Micellar rate effects: assumptions and approximations

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This article is dedicated to Prof. Rita H. Rossi in recognition of her contributions to physical organic chemistry

Abstract

Surfactants with ionic or polar head groups and extended apolar groups form micelles in water with hydrocarbon-like interiors and ionic or polar groups at the surface and bind ionic and nonionic solutes. They act as reaction regions, *i.e*., as pseudophases distinct from the bulk solvent, and can accelerate or inhibit reactions, depending on rate constants and reactant concentrations in the two regions. Theoretical treatments and experimental evidence of reactant partitioning between water and micelles allow estimation of rate constants in the micellar pseudophase for both uni-and bimolecular reactions, provided that they are slower than reactant transfers between water and micelles, but some treatments apply only to dilute electrolyte. Competition between reactive and inert ions inhibits bimolecular ionic reactions and is treated by ion-exchange equations and some local ionic concentrations can be estimated by dediazonization trapping or physical methods. Ionic micelles affect rates of unimolecular and bimolecular water-catalyzed reactions because the reaction region at the micelle-water interface is less polar than water. Zwitterionic micelles have no net charge but they interact with ions, although ion-binding is weaker than with ionic micelles and there are limitations in the use of the theoretical treatments applied to ionic micelles. Micelles can control product composition, but product isolation limits use of surfactants in some reactions

Keywords: Association colloids, micelles, surfactants, kinetics, reaction mechanisms

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1. Introduction

This article covers reactivity in solutions of ionic and zwitterionic micelles in water for simple reactions with known mechanisms, and covers the assumptions and approximations involved in the theoretical kinetic treatments. There is extensive literature summarizing early and recent kinetic work and covering reactivity in micelles and other association colloids, such as microemulsions and vesicles, in water and organic solvents.[1,2] Most work has involved organic reactions, generally in water, mediated by organic micelles which absorb reactants, providing a reaction region distinct from the bulk solvent. The treatments which allow estimation of rate constants in the micelles were developed over many years and make it possible to relate micellar reactivities to reaction mechanism and well-studied kinetic solvent effects. Reverse micelles form in some aprotic solvents containing small amounts of water and have unique properties, but are not considered here. The discussion largely covers self association of chemically simple surfactants, also called amphiphiles or detergents, with an ionic or polar head group and a long alkyl tail, and in water, above a critical micelle concentration, cmc,[3] they form normal micelles which are approximately spherical with the head groups in contact with water. With higher surfactant concentration micelles grow and become rod-like, especially in salt solutions. Micelles in water have a hydrocarbon-like interior, with ionic head groups and counter-ions in the Stern layer at the surface in contact with water and ions are oriented around the micelle in the Gouy-Chapman layer. In the widely used Gruen model of a spherical ionic micelle[4] the radius is similar to the length of the extended surfactant chain and aggregation numbers are usually 70-100, but increase as micelles become rod-like. Physical properties of micelles are considered only to the extent that they affect reaction rates and reverse micelles in apolar organic solvents are not considered.

Early work on association colloids was largely on physical properties, generally in water, and involved interactions with ionic and nonionic solutes and development of treatments of surfactant association, ion binding, effects of ionic charge on micellar growth and the cmc.[3,5] Micellar aggregation numbers, cmc values, and extents of incorporation of counter-ions, which follow the Hofmeister series, were very important in subsequent kinetic work. Surfactants are industrially important, with a wide range of structures,[5] and much of the research on micellar properties has involved readily available and easily purified ionic surfactants, with long alkyl tail groups, $e.g.,$ C_nH_{2n+1} , n = 10-18, and cationic, $e.g.$, R_3N^+, or anionic, $e.g.$, OSO, head groups. The head groups can also be zwitterionic, $e.g.$, $R_2N^+(CH_2)_nSO_3^-$, and R is usually small, $e.g.$, methyl or ethyl, although larger groups such as t-butyl, phenyl or pyridinium, affect micellar

properties and kinetic effects. Nonionic surfactants, typically with long alkyl groups and polar head groups, *e.g.,* polyethylene oxide, are widely used industrially[5] and can inhibit reactions by excluding ionic reagents.[1,2] Other structures include twin-tail surfactants, bolaform surfactants with head groups at each end of the alkyl chain, and gemini surfactants with two surfactant chains linked by a tether group, *e.g.*, $(CH_2)_n$. All are of interest because of their unique properties,[2,6] although single chain micelles are generally considered here. Many surfactants are made from natural oils and some nonchemical names indicate these origins. The surfactant head group can include a reactive group, typically a nucleophile, and examples are cited in the literature.[2]

