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Electron Transfer Reactions of Transition Metal Aminocarboxylates in the Presence of Micelle-Forming Surfactants. Catalysis by Cetyltrimethylammonium Bromide of the Reduction of $Mn(cydta)^-$ by $Co(edta)^{2-}$ and $Co(cydta)^{2-}$

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Abstract: The reduction of $Mncydta^-$ by $Co(edta)^{2-}$ and $Co(cydta)^{2-}$ is catalyzed by aqueous micellar cetyltrimethylammonium bromide (CTAB). The maximum rate enhancements are ca. 600× and 160×, respectively. The binding between $Co(cydta)^-$ and CTAB micelles was investigated by gel filtration chromatography using a Sephadex G-25 gel. The binding constant of $Co(cydta)^-$, defined in terms of partitioning between bulk aqueous phase and micellar pseudophase, is 325 M^{-1} (25 °C) and incorporates contributions from electrostatic as well as hydrophobic interactions. The kinetic data have been interpreted in terms of Berezin's theory (assuming similar binding constants for $Co(cydta)^-$ and $Mn(cydta)^-$) and current theories about the mechanism of electron transfer processes. This reveals that the rate constant for the bimolecular reaction in the micellar pseudophase (k_M) is smaller than the rate constant in aqueous solution, whereas the rate constant for the interphase reaction (k_M') involving $Co(edta)^{2-}$ on the micellar surface and $Mn(cydta)^-$ in bulk aqueous phase is higher than k_M and the rate constant in aqueous solution. Various factors which affect k_M and k_M' are discussed taking into account the micellar surface solvent properties.

Among the biochemical functions of metalloproteins which are being studied at the molecular level, the redox processes in which these electron transport enzymes participate are of paramount importance. However, the mechanistic details of the redox processes of these enzymes are not well understood. This is not surprising, for biological systems offer a multitude of subtle factors influential in determining the reactivities of electron acceptor–donor centers. Moreover, these factors in themselves exhibit exceeding complexities which are not usually encountered in normal aqueous solutions. On the other hand, the knowledge of electron transfer reactions, for example, between simple complexes of transition metal ions, is now well matured.[1] The principles which are operative in these simpler systems should apply, with relevant modifications, to the biological realm. To acquire better insight into these factors, various approaches can be adopted. One such line of approach involves the investigation of nonphysiological redox reactions of metalloproteins in aqueous media[1b,2-6] which are designed to serve as model systems for the physiological processes. Another approach involves the study of pseudobiological environments offered to elementary reactions. This has been achieved by coupling, for example, of micelles of micelle-forming surfactants with the elementary reactions, assuming that the micellar systems mimic important features of the reaction environment at biological interfaces.[7] Micelles of micelle-forming surfactants in aqueous media and also inversed micelles in aprotic solvents resemble enzymes in that they possess distinct regions of hydrophobic and hydrophilic character. Furthermore, the catalytic mechanisms show important similarities with those of enzymic processes.[7c] To date this line of approach has been extensively adopted to elementary reactions of organic and bioorganic chemistry.[7] It is likely that investigations of coupled systems composed of electron-transfer reactions and micelles of micelle-forming surfactants may contribute in a unique way to our understanding of the redox processes of electron transport enzymes and, in addition, will offer an opportunity to learn more about the behavior of the biological interfaces.

Grätzel et al.[8a-c] have incorporated micellar systems in electron transfer reactions of aquated electrons from the aqueous phase through an electrical double layer into an acceptor molecule solubilized in the lipoidic part of a micelle and vice versa (to form aquated electrons). However, electron transfer reactions between transition metal complexes in the presence of aqueous micellar systems have hardly been assessed. Only very recently, some experiments have been carried out on the kinetics of electron transfer to $Ru(bpy)_3^{2+}$ in micellar sodium dodecyl sulfate solutions.[8d] Since previous studies have revealed that electron-transfer reactions are relatively simple, at least those operating via outer-sphere pathways, and are highly sensitive to environmental changes,[1] we have investigated in some detail the reduction of $Mncydta^-$ (**1**) by $Coedta^{2-}$ (**2a**) and $Cocydta^{2-}$ (**2b**) in presence of cetyltrimethylammonium bromide (CTAB), a cationic micelle-forming surfactant. Here $cydta^{4-}$ denotes *trans*-1,2-diaminocyclohexane-*N,N,N',N'*-tetraacetate ion and $edta^{4-}$ denotes 1,2-diaminoethane-*N,N,N',N'*-tetraacetate ion. The formulation of the complexes adopted here is for convenience only and in no way precludes possible coordinated water or uncoordinated positions of the chelating ligand. The choice of the

