectric constant. With use of mixture of
H₂O and EG as solvents, the aggregation behaviour of some surfactants including Aerosol OT, cetylpyridinium bromide, cetyltrimethylammonium bromide, tetradecyltrimethylammonium bromide, sodium dodecyl sulfate, and octyl and nonyl phenyl polyoxyethylene ethers have been investigated.

4.1 REVIEW OF THE EARLIER WORK

Many results have been published in the literature showing typical behaviours of solvents on the α-effect. Various proposals have been advanced to account for the α-effect phenomenon, including destabilization of the ground state through electronic repulsion between non-bonding electron pairs, stabilization of product and stabilization of transition state. However, up to this time there is no general agreement as to which factors are predominant as the origins of this phenomenon.

Solvent effect is a subject of wider study to account the α-effect of the nucleophiles in different solvent systems. The first systematic study of the effect of solvent on the α-effect was reported by Terrier et al. for the reaction of p-nitrophenyl acetate (PNPA) with α,α,α-trifluoro acetophenone oximate (TFA-Ox⁻) (I) (an α-nucleophile) and p-chlorophenoxy (p-ClPhO⁻, as a corresponding normal nucleophile) in DMSO-H₂O mixtures of varying composition. The reactivity of the α-nucleophile, TFA-Ox⁻ is enhanced considerably relative to that of the similarly basic p-ClPhO⁻ on addition of DMSO to the medium.

Buncel and Um et al. reported solvent effects in MeCN-H₂O upto 80 mol % (v/v) for the reactions of PNPA with benzohydroxamate (BHA⁻), p-methylbenzohydroxamate (MBHA⁻) and p-methyl-N-methylbenzohydroxamate
Medium Effect on the reactions of carboxylic and phosphorus esters with hydroxamate ions

(M₂BHA⁻) ions. The α-effect showed a decreasing trend with increasing mol % solvent in case of BHA⁻ and MBHA⁻ whereas, M₂BHA⁻ reaction increased with increasing MeCN composition. Buncel and his group has also extensively studied the reaction of PNPA with butane-2, 3-dione monoximate anion (pKₐ=9.29) as the α-nucleophile and p-chlorophenoxide ion (pKₐ= 9.35) as the normal nucleophile.

Increased nucleophilic reactivity of small (hard) anions in DMSO with respect to water was first highlighted by Parker. Some years ago, Buncel et al. performed nucleophilic substitution reactions of p-nitrophenyl acetate with butane-2,3-dione monoximate (Ox⁻, α-nucleophile ) and p-chlorophenoxide ( p-ClPhO⁻, the reference nucleophile ) in dimethyl sulfoxide (DMSO)-H₂O mixtures at 25 °C. The α-effect is markedly dependent on the solvent, increasing from 100 in water to 290 in 50 mol % DMSO.

Moss et al. have found that for the reactions of PNPA with o-iodosobenzoate as the α-effect nucleophile and p-ClPhO⁻ as reference nucleophile, i.e., the α-effect decreased steadily as the mol % DMSO was increased.

Despite several reports on the solvophobic effects of EG in micellization process of cationic, anionic, nonionic and zwitterionic surfactants, no attempt has been made to predict the thermodynamic properties of micellization of alkanol amine surfactants. The presence of both amine and hydroxyl groups in alkanol amines makes them versatile intermediates for countless industrial applications, particularly in textile, pharmaceutical and household product industries. Nagarajan et al. explored the solution behavior of alkyl (C₁₂, C₁₄, C₁₆)
pyridinium bromides and alkyl \( (\text{C}_{10}, \text{C}_{12}, \text{C}_{14}, \text{C}_{16}) \) trimethylammonium bromide in ethylene glycol.

Moya and co-workers\(^{22-27}\) have reported the kinetic studies of spontaneous hydrolysis of phenyl chloroformate and various \( S_N2 \) reactions in water-ethylene glycol mixtures in the presence of cationic, zwitterionic, nonionic, and anionic surfactants\(^2\). Similarly, Ionescu et al\(^{71-72}\) reported the effect of solvent on micellization of CTAB and described the application of the pseudophase ion exchange model to a micellar-catalyzed hydrolysis of \( p \)-nitrophenyl diphenyl phosphate in water-glycerol solutions. In the case of bimolecular reactions, the concentration or depletion of reactants in the interfacial region have two major effects on the reaction rates, i.e. micellar concentration effects and medium effects on the reaction rates. This issue needs substantiation, and we have investigated the nucleophilic reactivity of hydroxamate ions in water-ethylene glycol using novel cationic micellar media for ester hydrolysis.