The reactions discussed here are mechanistically simple and can be followed by uv/vis spectroscopy. The substrates have apolar groups which favor micellar binding and were selected so that mechanisms are the same in micelles and aqueous solvents.

2. Discussion

In early work on chemical reactions acid-base equilibria were examined by using visual indicators and apparent acid dissociation constants were sensitive to ionic micelles. Hartley explained these observations in terms of charge-charge interactions between micelles and ions in solution, with anionic micelles attracting cations and repelling anions, cationic micelles having the opposite behavior, and nonionic micelles having little effect.[1,7] These so-called "Hartley's Rules" played a major role in subsequent development of treatments of micellar effects on reactions, and extensive study of kinetic micellar effects had to wait for instrumental development.

In the 1930's there was increasing study of chemical kinetics and mechanisms, but reactions were generally in moderately concentrated solutions and were typically monitored by chemical analysis, electrolytic conductance or dilatometry. These methods could not be easily applied to reactions in micelles, or other association colloids, where the surfactant is in large excess over the organic substrate to avoid perturbation of the colloidal structure.[1,2] The situation changed with the introduction of low cost uv/visible spectrophotometers so that reactions could be followed with very dilute substrate. Bimolecular reactions were usually followed with one reagent in large excess, giving first-order kinetics, and making nucleophilic reactions of nitrophenyl derivatives very popular. Duynstee and Grunwald[8] showed that reactions in aqueous micelles could be followed kinetically and Menger and Portnoy[9] examined an ester reaction with OH^- in anionic micelles and showed that inhibition follows entry of the ester into the micelles which exclude OH^-. The theoretical treatment of substrate transfer was the basis for quantitative models of micellar rate effects.

Normal aqueous micelles can take up reactants and behave as a reaction region distinct from water. They influence spontaneous unimolecular reactions, for example, S_N1 nucleophilic substitutions, dephosphorylations and decarboxylations, and a wide variety of bimolecular, water

catalyzed, reactions.[1,2] Unimolecular reactions are inhibited or accelerated, depending on the mechanism, for example S_N1 reactions are inhibited and some decarboxylations and dephosphorylations are accelerated, while bimolecular water-catalyzed reactions are typically modestly inhibited, because of the lower polarity and water content of the micellar reaction region. The dependence of first-order rate constants on [surfactant] is typically governed by partitioning of the substrate between water and micelles and fits simple transfer equations.[1,2]

As expected, cationic micelles accelerate reactions of organic substrates with OH^- and other nucleophilic anions,[1,2] this behavior was often described as "micellar catalysis", and anionic micelles inhibited these reactions. There was typically little rate effect at surfactant concentrations below the cmc, but above the cmc both reactants could bind to the micelles, and for accelerated reactions rate constants increased and generally went through maxima due to competition between the ionic reactant and the surfactant counterion.[1,2] Cetyl trimethyl-ammonium bromide, $n\text{-}C_{16}H_{33}N^+(CH_3)_3Br^-$, CTABr, was a widely used cationic surfactant in examination of bimolecular anionic reactions and as its concentration increased Br^- competed with OH^-, or other anionic reactant, giving the rate maxima and the kinetic form was similar for acid catalyzed reactions in anionic micelles. Rates did not go through maxima with micelles of surfactant in which the counter-ion was the ionic reagent, *e.g.*, an anionic nucleophile, or the hydrogen ion in acid catalyzed reactions.[2,10].