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redox systems was largely governed by amenability to conventional kinetic techniques, since electron transfer reactions are known to be among the fastest group of reactions. The present study also serves to demonstrate some subtle features associated with the investigation of reactions between ionic reactants in aqueous micellar systems and which are not generally important in the case of the nonionic reactants.

Experimental Section

The following complexes were prepared by methods reported earlier: KCocydta·3H_2O,[9] KCoedta·2H_2O),[10] KMncydta·H_2O,[11] Na_2Cocydta·3H_2O,[11,12] and Na_2Coedta·2H_2O.[11,12] Hexadecyltrimethylammonium bromide (CTAB, Merck, p.a. quality) was purified by the method of Duynstee and Grunwald.[13] Sephadex G-25 Fine was from Pharmacia Fine Chemicals AB, Uppsala, Sweden. Other chemicals used were of the highest grade (purity) available. In all runs a concentration of 2×10^{-5} M hydrochloric acid was maintained so that protonated and hydroxo species of the complexes used become unimportant.[14,15] Since the reactants in the present report are ionic species, their concentrations employed for kinetic runs must be as low as possible to avoid electrolyte effects. Thus, 1×10^{-5} M of **1**, 1×10^{-4} M of **2b**, and 9.7×10^{-5} M of **2a** were used so that the reductant was about 10 times in excess over the oxidant to create pseudo-first-order conditions. All reactions were performed in 2-cm quartz cells which were placed in a thermostated (25 ± 0.05 °C) cell compartment (equipped with a magnetic stirring device) of a Zeiss PMQ 11 spectrophotometer. The reactions were initiated by injecting the oxidant with the help of an all-Teflon syringe (previously brought to 25 °C) into the thermostated quartz cell containing the other components of the reaction mixture. In all cases good pseudo-first-order plots were obtained up to >75% conversion and the reproducibility of individual rate constants was within 3%. The UV charge transfer bands of **2a** and **2b** were employed to monitor the rate of reactions. The rate constant for the oxidation of **2b** by **1** was found to be independent of the wavelength used between 230 and 280 nm, indicating that even though Cocydta·H_2O^- is a major immediate product of oxidation owing to the dominant operation of an inner-sphere path,[16] its rate of conversion to Cocydta⁻ is much faster as was also reported earlier.[17] Thus this reaction was monitored at 230 nm. Contrastingly, the rate constant for the oxidation of **2a** by **1** was not independent of the wavelength used, confirming that the postoxidation ring-closure process contributes significantly to the rates, even though the outer-sphere path is now dominant.[16,18] Therefore, this reaction was monitored at 258 nm where Coedta⁻ and Coedta·H_2O^- species have about the same extinction. This was established by recording the absorbance change with time, at various wavelengths between 230 and 280 nm, of a solution of CoedtaOH^{2-} adjusted to pH 5. No further attempts were made to determine the order of the reaction; it was assumed to be two as reported earlier.[15,16]

The binding constant of Cocydta⁻ (**3**) to CTAB micelles was determined in terms of its partition coefficient between bulk aqueous phase and micellar pseudophase, using gel filtration chromatography employing Sephadex G-25 Fine.[19,20] A column (typically 2-cm diameter, bed height 34 cm) with an outer jacket for circulating water from a thermostat (25 °C) was used. Using Blue Dextran 2000 in 1.0 M sodium chloride the void volume V_0 and the sum of void volume and imbibed volume, $(V_0 + V_i)$, of the packed column were determined to be 45.9 and 94.4 mL, respectively.[21] Prior to each run the column was equilibrated overnight with the appropriate eluent (i.e., water or aqueous solutions of sodium chloride or of detergent of appropriate concentration). The runs were initiated by the addition of approximately 0.5 mL of a 1×10^{-3} M Cocydta⁻ solution. Elution with the appropriate eluent was followed at a rate of 0.3 mL min^{-1}. Fractions of 1.0 mL were collected by means of an automatic fraction collector, and the absorbance between 230 and 270 nm of each fraction was monitored manually in a Zeiss PMQ II spectrophotometer. The elution volume, V_e, was calculated corresponding to the fraction of maximum absorbance. In determining $(V_0 + V_i)$ the conductivity of each sample was measured with a Radiometer, Copenhagen conductivity bridge, and the absorbance of Blue Dextran 2000 was monitored at 620 nm for the determination of the void volume, V_0.