4.2 PRESENT INVESTIGATION

This chapter is divided into two sections:


[B] Nucleophilic Substitution Reaction of \( p \)-Nitophenyl Diphenyl Phosphinate with Acetohydroxamate Ion in the Presence of DMSO.

In Section A, the micellar behavior of alkyl \( (R = \text{C}_{12}\text{H}_{25}, \text{C}_{14}\text{H}_{29}, \text{C}_{16}\text{H}_{33}) \), dimethyl \( (\text{R}'=\text{CH}_3),(\text{CDMEAB}) \) (I) and diethyl \( (\text{R}'=\text{C}_2\text{H}_5),(\text{CDEEAB}) \) ethanolammonium bromides (II) in water-ethylene glycol mixtures (0-50 % v/v)
have been investigated. Kinetics of the nucleophilic bimolecular reaction of the $p$-nitrophenyl acetate with hydroxamate ion has also been studied to explore the solvation effects on micellar catalyzed reaction. This reaction has a well-known mechanism and has been studied in different aqueous micellar solutions$^{11-16}$.

To investigate the dependent rate effects on the structure of micelles the kinetics has been studied with changing the head and tail groups of surfactants (Scheme 4.1).

\[
\begin{align*}
\text{H}_2\text{C} & \text{C} \rightarrow \text{O} + \text{Nu'} \xrightarrow{\text{Surfactant}} \text{H}_2\text{C} \rightarrow \text{O} + \text{Nu} \rightarrow \\
\text{H}_2\text{C} & \text{C} \rightarrow \text{O} + \text{Bu} \rightarrow \\
\text{H}_2\text{C} & \text{C} \rightarrow \text{O} + \text{Bu} \rightarrow \\
\text{H}_2\text{C} & \text{C} \rightarrow \text{O} + \text{Bu} \rightarrow \\
\text{H}_2\text{C} & \text{C} \rightarrow \text{O} + \text{Bu} \rightarrow
\end{align*}
\]

$\text{EG} =$ Ethylene Glycol

\[
\text{benzohydroxamate ion}
\]

**Surfactants**

\[
\begin{align*}
\text{Br} & - \\
\text{R} & - \text{N}^+ \rightarrow \text{CH}_3 \\
\text{CH}_3 & - \text{OH}
\end{align*}
\]

$R = C_{10}H_{21}, C_{12}H_{25}, C_{14}H_{29}, C_{16}H_{33}$.

\[
\begin{align*}
\text{Br} & - \\
\text{R} & - \text{N}^+ \rightarrow \text{C}_2\text{H}_5 \\
\text{C}_2\text{H}_5 & - \text{OH}
\end{align*}
\]

$R = C_{12}H_{25}, C_{14}H_{29}, C_{16}H_{33}$.

**Scheme 4.1**

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In Section B, in order to obtain more conclusive information on the role of solvent, a systematic study for the reaction of \( p \)-nitrophenyldiphenyl phosphinate (PNPDP) with acetohydroxamate ions in DMSO-H\(_2\)O mixture systems have been investigated. (Scheme 4.2).

\[
\begin{align*}
\text{C}_6\text{H}_{5}\text{P} & \quad \text{O} \quad \text{C}_6\text{H}_{5} \quad \text{C}_6\text{H}_{5} \quad \text{NC}_2 \quad \text{Nu}^- \quad \text{DMSO} \\
\text{C}_6\text{H}_{5}\text{P} & \quad \text{O} \quad \text{C}_6\text{H}_{5} \quad \text{C}_6\text{H}_{5} \quad \text{NC}_2 \quad \text{Nu}^- \\
\text{p-Nitrophenyl diphenyl phosphinate} & \\
\text{DMSO} & = (\text{CH}_3)_2\text{SO} \\
\text{Nu}^- & = \text{C}_6\text{H}_3\text{C} = \text{N} - \text{H} & \text{(Acetohydroxamate ion)}
\end{align*}
\]

\textbf{Scheme 4.2}

\textbf{4.3 EXPERIMENTAL}

\textbf{Materials}

Benzohydroxamic acid was prepared by literature method\(^{74-75}\). \( p \)-Nitrophenyl acetate (PNPA) was obtained from SD fine chemicals. \( p \)-Nitrophenyl diphenyl phosphinate (PNPDP) was prepared at Defence Research Development Establishment, Gwalior. EG and DMSO were procured from Qualigens. All the surfactants were obtained from the laboratory of Prof. R. M. Palepu, St. Francis
Xavier University, Canada. Their cmc's in the aqueous solutions being in agreement with literature data. The purity of these surfactants was checked employing conductometric titration of bromide ion with standard silver nitrate solution. In all cases the surfactants were found to be > 99.5 % pure.