Specific hydrogen ion catalyzed hydrolyses are accelerated by anionic micelles, *e.g.*, of sodium dodecyl sulfate, $n\text{-}C_{12}H_{25}OSO_3^-Na^+$, SDS, which was used in much of this early work, and rates increased as the substrate and H^+ became micellar bound and then went through maxima due to competition between H^+ and Na^+ [1,2]. Ionic competition by inert counterions was observed with a variety of added electrolytes, following the Hofmeister series, and it was assumed that co-ions remained in the water and did not affect reactivity. These rate effects were as expected from Hartley's evidence on indicator equilibria[7] with the micellar reaction region treated as a pseudophase distinct from the bulk solvent. Solute and surfactant monomer transfers between water and micelles are much faster than the thermal reactions but not for rapid photochemical or radical reactions. Observations of NMR spectra are useful in examining micelle-ion structures, and sharp signals indicate rapid reagent transfer and show that monomers have free movement in spherical micelles, but less so in large rod-like micelles.

Extensive kinetic studies showed that for many micellar inhibited second-order ion-molecule reactions this simple model fits changes in substrate hydrophobicity and surfactant structure, and addition of inert electrolytes. For such spontaneous reactions as water-catalyzed and S_N1 or S_N2 hydrolyses first-order rate constants follow micellar binding of the substrate,[1,2,10] and the lower polarity of the reaction region relative to that of water.[1,2] A theoretical treatment of the kinetic data for spontaneous reactions involved transfer of the organic substrate between water and micelles which could be monitored for slow reactions. This kinetic work was largely on organic reactions with known mechanisms which could be followed spectrophotometrically, but quantitative treatment of bimolecular ionic reactions required development of theoretical models of ion transfer. The basic equations applied to micellar rate effects are not shown, in part because

there is no general agreement on the formalism and use of symbols and abbreviations in the equations, or on the value of partial molar volumes of the micellar reaction region. These questions are covered in a variety of reviews, with consideration of the assumptions involved in the numerical treatments.[1,2,10,11]

The problem in treating bimolecular ionic reactions was estimation of local ionic concentrations of inert and reactive counter-ions in the micellar pseudophase assuming that co-ions are not micellar bound. In some cases, *e.g.*, for dilute halide or hydrogen ions, relative concentrations in micelles and water can be estimated with ion specific electrodes, and converted into local molecularity in the micellar pseudophase in terms of the total concentration and the estimated molar volume of the micellar reaction region, but this treatment is only applicable to dilute electrolyte. The fractional charge, α, of ionic micelles is approximately 0.25, *i.e.*, the fractional coverage by counterions, β = 0.75, for a variety of ions. However, ion-exchange experiments show that ions compete specifically for the micelle, for example OH^- or F^- are driven out of cationic micelles by such monoanions as Br^- or NO_3^- and the competition follows the Hofmeister series. Romsted concluded that ion-exchange must occur on an approximate 1:1 basis, despite differences in ion affinities, and with this assumption fitted ion exchange competition in terms of ion affinity ratios for the micelle, and the value of the fractional micellar charge, α.[11] This Pseudophase Ion Exchange, PIE, treatment, with the assumed molar volume of the micellar reaction region, fitted extensive kinetic data, and for many reactions of ionic nucleophiles second-order rate constants are similar in the aqueous and micellar reaction regions.[11,12] The overall micellar rate enhancement of bimolecular reactions is therefore due largely to concentration of both reactants in a small volume at the micellar surface. This model is similar to that developed by Berezin *et al* for treatment of bimolecular reactions of nonionic organic molecules.[13]

The PIE treatment has been applied successfully to very many bimolecular reactions and indicates that the generalization regarding similarities of second-order rate constants in the micellar and aqueous pseudophases, which fits reactions of nucleophilic anions, is not universal, in that some reactions, *e.g.*, anionic oxidations, are significantly slower in micelles than in water.[2] Micellar effects on uni-and bimolecular reactions in aqueous micelles fit the assumption that the polarity of the micellar reaction region is lower than that of water, but higher than of most aprotic organic solvents.