It can be shown[20] that the observed elution volumes and the partition coefficient of the solute are related as follows:

$$\frac{V_i}{V_e - V_0} = \frac{\bar{v}(P-1)}{k'K_D} C_m + \frac{1}{k'K_D} \qquad (1)$$

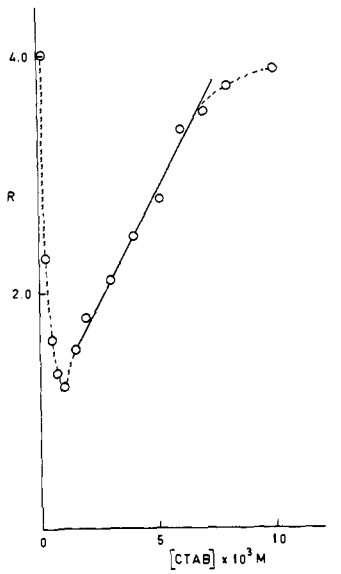

Figure 1. Plot of $R = V_i/(V_e - V_0)$ vs. CTAB concentration for Co(cydta)⁻.

where V_i, V_e, and V_0 are the imbibed (stationary), elution, and void volumes, respectively, $\bar{v}$ is the partial (or effective) specific volume of the detergent molecule in the micelle, K_D is the "molecular sieving" constant which is equal to the ratio of the solute concentration in the imbibed liquid to the concentration in the nonmicellar portion of external liquid, C_m is the concentration of micelles (in g mL^{-1}), $C_m = C - \text{cmc}$ where C is the stoichiometric surfactant concentration in g mL^{-1}, and cmc is the critical micelle concentration (in g mL^{-1}), P is the partition coefficient of the solute between the micellar and the aqueous phase, and k' is defined by

$$k' = (kV_g + V_i)/V_i = (kA_g + A_i)/A_i \qquad (2)$$

In eq 2 k is the constant of proportionality between the solute adsorbed per unit volume of gel matrix and the equilibrium concentration of monomer solute in the liquid (linear adsorption isotherm assumed), V_g is the total volume of the gel matrix, and A_g and A_i are cross-sectional areas of the gel matrix and the imbibed liquid.

In the absence of micelles and adsorption effects, eq 1 reduces to the usual gel filtration equation

$$V_i/(V_e - V_0) = 1/K_D \qquad (3)$$

We will designate the ratio $V_i/(V_e - V_0)$ by R. The observed values of R for **3** with H_2O, 0.2 M NaCl, and 1.0 M NaCl solutions as medium are 10.33, 1.16, and 1.12, respectively. In the absence of adsorption effects the value of R on Sephadex G-25 should be unity for small molecular weight solutes like sodium chloride.[21] However, for **3** the value of R observed is very high and it approaches 1.1 at high salt concentrations. It is well known that the Sephadex gel matrix contains a small number of negative charges due to carboxyl groups. Therefore, the large value of R for the aqueous medium can be attributed to a negative adsorption effect (i.e., the repulsion by gel matrix). In 0.2 or 1.0 M sodium chloride the negative charges of the gel matrix are essentially totally shielded by sodium chloride leading to a large decrease in R.