**Kinetics**

All of the reactions were followed at 27°C ± 0.2°C with a UV 2-300 Unicam spectrophotometer equipped with Techné circulator (C-85A) thermostated cell holder and Cary 50 Varian UV-vis spectrophotometer. The rate of nucleophilic reaction with PNPA and PNPDPA were determined by following the increase in absorption of p-nitrophenoxide anion (400 nm). All of the kinetic experiments were performed at an ionic strength of 0.1 M (with KCl). Phosphate buffer was employed to control the pH of the media. All reactions were conducted under pseudo-first-order conditions. For all of the kinetic runs, the absorbance/time result fit very well to the first-order rate equation

\[
\ln (A_o - A_t) = \ln (A_o - A_0) - kt
\]

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. The breakdown of PNPA was confirmed by the appearance of peak at 400 nm, when nucleophiles were added to the reaction medium. The absorption spectra exhibit an increase in absorbance at 400 nm with the formation of p-nitrophenoxide ion during the course of reaction as shown in Figures 4.1 and 4.2. The pKₐ values of hydroxamic acids were determined pHmetrically using Systronics (Type-335) pH meter.
Figure 4.1: Repeat scans every one minute showing the increasing absorbance at 400 nm. [BHA] = 1.0 mM, [PNPA] = 0.1 mM, [CDMEAB] = 5 mM, [EG] = 10 %, pH = 8.0

Figure 4.2: Repeat scans every one minute showing the increasing absorbance at 400 nm. [BHA] = 1.0 mM, [PNPA] = 0.1 mM, [CDMEAB] = 5 mM, [EG] = 10 %, pH = 8.0
Conductivity measurements

The conductivity was measured with a Systronics (Type-304) direct reading digital conductivity meter. The conductivity cell was calibrated with KCl solutions in appropriate concentration range.

4.4 RESULTS AND DISCUSSION


4.41 Determination of Micellar Parameters

The critical micelle concentration, \( cmc \) of all the surfactants under conditions has been determined from the plots of specific conductivity, \( \kappa \), versus surfactant concentration (Figures 4.3-4.4). Subsequently, the degree of ionization is calculated from the ratio of the slope of \( \kappa \) versus [surfactant] above and below the \( cmc \). The \( cmc \) values of \( C_{12}DMEAB \), \( C_{16}DMEAB \) and \( C_{16}DEEAB \) for various water-EG solutions are listed in Table 4.1. The \( cmc \) values obtained for these surfactants in aqueous solutions are in close agreement with the literature data. The micellar ionization degree, \( \alpha \), of the cationic surfactants in water-EG micellar solutions are also listed in Table 4.1. For all the surfactant studied an increase in the amount of EG present in the solution results in an increase in the critical micelle concentration and an increase in the degree of ionization.

The dependence of \( cmc \) upon the temperature was used to evaluate the standard thermodynamic parameters of micellization for \( C_{16}PPh_3Br \)-solvent systems. The change in the \( cmc \) value with temperature is generally analyzed in
terms of the phase separation or equilibrium model for micelle formation. The micellization takes place where the energy as result of association of hydrocarbon chain of the monomer is sufficient to overcome the electrical repulsion between the ionic head group and decrease in entropy accompanying the aggregation. Therefore, in the study the increase in temperature results in an increase in cmc values because the kinetic energy of monomer has been raised. The latter is preferable for the ionic surfactants since the effect of counter ion can be explicitly considered. According to this model, the equilibrium between monomers and micelles can be represented by eq.2

\[ nS^+ + (n-p)Br^- \rightleftharpoons M^{+P} \]  (2)

Where \( S^+ \) represents the cationic surfactants and \( M \) represents the micelle. The standard free energy of micelle formation per monomer unit is

\[ \Delta G^0_m/RT = -1/n \ln m^{+P} + C_s^+ + (1-P/n) \ln C_{Br} \]  (3)

Since \( n \) is larger (50-100) the \( C_m^{+P} \) is smaller and in sensitive to larger error in the estimated \( C_m^{+P} \), both \( C_s^+ \) and \( C_{Br}^- \) can be replaced by the cmc (expressed in mole fraction). Equation (3) gives

\[ \Delta G^0_m = (2 - \alpha) RT \ln X_{cmc} \]  (4)

where \( R \) is the gas constant, \( T \) is the absolute temperature, \( \alpha \) is the degree of ionization and \( X_{cmc} \) is the mole fraction of the surfactant at the cmc.

The Gibbs free energy of micellization, \( \Delta G^0_m \) for all the surfactants in the presence and absence of EG are listed in Table 4.1. For all the surfactant studied,
an increase in the amount of EG present in the solution results in an increase in the critical micelle concentration and an increase in the degree of dissociation. The observed values of $\Delta G^o_m$ show that the micellization process is less spontaneous in the higher volume percentage of EG in the mixture.