Counter-ion binding to micelles can also be treated in terms of a Langmuir isotherm and this method is convenient in treating bimolecular reactions in which the micellar counter-ion, *e.g.*, OH^-, Br^- or H^+, is the reagent, and it is also applicable to the competition between reactive and inert ions.[14-16] The Langmuir binding parameters for reactive and unreactive ions follow the Hofmeister series and their ratios are similar to those from the PIE treatment.

Another theoretical model for micellar-mediated bimolecular reactions involves estimation of local ionic concentrations in the micellar reaction region by using the Poisson-Boltzmann equation, PBE, to estimate electrostatic interactions between hypothetical point-charge ions and the micelle-water interfacial region.[17] However, ions are not point-charges, and the treatment

includes an empirical term for the ion specific, non-Coulombic, interactions in estimation of ionic concentrations at the micelle-water interface with the ion order following the Hofmeister series, as in the PIE model.[18,19] This treatment is more complicated than the classical PIE model, but includes possible interactions of co-ions with micelles, which should be unimportant in dilute electrolyte but have to be considered in some conditions. The various treatments lead to similar values of second-order rate constants in the micellar pseudophase for reactions of dilute electrolytes in ionic micelles.[2]

The various quantitative treatments of ion binding to micelles in water estimate relative ionic concentrations in water and micelles but give local concentrations as molarities in terms of assumed molar volumes, V_m , of the micellar reaction region. These volumes depend on assumptions regarding this region and cited values vary between 0.14 and 0.5 M^{-1}, and probably depend on the reaction conditions, which limits comparisons of second-order rate constants in micelles and water.[2]

Diazonium ions are very effective trapping agents for many nucleophiles and comparison of extents of this trapping in water and in micelles allows estimation of concentrations of nucleophiles in the two regions.[20] The location of the diazonium ion is controlled by the hydrophobicity of its substituent group, whose size should not affect trapping rates in either medium, so that the extent of trapping relates nucleophilic molarity in micelles to the known nucleophilic molarity in water. This method gives micellar concentrations for many nucleophiles, ranging from halide to sulfate and sulfonate ions and including micellar-bound water, depending on the specificity of the trapping reaction, and it is applicable to a variety of colloidal media.[21] In general local and relative concentrations in micellar pseudophases are similar to those estimated by the various theoretical models. The method is not applicable to cations or OH^-, but ion exchange constants for it and halide ions are known from kinetic work [2] which allows estimation of local molarity.

The simple models treat micelles and water as independent reaction regions with definable reactant concentrations in each region, rapid reactant transfer between regions and, for ionic micelles, no uptake of co-ions.[1,2,10,11] For bimolecular reactions with co-ions rate constants should therefore decrease to zero as the substrate is fully micellar-bound, and early results for reactions with OH^- fitted this assumption. Reactions of *p*-nitrophenyl octanoate, decanoate and dodecanoate with OH^- in aqueous NaOH and NaCl are strongly inhibited by micellized SDS, but rate constants do not go to zero in high [SDS] and go through a mild minimum at 5 mM SDS for the dodecanoate.[22] This general behavior was also observed for the reaction of *p*-nitrophenyl diphenyl phosphinate with OH^- in SDS. With, and without, added NaCl, rate profiles for these reactions were fitted by the PBE with substrate binding constants estimated in dilute SDS and micellar radii and aggregation numbers from the literature.

The pseudophase ion exchange, PIE, model involves an assumed limit to ion incorporation when *ca.* 75% of the surfactant head groups are neutralized by counterions, corresponding to α ≈ 0.25, in dilute electrolyte, < 0.05 M, as in most kinetic work, but has limitations at higher concentrations. Bimolecular reactions can be followed in micellar solutions with a reactive