Figure 1 and Table I show the variation of the R values upon varying the medium from 1×10^{-4} to 1×10^{-2} M CTAB. At low concentrations of CTAB when no micelles are present, the decrease of R with increasing CTAB concentration will be primarily due to shielding (or neutralization) of negative charges on the gel matrix by the adsorption of positively charged surfactant molecules. This then may be varified quantitatively in conjunction with the Langmuir adsorption isotherm[22] for the adsorption of surfactant molecules on the gel matrix using the following equation (Appendix A):

$$\frac{R_a}{R_1 - R_a}\frac{R_1 - R_w}{R_w} = 1 + bC \qquad (4)$$

where b is a constant related to the adsorption of surfactant molecules on the gel matrix, R_a, R_1, and R_w are the values of R, at a certain

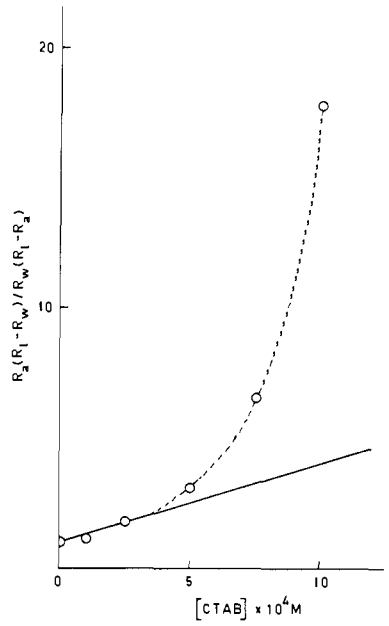

Figure 2. Plot of $R_a(R_1 - R_w)/R_w(R_1 - R_a)$ vs. CTAB concentration for the descending portion of Figure 1.

surfactant concentration, when the adsorption effect vanishes, and when the medium is water, respectively, and C is the equilibrium concentration of surfactant in solution. Since prior to each run the column is equilibrated with the appropriate detergent solution by elution, the equilibrium surfactant concentration will be equal to the surfactant concentration used in each run. A plot of the left-hand side of eq 4 against CTAB concentration is depicted in Figure 2 corresponding to the descending portion of Figure 1 (R_1 = 1.14 was substituted in eq 4 which is an average of the values for 0.2 and 1.0 M sodium chloride medium). A reasonably good correlation is observed for low concentrations of CTAB but above 5×10^{-4} M CTAB a substantial deviation from linearity is observed. These deviations beyond 5×10^{-4} M CTAB cannot be attributed to the appearance of micelles, because then the value of R should increase with increasing CTAB concentration according to eq 1 or should remain almost constant if the decrease in the partition coefficient, P, for ionic solutes, due to an increase in the total concentration of gegenions,[23-25] is compensated by an increase in the concentration of micelles. We propose that the decrease of R beyond 5×10^{-4} M up to 1×10^{-3} M CTAB may be rationalized by postulating premicellar aggregation.[26-29] The appearance of premicellar aggregates implies that a further small increase in surfactant concentration only increases the concentration of these aggregates and that the monomer concentration remains constant. A quantitative treatment[30] indicates that both in the presence and absence of molecular sieving for premicellar aggregates, R will decrease only if there is a binding of **3** to these premicellar aggregates.

From Figure 1 it can be seen that on going from 1×10^{-3} M CTAB to 1.5×10^{-3} M CTAB there is a sharp increase in the R value. Beyond 1.5×10^{-3} M CATB, the R value increases linearly with CTAB concentration but less sharply. This can be explained by assuming that the cmc for CTAB on a Sephadex G-25 column and in the presence of 3 is ca. 1×10^{-3} M. Upon increasing the concentration of CTAB from 1×10^{-3} to 1.5×10^{-3} M the total micelle concentration will increase, but owing to a concomitant increase in gegenion concentration, the partition coefficient of **3** between the aqueous and micellar phase will decrease simultaneously.[23,24] Beyond 1.5×10^{-3} M CTAB the partition coefficient appears to remain practically constant. We note that above 8×10^{-3} M CTAB, the R value tends to become independent of the detergent concentration. This is indicative of a limiting situation for which practically all solute molecules move with the micelles. Now if the binding constant of **3** to CTAB micelles is defined as

$$K = \bar{V}(P - 1) \tag{5}$$

where $\bar{V}$ is the partial molar volume of the monomer in the micelle, the unit of the binding constant, K, will be M^{-1}. Therefore, if the partial specific volume, $\bar{v}$, is replaced in eq 1 by the partial molar volume, $\bar{V}$, C_m should be substituted in molarity. Hence, the binding constant, K (M^{-1}), in terms of the partition coefficient can be calculated from the ratio of slope to intercept employing eq 1. If the cmc on the Sephadex G-25 column is taken as 1×10^{-3} M (vide infra), we obtain K = 325 M^{-1} from Figure 1 for **3**.