The influence of EG on the thermodynamic parameters can be explained by considering the following solvent dependent contributions to the $\Delta G^o_m$: (a) the surfactant tail transfer free energy, which accounts for the solvophobic effect (b) the aggregate core-solvent interfacial free energy (c) the electrostatic head group interaction free energy. The magnitude of the surfactant tail transfer free energy is considerably smaller in ethylene glycol than in water, and it is the dominant contribution responsible for the increase in the cmc of ionic, nonionic, and zwitterionic surfactant as the amount of EG in the mixture increases. The aggregate-core solvent interfacial free energy is smaller in ethylene glycol solutions than in water because of the considerably smaller ethylene glycol hydrocarbon interfacial tension compared to the water-hydrocarbon interfacial tension. In regard to the head group interaction free energy, the importance of this contribution follows the trend ionic > zwitterionic > nonionic.

The ethylene glycol is acting as a cosolvent and structure breaking solute in the present study. Structure breaking solutes are known to decrease the hydrophobic effect thereby increasing the cmc values. The effect of EG on the micellization process was calculated through the Gibbs free energy of transfer, $\Delta G^o_{\text{trans}}$, which can be written as:

$$\Delta G^o_{\text{trans}} = (\Delta G^o_m)_{\text{water-EG}} - (\Delta G^o_m)_{\text{water}}$$
Table 4.1

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>CA MDEAB</th>
<th>CA MDEAB</th>
<th>CA MDEAB</th>
<th>CA MDEAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.1</td>
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<td>14.1</td>
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<td>14.5</td>
<td>14.5</td>
<td>14.5</td>
<td>14.5</td>
</tr>
</tbody>
</table>

Note: Literature values are given in the parentheses at 298 K.

Critical micelle concentrations, cmc; Micellar Lociation Degree, c, and Gibbs Free Energy of Micellization, AG°m

TABLE 4.1
Medium effect on the reactions of carboxylic and phosphorus esters with hydroxamate ions

Figure 4.3 Plots of specific conductance versus [surfactant] in aqueous and water-EG media for the determination cmc of C₁₆DMEAB.

Figure 4.4. Plots of specific conductance versus [surfactant] in aqueous and water-EG media for the determination cmc of C₁₆DEEAB.
Medium Effect on the reactions of carboxylic and phosphorus esters with hydroxamate ions

4.42 Kinetic Studies in Water-Ethylene Glycol Micellar media.

Pseudo-first order rate constants ($k_{obs}$) for the nucleophilic reaction of $p$-nitrophenyl acetate with benzohydroxamate ion (Scheme 4.3) in water-ethylene glycol micellar solution of cetyltrimethyl ammonium bromide and cetyltrimethyl ammonium bromide have been summarized in Table 4.2. Typical profiles for the pseudo-first order rate constants, as a function of the concentration of $C_{16}$DMEAB and $C_{16}$DEEAB for the hydrolysis of PNPA at $2^\circ C$ using benzohydroxamate ion in different ethylene glycol solutions (0-50% v/v) are depicted in Figures 4.5 and 4.6. The presence of EG exerts rate retardation effect for the reactions in the micellar medium. The effects depend on the transfer of the substrate from water to micelles, the reaction mechanism, and properties of the interfacial region.

The $k_{obs}$ of the nucleophilic substitution reactions obtained are characteristic micellar catalyzed reactions. The hydrophobic interaction of the substrate and the electrostatic attraction of the anionic nucleophile into the micelle are the two factors that governed the rate enhancement. The hydrolytic reactivity of the PNPA is expected to occur at the micellar interfacial region.

The $k_{obs}$ values increases upon increasing surfactant concentrations. This dependence can be explained by considering that an increase in the surfactant concentration results in further incorporation of PNPA into the micelles, where the benzohydroxamate ions concentration is higher than that in the bulk phase since cationic micelles bind anionic nucleophiles. When the PNPA molecules fully bound to the micelles, the process occurs wholly in the micellar pseudophase, and the observed rate constants reaches its maximum value.
### Table 4.2

**Kinetic Rate Data for the Nucleophilic Substitution Reaction of p-Nitrophenyl Acetate with Benzohydroxamate Ion in Alkaline Amino-based Cationic Micellar Media.**