counterion, typically a nucleophile or base, *e.g*., OH$^-$ or Br$^-$and no ionic competition.[2,10] In terms of the PIE model reaction rates with fully micellar bound substrate should become constant when the interfacial reaction region is saturated with reactive ion, but in some conditions reaction rates increase on addition of large amounts of the reactive ion.[24] This phenomenon, called "invasion" or "percolation", indicates the limitations in the simple models of ion binding and in 1 M electrolyte average interionic distances are approximately 9.4 Å [25] so that the micelle will be in contact with a congested, nonuniform, concentrated salt medium, rather than water. The initial concept of distinct micelle and water as reaction regions therefore fails and ions, regardless of charge, can interact with substrate at the micellar surface, because ionic interactions with micelles are governed by the balance between entropic and enthalpic forces, as in the PBE treatment.[17,18,19]. In these conditions of high electrolyte the concept of micellar and water reaction regions has limitations because the micelles are not in "pure" water but in a nonuniform ion-water region with significant ionic gradients.
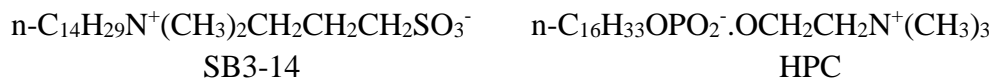
2.1. Premicellization

These various models of micellar rate and equilibrium effects involve the assumption that they will be observed only with [surfactant] > cmc.[1,2] However, reaction rates often increase slightly at surfactant concentrations below the cmc, possibly due to reactant-induced micellization, and an assumed "kinetic" cmc is often used in fitting the kinetics,[1,2] but premicelles may exist and affect reaction rates, because some hydrophobic nonmicellizing quaternary ammonium ions increase reaction rates.[26] There is physical evidence for premicellization of gemini surfactants[27] and Ralston *et al* used conductance to show that dimethyldidodecylammonium halides, $(CH_3)_2N^+(C_{12}H_{25})_2X^-$, X = Cl, Br, DDDAX, and related twin tail surfactants, form premicelles[28] and their conclusions are consistent with kinetic data and NMR spectroscopy.[29,30]

Decarboxylations of nitrobenzisoxazole-3-carboxylate ions are strongly accelerated by decreases in the polarity of the reaction medium[31] and are much faster in cationic and zwitterionic micelles than in water.[2,32] The affinity of benzisoxazoles for colloidal surfaces is strongly increased by bulky alkoxy substituents in the benzene ring and decarboxylation rates increase sharply in some very dilute surfactant, go through maxima and then increase above the cmc as micelles form.[32] These results show that premicelles can exist and accelerate decarboxylation, but do not exclude the possibility that their formation is induced by the anionic substrate. However, this kinetic behavior is observed with DDDACl, and its ^{1}H NMR signals at 0.025 mM in D$_2$O are sharp, as expected for free surfactant ions, broaden at 0.106 mM as premicelles form, and at 0.26 mM sharpen as normal micelles form.[30] The micelles grow at higher surfactant concentrations and the signals become much broader, as with single chain micelles. This physical evidence confirms that twin tail and gemini surfactants can form premicelles without interacting with organic solutes and that premicellar structures can be more ordered than those of micelles.

2.2 Zwitterionic Micelles

Zwitterionic surfactants have no overall charge and in the head group the anion and cation are separated by a short spacer group, as with the sulfobetaine and phosphocholine surfactants, SB3-14 and HPC shown here.

$$n\text{-}C_{14}H_{29}N^+(CH_3)_2CH_2CH_2CH_2SO_3^- \qquad n\text{-}C_{16}H_{33}OPO_2^-\cdot OCH_2CH_2N^+(CH_3)_3$$

$$\text{SB3-14} \qquad\qquad\qquad\qquad \text{HPC}$$

The surfactants differ in the ion order and the tether groups, they are structurally similar to other widely used zwitterions and are related to many biologically important amphiphiles. The reactions studied to date are mechanistically simple and substrates have hydrophobic groups so that reactions are largely in the micellar pseudophase.