Results and Discussion

The binding constant of **3** to the CTAB micelles and other information obtained from gel filtration chromatographic experiments are subsequently used in the treatment of the kinetic data. Therefore, we will first discuss some aspects of the partitioning of **3** between the micellar pseudophase and bulk water.

Binding of 3 to CTAB. In principle, the partition coefficient of an ionic solute between an aqueous phase and a micellar pseudophase can be calculated using the relation[24,31]

$$P = e^{-Z\psi/25.69} \text{ (at 25 °C)} \tag{6}$$

where Z is the ionic charge on the solute and ψ the surface potential of the micelle in millivolts. The surface potential is highly sensitive to several factors, including the ionic strength of the medium, the nature of the counterions, pH, etc., and its determination or even reasonable estimation is not straightforward. However, from the data of Mukerjee and Banerjee[32] one can estimate that the value of ψ for CTAB at the cmc will be in the range from 100 to 200 mV. Using these values, the partition coefficient for univalent ions would range from ca. 50 to 2440 solely on electrostatic grounds. This in turn reduces eq 5 to

$$K = P\bar{V} \tag{7}$$

Recently, partial specific volumes, $\bar{v}$, for several detergents above the cmc have been determined very accurately by Tanford et al.[33] From their data, we calculate 0.363 M^{-1} as the partial molar volume of CTAB. Using this value and eq 7 the binding constant for univalent ions would range from about 18 to 890 M^{-1}. If it is assumed that the binding constant for **3** (325 M^{-1}) as determined by gel filtration chromatography (Experimental Section) is solely due to electrostatic interactions, then the surface potential is calculated to be about 175 mV. However, such a high value is hardly acceptable because the experimental binding constant has been determined from the data well above the cmc where the surface potential must be considerably lower than that at the cmc. Consequently, we presume that the observed binding constant has contributions from electrostatic as well as from hydrophobic interactions. Furthermore, it is an established fact that the free-energy change associated with the transfer of the hydrophobic part of an amphiphile from the aqueous medium to the micelle interior is independent of the ionic strength of the medium and aggregation number.[34-36] It may then be inferred that the changes in surface potential, which are only caused by electrostatic interactions, only affect the electrostatic contribution to the binding constant of the solute and that the hydrophobic contribution remains largely unaffected. In view of the low total ionic concentration the assignment of a value of 150 mV to the surface potential appears reasonable. Then the electrostatic contribution to the binding constant will be about 125 M^{-1}. If this value is accepted, then the electrostatic contribution to the binding constant of $Cocydta^{2-}$, which is identical with the $Cocydta^{-}$ species except for the charge, the oxidation state of the central cobalt ion, and a probable water molecule in the first coordination sphere of the metal ion, can be estimated from eq 6 and 7 to be 4.31×10^4 M^{-1}. The incorporation of the hydrophobic contribution will then change the binding constant to 4.33×10^4 M^{-1}. Hence, for bivalent ions it appears that the electrostatic part of the binding constant will completely dominate the hydrophobic contribution. The

high value of the binding constant for bivalent ions is not surprising. Recently, Lindman et al.[29] from ESR measurements on the vanadyl ion, VO^{2+}, in aqueous solution of sodium dodecyl sulfate have concluded that virtually all VO^{2+} ions become attached to the micelles at concentrations only slightly above the cmc. Therefore, it is likely that a very strong binding for bivalent ions[8d] is a general phenomenon regardless of the nature of the micelles, provided that the charge sign on the solute is opposite to that on the micellar surface.