<table>
<thead>
<tr>
<th>Condition: pH 7.9, [p-NPA] = 1.0 x 10^{-3} M, [BHA] = 1.0 x 10^{-3} M, [KCl] = 0.1 M</th>
<th>Surfactant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SDBAB</td>
</tr>
<tr>
<td></td>
<td>0% EG</td>
</tr>
<tr>
<td>Condition</td>
<td></td>
</tr>
<tr>
<td>pH 7.9</td>
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</tr>
<tr>
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<td>28.9</td>
</tr>
</tbody>
</table>

**Conditions:** pH 7.9, [p-NPA] = 1.0 x 10^{-3} M, [BHA] = 1.0 x 10^{-3} M, [KCl] = 0.1 M.
Figure 4.5  Plots of $k_{obs}$ vs. [C$_{16}$DMEAB] for the hydrolysis of PNPA (1.0 x $10^{-4}$ M) by BHA, at pH 7.9, in the presence of various compositions of water-EG co-solvent: 0% (v/v) EG ($\bullet$); 10%(v/v) EG ($\square$); 30% (v/v) EG (▲) and 50% (v/v) EG (Δ).

Figure 4.6  Plots of $k_{obs}$ vs. [C$_{16}$DEEAB] for the hydrolysis of PNPA (1.0 x $10^{-4}$ M) by BHA, at pH 7.9, in the presence of various compositions of water-EG cosolvent: 0% (v/v) EG ($\bullet$); 10%(v/v) EG (□); 30% (v/v) EG (▲) and 50% (v/v) EG (Δ).
For a given surfactant concentration, the observed rate constant decreases as the volume percent of EG present in the mixture increases. These variations in $k_{\text{obs}}$ upon changing (v/v) % EG are a reflection of the thermodynamic and structural changes produced in the micellar solutions by the presence of different amounts of the organic solvent. If the pseudophase kinetic models are considered, the observed rate of the reaction is assumed to be equal to the sum of the reaction occurring in the bulk phase (water and water-EG mixtures), and in the micellar pseudophase.

According to Moya et al\textsuperscript{23-27}, the binding of the substrate, is small compared to the aqueous micellar system for all of the water-EG micellar reaction media. Besides, an increase in the amount of EG present in the bulk phase results in a decrease in the interaction of PNPA and BHA for all the surfactants investigated. Change in binding of PNPA will depend on the changes in the characteristics of the two pseudophases in which PNPA and benzohydroxamate ion distributes. PNPA molecules are expected to be located at micellar surface. The small binding constants in the presence of EG could be explained by considering the polarities of the interfacial region. With regard to the effect of the addition of EG to the mixture, the interfacial region becomes more polar when the amount of EG present in the mixture increases, although the greater change have been observed in 35 to 50% (v/v) EG.

It is noted that the $k_{\text{obs}}$ values for the hydrolysis of PNPA is accelerated at above the cmc of the surfactants in the aqueous and water-EG mixture media. This is due to the micellar catalyzed nucleophilic reaction. However, it is likely that the extent of attack of benzohydroxamate ion at the carbon (C=O) is influenced by a number of factors apart from lipophilicity, including the nucleophilicity of $\alpha$-effect nucleophile, the aggregate size of the micelle and polarity of the interfacial region.
4.43 Effects of Head and Tail Groups on \( k_{\text{obs}} \) Values in Aqueous Micellar Media:

Table 4.3 summarizes the \( k_{\text{obs}} \) values for the nucleophilic reaction of \( p \)-nitrophenyl acetate with benzohydroxamate ion in aqueous and water-EG (0-30% v/v) micellar solutions of different alkanol amine-based cationic surfactant (C\(_{10}\)-C\(_{16}\)). The argument that the variation of \( k_{\text{obs}} \) values of the reactions depends on the micellar structure and medium effect can be further supported from the rate-surfactant profiles with varying hydrophobic tail length. The \( k_{\text{obs}} \) values for the reaction shows drastic change around the critical micelle concentration of the surfactants in the aqueous and water-EG micellar media. In this regards, the comparison of the \( k_{\text{obs}} \) values with decreasing hydrophobic tail will be highly informative. The hydrolytic rate of PNPA in C\(_{16}\)DMEAB and C\(_{16}\)DEEAB micelles are 17.8 x 10\(^3\)/s\(^{-1}\) and 24.8 x 10\(^3\)/s\(^{-1}\) at the surfactant concentration 0.9 x 10\(^{-3}\) M, i.e. at \( \sim \text{cmc} \)'s of both the surfactants. Similarly the \( k_{\text{obs}} \) in the tetradecyl dimethyl and diethyl ethanolammonium bromides (C\(_{14}\)H\(_{29}\)) shows high reactivity in the range of \( \sim 3 \times 10^{-3} \) M. This behavior is due to the micellar driving rate effects on the hydrolytic reactions.