Despite their zero overall charge zwitterionic micelles bind anions and cations, although less effectively than ionic micelles, and the binding order follows the Hofmeister series.[2] Initially the preferential binding of anions to betaine micelles was ascribed to different charge densities at the assumed spherically oriented ammonium and sulfonate surface regions.[33] This electrostatic interaction, without ion specificity, was treated theoretically with simplifying approximations,[34a] and later with inclusion of terms for specific ion binding,[34b] but the model of preferred anion binding to sulfobetaine micelles and cation binding to phosphocholine micelles is inadequate, as shown by diazo trapping.[35] Ion-binding to zwitterionic micelles is specific for both co-and counter-ions, although it is much weaker than with ionic micelles. It is monitored by a variety of physical methods, including ionic conductance, the use of ion-specific electrodes, electrophoresis, and NMR spectroscopy and examples are given in the cited references. Results from these physical methods can be related to those from diazo trapping[35] and kinetic studies of reactions with known mechanisms. The physical methods have limitations[36] in that only dilute electrolytes can be studied with ion specific electrodes and electrophoresis, while NMR spectroscopy is limited to some nuclei and diazo trapping cannot be used with very dilute solutions and some ions. Theoretical treatments of ion binding to ionic micelles give considerable weight to electrostatic interactions[1,2] but ion-specific interactions play major roles in ion binding to zwitterionic micelles where electrostatic interactions are less important.

Kinetic results provide considerable evidence on ion-surfactant interactions. For example, spontaneous ionic decarboxylations and dephosphorylations are strongly accelerated by both cationic and sulfobetaine micelles and the latter do not suppress bimolecular reactions of OH$^-$ and accelerate reactions with less hydrophilic anions.[2,33] Unlike reactions in ionic micelles dilute inert electrolytes can inhibit or accelerate reactions in zwitterionic micelles, depending on competition with the ionic reactant and the effect on the apparent micellar charge. Treatments of kinetic results therefore require physical evidence on specific ion-micelle interactions. Kinetic studies with zwitterionic micelles have generally involved reactions with known mechanisms so that kinetic and physical evidence can be related.

Diazo trapping with halide salts and both sulfobetaine and phosphocholine micelles, showed that halide ion uptake is higher with dicationic than monocationic salts,[35] indicating that both anions and cations are micellar bound . The simple rules applied earlier to micelle-ion interactions do not apply to zwitterionic micelles, except that ion-orders follow the Hofmeister series.

Perchlorate ion has a strong affinity for sulfobetaine micelles and displaces Br^- from them and inhibition of reactions of Br^- and fully bound substrate closely follows physical evidence from NMR spectroscopy.The reaction of Br^- with methyl naphthalene-2-sulfonate (MeONs), accelerated by sulfobetaine micelles, is strongly inhibited by $NaClO_4$ and physical measurements and NMR spectroscopy monitor the displacement of Br^- by ClO_4^-.[36,37] For the corresponding reaction of I^- with MeONs in micelles of sulfobetaines with variable tail length and fully micellar bound substrate rate constants follow the binding of I^- estimated by capillary electrophoresis.[38] (NMR spectroscopy is of limited value in studying the reaction with I^-.) Rate constants and binding of I^- increase slightly with increasing length of the surfactant chain and with fully bound substrate and $KI < 0.1M$ rate constants increase with increasing [KI], as predicted by simple pseudophase models, but then increase linearly with increasing [KI].[38] This "invasion"or "percolation" by a nucleophilic anion is similar to that observed earlier in solutions of cationic micelles, but only with concentrated nucleophilic anions.[24]

The different effects of ionic micelles on bimolecular ionic reactions had been rationalized in terms of electrostatic and ion-specific interactions, as given by Hartley's Rules,[1,2] but they are limited for reactions in zwitterionic reactions, for example, hydrogen ion catalyzed and anionic nucleophilic reactions are observed in solutions of sulfobetaine and phosphocholine micelles. The specific hydrogen ion catalyzed hydrolysis of 2-(*p*-heptoxyphenyl)-1,3-dioxolane, (HPD), in SB3-14 micelles, with fully micellar bound substrate, is faster in $HClO_4$ than in HCl, and in dilute HCl is accelerated by added salt in the sequence $NaClO_4 \gg NaNO_3 > NaBr > NaCl$. Protonation of 1-hydroxy-2-naphthoate ion (HNA) in dilute HCl follows this salt order, showing that added anions are increasing the hydrogen ion uptake in the zwitterionic micelle.[39] These, and similar results with a wider range of sodium salts, show that this anion dependence is general, and capillary electrophoresis confirms the apparent negative micellar surface potential dependence on the Hofmeister anion order and hydration free energies.