For a given ionic head group, the critical packing parameter of the surfactants decreased and the critical micelle concentration increased. The similar observation can also be compared in the presence of EG. If we compare the reaction rate at the \( \text{cmc} \)'s of the surfactants in aqueous and water-EG micellar solution, the depletion of the rate has been observed with increasing amount of EG. For example, the \( k_{\text{obs}} \) value of PNPA hydrolysis is 17.8 x 10\(^3\)/s\(^{-1}\) at 0.9 x 10\(^{-3}\) M \( (\sim \text{cmc}) \) of C\(_{16}\)DMEAB in aqueous micellar solution and 5.33 x 10\(^3\)/s\(^{-1}\) at 5.0 x 10\(^{-3}\) M \( (\sim \text{cmc}) \) in 50% EG. This effect is due to medium effect of the reaction rate and the structural variation of the micelles.
The influence of the $k_{obs}$ values for the nucleophilic bimolecular reactions can be rationalized by considering the micellar parameters and the reagent incorporations into the micelles. The rate constants in a variety of association colloids are slightly higher than in water and increase modestly with increasing size of quaternary ammonium head group$^{44}$. The differential reactivity in the micellar media involves variation in the surfactant head and tail groups and changes in the interfacial region. Analysis of kinetic data indicates that the alkylidithionyl ethanolammonium bromide show higher reactivity over the reaction in the presence of alkyltrimethyl ethanolammonium bromide under the identical conditions. Comparison of $k_{obs}$ values at [surfactant] = 1.8 x $10^{-3}$ M, it is evident that reactivity pattern are in the order of RDEEAB>RDMEAB with the rate constants, $k_{obs}$, $R = C_{16}H_{33}, 31.2 \times 10^{3}/s^{-1}$, $R = C_{14}H_{29}, 12.1 \times 10^{3}/s^{-1}$, $R = C_{12}H_{25}, 7.22 \times 10^{3}/s^{-1}$ for the RDMEAB micelles and $R = C_{16}H_{33}, 40.1x 10^{3}/s^{-1}$, $R = C_{14}H_{29}, 24.5 \times 10^{3}/s^{-1}$, $R = C_{12}H_{25}, 7.25 \times 10^{3}/s^{-1}$, respectively.

The increase of $k_{obs}$ values with increasing alkyl chain lengths of the surfactants, i.e., with increasing aggregation number of micelle mainly due to the increase in the electrical surface potential of the micelle and partially due to an increase of hydrophobicity of the palisade layer of micelle.

This report supports our results significantly. Similar trends are expected in the aqueous- EG mixtures for these surfactants with lower values for aggregation number.
TABLE 4.3

Kinetic Rate Data for the Nucleophilic Substitution Reaction of p-Nitrophenyl Acetate with Benzoh~ammatc Ions in aqueous and water-EG micellar solutions of Alkanol Amine-Based Cationic surfactants at 300 °K.

<table>
<thead>
<tr>
<th>Conditions: pH 7.9, , [PNPA] = 1.0 x 10^-4 M, [BHA] = 0.1 M</th>
<th>K, 10^-4</th>
<th>1.0</th>
<th>0.1</th>
<th>0.01</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>128</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30%</td>
<td>4.32</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>3.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td>2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>120%</td>
<td>2.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150%</td>
<td>2.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>180%</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>210%</td>
<td>1.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>240%</td>
<td>1.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>270%</td>
<td>1.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>300%</td>
<td>1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*R = CH3*: R = CH3, R = C2H5, R = C3H7, R = C4H9, R = C5H11, R = C6H13, R = C7H15, R = C8H17, R = C9H19, R = C10H21.
4.44 Application of the Pseudophase model:

The results presented in Table 4.4 allow us to study the influence of the nature of the micelles for the reaction of PNPA with varying composition of ethylene glycol. The micellar binding constants of the PNPA and BHA in the C_{16}DMEAB and C_{16}DEEAB micelles provides the conclusive information on the reactivity patterns. This association constant of PNPA is obtained by fitting data in micellar systems with the value of $K_m^{PNPA} = 150 \text{ M}^{-1}$ for the C_{16}DMEAB and $190 \text{ M}^{-1}$ for the C_{16}DEEAB micellar systems in the absence of EG. The values of distribution constants of the BHA ($K_m^{HA}$) decrease with increasing %EG (v/v) in the reaction medium. Taking into account these micellar parameters, the changes in the polarity of the interfacial region and aggregation number of the micelles are the key factor for the decrease in $k_{obs}$ values in the presence of EG. The equation of pseudophase model has already been discussed in Chapter-II (Section 2.44).

The medium effect exerted by micelles on the nucleophilic hydrolysis of $p$-nitrophenyl acetate can be due to various factors. Among them, the transfer of PNPA from water-EG bulk phase to the micelles, electrostatic binding of the nucleophile (BHA), and the polarity of the reaction medium perform major contributions. The second order rate constants at the micellar interface for both micellar systems (C_{16}DMEAB and C_{16}DEEAB) decrease with increasing amount of EG. The variation in the quotient $k_2^w / k_2^m$ varies from 30 (0 % EG) to 150 (50% EG) for C_{16}DMEAB micelles and from 40 (0% EG) to 250 for C_{16}DEEAB. This fact confirms the variation in the polarity of the medium with the increase of the percentage of EG. For the present reaction system the binding constant of BHA decreases with increasing amount of EG, indicating the reaction involved in the bulk water-EG phase rather than micellar pseudophase. This result also supports the decrease in second order rate constants in C_{16}DMEAB and
C_{16}DEEAB micellar systems with increasing %EG. Rate constants of nucleophilic hydrolysis decrease upon addition of organic solvent to water. This can be explained taking into account that the addition of an organic solvent diminishes the water content and decrease the polarity of the reaction medium.

The rate effects in colloidal assemblies are sensitive to the length of hydrocarbon tail, the nature of cationic head group, counterion, and the head group bulk, giving information about the structural variation of the submicroscopic reaction environments. A decrease in polarity results in a large destabilization of the polar transition state with respect to the initial state, thus retarding the reaction. The micellar incorporation of the substrate, nucleophile or the transition state form during the reaction causes the catalytic effects on the reaction. The results obtained from the present study, strongly support the effects of the structural variation on the rate of the hydrolytic reactions.

The hydroxamate ion concentration in the vicinity of the micellar surface is expected to increase with increase in the aggregation number. Palepu et al.\textsuperscript{23} investigated the aggregation behavior of the RDMEAB and RDEEAB surfactants with varying alkyl chain length. They documented values of aggregation number C_{12}DMEAB = 42, C_{14}DMEAB = 44, C_{16}DMEAB = 45, C_{12}DEEAB = 38, C_{14}DEEAB = 41 and C_{16}DEEAB = 43 within the ± 2 units.
TABLE 4.4  
Kinetic parameters obtained by applying pseudophase model for the nucleophilic reaction of PNP with benzohydroxamate ions in the presence of C<sub>16</sub>DMEAB and C<sub>16</sub>DEEAB cationic micelles.

<table>
<thead>
<tr>
<th>C&lt;sub&gt;s&lt;/sub&gt;DMEAB</th>
<th>C&lt;sub&gt;s&lt;/sub&gt;DEEAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>v(v)</td>
<td>0% EG</td>
</tr>
<tr>
<td>k&lt;sub&gt;in&lt;/sub&gt;/M&lt;sup&gt;-1&lt;/sup&gt;s&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>43.4</td>
</tr>
<tr>
<td>KmPNPA/M&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>150</td>
</tr>
<tr>
<td>KmBHA/M&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>70</td>
</tr>
<tr>
<td>k&lt;sub&gt;2&lt;/sub&gt;/M&lt;sup&gt;-1&lt;/sup&gt;s&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>1.367</td>
</tr>
</tbody>
</table>
| Conditions: pH 7.9, 0.1 M KCl, [PNPA] ~ 1.0 x 10<sup>-4</sup> M, [BHA] ~ 1.0 x 10<sup>-3</sup> M, [C<sub>16</sub>DMEAB] = [C<sub>16</sub>DEEAB] = 0.1 M

K<sub>in</sub> kinetic parameters obtained by applying pseudophase model for the nucleophilic reaction of PNP with benzohydroxamate ions in the presence of C<sub>16</sub>DMEAB and C<sub>16</sub>DEEAB cationic micelles.
Nucleophilic substitution reactions of \( p \)-nitrophenyl diphenyl phosphinate with acetohydroxamic acid in DMSO-H\(_2\)O mixtures of varying compositions (10-80 % v/v) at 27°C have been studied. As shown in Figure-4.5, the pseudo-first rate decreases up to 10 % and then increases. This decrease in rate constants persists into higher DMSO contents for the less reactive substrates. The rate constant is more significant in the DMSO rich region: the second order rate constant increases from 10.5 M\(^{-1}\)s\(^{-1}\) to 2779.0 M\(^{-1}\)s\(^{-1}\) as the medium changes from pure water to 80 % (v/v) DMSO, respectively.

Since anionic nucleophiles would be strongly desolvated in dipolar aprotic solvent, one might expect significant rate acceleration for the reactions with anionic nucleophiles upon addition of these solvents.