Hexadecyl phosphorylcholine (HPC) and sulfobetaine (SB3) surfactants differ in the charge orientation of the head group ions, but diazo trapping and kinetic results show that their micelles can bind both anions and cations and affect hydrogen ion catalyzed reactions and reactions with OH^- [35,40]. The negative zeta potential of HPC micelles is very low but increases markedly on addition of $NaClO_4$, while NaCl has little effect.[40] Consistently the reaction of OH^- with naphthoic anhydride in HPC micelles is strongly inhibited by $NaClO_4$ and weakly by NaCl, in agreement with the negative zeta potentials, while the hydrogen ion catalyzed hydrolysis of the dioxolane, HPD, is strongly accelerated by $NaClO_4$ and weakly by NaCl. This anion order is similar to that for sulfobetaine micelles, despite the different head group charge orientations and the strong interaction of ClO_4^- with the ammonium ion in the sulfobetaine micelle. In

phosphocholine micelles the terminal ammonium ion is probably oriented towards the anionic phosphate, but on addition of $NaClO_4$ the tether group and the ammonium ion can be extended into the surface region. The postulated salt effects on head group conformations in zwitterionic micelles show that generalizations regarding ion specific interactions with ionic micelles fail for zwitterionic micelles and the conformational control of ion binding should be important at some biological surfaces.

Early work with anionic micelles of SDS showed that Na^+ and H^+ have similar affinities for the micelles and anion effects could be neglected.[1,2,11] The situation is different for reactions in concentrated salt solutions[22,23] and in zwitterionic micelles where interactions with both anions and cations have to be considered. Preliminary observations show that hydrogen ion catalyzed reactions in sulfobetaine micelles are strongly accelerated by lithium, sodium and potassium perchlorate, but to similar extents, *i.e*., the rate increase is not sensitive to cation properties, so that these cations apparently compete weakly with H^+, unlike the situation in anionic micelles,[11] where electrostatic interactions are important, relative to ion-specific forces. Alkali metal cations and hydronium ions differ in that the former are spherical, but the nonspherical hydronium ion, as the Eigen cation, $H_9O_4^+$, has a strong, transient, dipole, which could interact readily with a dipolar tether group in a zwitterionic micelle. These speculations may not apply to the behavior of salts of di- and tri-cations.[35]

2.3 Preparative Applications

Micelles and other association colloids control reaction rates and products of competing reactions.[1,2] A typical example of this behavior is the control of isomer ratios in bromination of N,N-dialkyl anilines.[41] In micellized 1-hexadecylpyridinium tribromide the brominating agent is the counter anion and reaction at 25°C gives largely the *para* isomer, but significant amounts of *ortho* isomer are formed in reaction at 0° C, and similar examples of this selectivity are cited. Micelles and other association colloids can affect both the rate and products of the very important Diels-Alder reactions, as discussed in detail.[42] However, use of these systems in organic synthesis is limited to the extent that reactions are usually carried out with surfactant in large excess over reactants and subsequent recovery of surfactant and product isolation can be difficult, especially for large scale syntheses. Jaeger and coworkers attacked this problem by designing labile surfactants to simplify product isolation in micellar-mediated reactions.[43]

2.4 Approximations

Theoretical treatments involve approximations and assumptions and colloid science is no exception to this generalization. Micelles in water have mobile structures with monomer, counter ions and associated solutes entering at diffusion controlled rates, so that only averaged properties are considered, and kinetic treatments are written for uniform interfacial reaction regions, with assumed geometries, although reactant concentrations in this postulated region may not be uniform. Estimations of local concentrations in water and micelles with the pseudophase models[1,2] involve empirical terms and assumptions, for example the PIE treatment is based on

assumed 1:1 ion-exchange,[11,12] and other treatments do not involve this, but involve other, assumptions.[15,16,18,19] Kinetic treatments generally neglect both ionic effects on the neighboring water and micellar growth with sphere to rod transitions in high electrolyte, which should be important in the use of micelles in preparative chemistry.