The magnitude of the \( \alpha \)-effect (\( k_{\text{AHA}}/k_{\text{ClPhO}} \)) increased upon addition of DMSO in the reaction medium up to 50 % (v/v) DMSO and then decreased beyond that point, resulting in a bell shaped dependence on solvent composition (Table-4.5). Bell shaped \( \alpha \)-effect profile with a maximum \( \alpha \)-effect at 50 % (v/v) DMSO was observed for the reactions of \( p \)-nitrophenyl diphenyl phosphinate and \( p \)-nitrophenyl benzene sulfonate, with butane 2-3-dione monoxime and \( p \)-chlorophenoxide and a corresponding normal nucleophile respectively, suggesting that the bell shaped \( \alpha \)-effect trend is general for the reactions of the carbonyl, phosphiny1, and sulfonyl esters with \( \text{Ox}^- \) and \( \text{ClPhO}^- \) in DMSO-H\(_2\)O mixtures.
TABLE 4.5
Summary of rate constants for the Nucleophilic Substitution Reaction of PNpDP with Acetohydroxamate ion in DMSO-

<table>
<thead>
<tr>
<th>% DMSO</th>
<th>AHA</th>
<th>p-CIPhOH</th>
<th>10^(-4)K</th>
<th>10^(-4)k</th>
<th>10^(-9)k</th>
<th>10^(-12)k</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
<td>1.897</td>
<td>4.34</td>
<td>0.035</td>
<td>0.005</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>-</td>
<td>1.92</td>
<td>7.36</td>
<td>0.86</td>
<td>0.236</td>
</tr>
<tr>
<td>10</td>
<td>-</td>
<td>-</td>
<td>1.72</td>
<td>2.46</td>
<td>0.98</td>
<td>0.303</td>
</tr>
<tr>
<td>20</td>
<td>-</td>
<td>-</td>
<td>1.95</td>
<td>4.89</td>
<td>1.08</td>
<td>0.303</td>
</tr>
<tr>
<td>30</td>
<td>-</td>
<td>-</td>
<td>0.92</td>
<td>2.23</td>
<td>0.98</td>
<td>0.282</td>
</tr>
<tr>
<td>40</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>2.36</td>
<td>0.86</td>
<td>0.236</td>
</tr>
<tr>
<td>50</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>2.46</td>
<td>0.98</td>
<td>0.303</td>
</tr>
<tr>
<td>60</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>2.54</td>
<td>0.86</td>
<td>0.236</td>
</tr>
<tr>
<td>70</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>2.63</td>
<td>0.86</td>
<td>0.236</td>
</tr>
<tr>
<td>80</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>2.72</td>
<td>0.86</td>
<td>0.236</td>
</tr>
</tbody>
</table>

a Data taken from ref. 75

H2O mixtures at pH=9.1

Summary of rate constants for the Nucleophilic Substitution Reaction of PNpDP with Acetohydroxamate ion in DMSO.
Figure 4.7 Plot of log $k_2$ vs (v/v) composition DMSO for the reaction of AHA and $p$-ClPhO$^-$ with $p$-nitrophenyl diphenyl phosphinate at 27°C

The present result clearly shows that the effect of solvent on the $\alpha$-effect is significant and supports the argument that a two-point analysis of the $\alpha$-effect could be misleading.

4.5 CONCLUSIONS

Studies on the effect of solvent on the micellization and kinetics of the hydrolytic reactions are of fundamental importance. The presence of ethylene glycol affects the micellization behavior of surfactants. Rate constants of hydrolysis of $p$-nitrophenyl acetate by benzohydroxamate ion in cationic micellar
Medium Effect on the reactions of carboxylic and phosphorus esters with hydroxamate ions

solutions of alkyldimethyl and diethyl ethanol ammonium bromides, decreases upon addition of organic solvents (ethylene glycol) to water because addition of an organic solvent diminishes the water content and decreases the polarity of the reaction medium. A decrease in polarity results in a larger destabilization of the polar transition state with respect to the initial state, thus retarding the reaction. The physicochemical properties of surfactants in different amount of ethylene glycol have also been studied. The reaction is accelerated by these surfactants, as compared to the bulk phase, in any of water-EG micellar solutions. But the observed rate constant decreases as the volume percentage of EG increases. The addition of ethylene glycol to alkyldimethyl and diethyl ethanol ammonium bromides micellar solutions results in an increase in the cmc and in an increase in the micellar ionization degree. The free energy of micellization includes three solvents-dependent contributions. The large magnitude of the cmc originates primarily from the small magnitude of the tail transfer energy from ethylene glycol compared with that of water.
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Medium Effect on the reactions of carboxylic and phosphorus esters with hydroxamate ions

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