Most useful theoretical treatments include assumptions and approximations, for example, the Debye-Hückel equation, without an empirical term, is applicable only in very dilute electrolyte. The practical world runs efficiently on Newton's equations, which for hundreds of years included the mysterious force of gravity, until it was treated theoretically by Einstein's equations, which have problems with some subatomic properties. In the 1950's C.K.Ingold set out to develop a theoretical treatment of S_N2 reactions in solution, with known values for most, but not all, terms in the equations, and in lecturing on this treatment he suggested that everyone should be entitled to include one adjustable parameter in a complete equation. Following this pattern theoretical models of micellar rate and equilibrium effects include assumptions and some terms whose values are uncertain, but reasonable, which allows one to explain some results and to predict others.

3. Conclusions

The pseudophase model of micellar rate effects depends on equations with terms describing reactant partitioning between two assumed reaction regions and rate constants in each region. Reactant transfers between the regions are faster than most thermal reactions and for unimolecular and water-catalyzed reactions rate constants depend on one transfer equilibrium constant and first-order rate constants in each region. The polarity of the micellar pseudophase is lower than that of water and with fully micellar-bound substrate rate effects are often similar to those in aqueous-solvent mixtures.

Kinetic treatments for bimolecular reactions involve transfers of both reactants and second-order rate constants in each pseudophase. Transfer of ionic reagents to aqueous micelles generally involves competition between the reactive ion and the surfactant counterion and added electrolyte. Treatment of the kinetics by the PIE model involves the assumption that counter-ion transfer equilibria are ion-specific, but with 1:1 exchange between mono-ions. This assumption is satisfactory for ionic micelles whose charge is largely neutralized by counter-ions, and accounts for specific kinetic salt effects in dilute solution which follow the Hofmeister series. The electrostatic contribution can also be treated in terms of the PBE with an empirical term for ion-specific interactions.

These treatments fit extensive experimental data in showing that the micellar rate enhancements of bimolecular reactions are due largely to concentration of both reactants at the micelle-water interface. It is assumed that free surfactant, below the cmc, does not affect reaction, but generally there are rate effects in this region because reactants induce micellization and reactions can be accelerated by premicelles.

The assumption in the PIE and similar models that micellar counter-ion populations are limited to *ca*. 75% of the ionic head group fails in high electrolyte where both co- and counter-ions enter the micellar region and reaction rates are higher than predicted. Some deviations from this model are fitted by the PBE treatment. Current simple treatments of micellar rate effects in aqueous ionic micelles are inadequate for zwitterionic micelles where ion-specific interactions play major roles, and regardless of head-group orientation anions and cations bind to the micelles, so that rules governing ion-binding to ionic micelles have limitations. Ion-binding is much weaker than with ionic micelles, but follows the Hofmeister series. Hydrogen-ion uptake by sulfobetaine or phosphocholine micelles is not very sensitive to salt monocations but is affected by the conjugate anion, and ClO_4^- is much more effective than Cl^- in increasing uptake of H^+ and decreasing that of OH^-. These observations are consistent with physical evidence on the specificity of ion binding to zwitterionic micelles. Kinetic salt effects in micellar solutions therefore provide evidence on micellar structure and the extent to which it can be controlled, especially for zwitterionic micelles.

4. Acknowledgements

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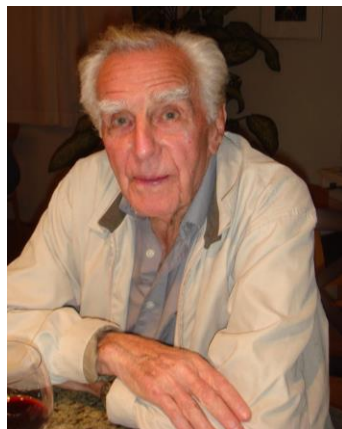
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