Kinetics and Mechanism of the Reduction of Mncydta⁻ (1) by Coedta²⁻ (2a) and Cocydta²⁻ (2b) in the Presence of CTAB. Wilkins et al.[15,16] have studied the reduction of **1** by **2a** and **2b** at 25 °C in the pH range 4.5–6.0 and ionic strength 0.5 M. The reactions may proceed via outer-sphere and inner-sphere pathways (see Experimental Section) which may be schematically represented as follows. 1. outer sphere

(i) $CoL^{2-} + MnLH_2O^- \longrightarrow CoL^- + MnLH_2O^{2-}$

(ii) $CoLH_2O^{2-} + MnLH_2O^- \longrightarrow CoLH_2O^- + MnLH_2O^{2-}$

$\downarrow$

$CoL^- + H_2O$

2. inner sphere

(i) $CoLH_2O^{2-} + MnLH_2O^- \rightleftharpoons LCo{-}OH{-}{-}MnL^{4-} + H_3O^+$

$\downarrow H_3O^+$

$CoL^- + H_2O \longleftarrow CoLH_2O^- + MnLH_2O^{2-}$

The reported rate constants are 0.9 M^{-1} s^{-1} for **2a** and 0.45 M^{-1} s^{-1} for **2b.** We find similar values. However, when these two reactions are carried out at very low concentration, virtually approaching infinite dilution (see Experimental Section), the rate constant for both reactions is 0.2 M^{-1} s^{-1}. Therefore, the different values at high ionic strength may be attributed to a slightly different ionic strength dependence and to specific cation catalysis for the two reactions.

In Figure 3 and Table II the dependence of the second-order rate constants for the two reactions on the CTAB concentration in the region 4×10^{-4} to 3.2×10^{-2} M is depicted. The most important features are that the apparent second-order rate constant increases sharply beyond 4×10^{-4} M CTAB and reaches for both electron transfer reactions a maximum value at about 1.5×10^{-3} M CTAB. Beyond this concentration the rate constant first decreases sharply and then gradually. The maximum rate enhancement for oxidation of **2a** and **2b** by **1** are about 600× and 160×, respectively.

In analyzing the catalytic effect of the CTAB micelles we will essentially follow Berezin's approach.[24] Accordingly, a solution above the critical micelle concentration may be viewed as a two-phase system, consisting of an aqueous phase and a micellar pseudophase. A quantitative relation for the bimolecular rate constant is then given by eq 8 for reactants A and B:

$$K_{EXP} = \frac{(k_M P_A P_B + k_M' P_A + k_M'' P_B) C\bar{V} + k_w(1 - C\bar{V})}{(1 + K_A C)(1 + K_B C)} \quad (8)$$

where $K_A = (P_A - 1)\bar{V}$ and $K_B = (P_B - 1)\bar{V}$ and the subscripts M, W, A, and B represent quantities relating to the micellar phase, aqueous phase, and reactants, respectively. k_M and k_W are the rate constants for the reaction occurring in the micellar phase and the aqueous phase, respectively, k_M' is the rate constant for the reaction due to encounters between reactant A in the micellar phase and reactant B in the aqueous phase, k_M'' refers to the exactly reverse situation, C is the stoichiometric concentration of surfactant minus cmc, P and K represent the partition coefficient and the binding constant, respectively, k_{exp} is the observed second-order rate constant

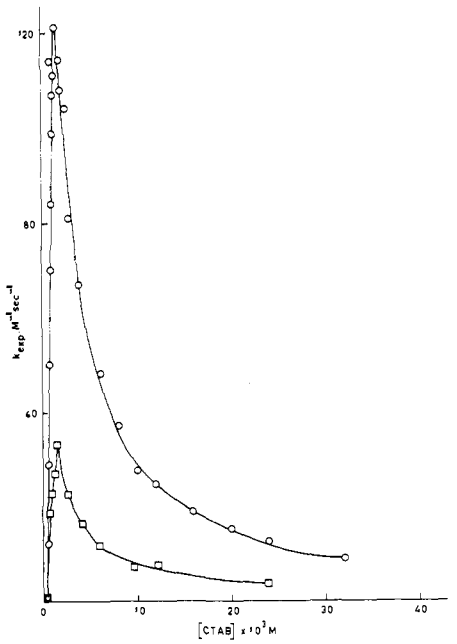

Figure 3. Plot of the second-order rate constant, k_{exp}, vs. concentration of CTAB for the reduction of **1** by **2a** (○) and **2b** (□).

in the aqueous micellar system, and $\bar{V}$ is the partial molar volume of a surfactant molecule in the micelle.[37]

Slightly above the concentration where micelles first appear, virtually all *bivalent* ions will be in the micellar phase, and therefore k_W and P_B (B represents the monovalent reactant) are assumed to be negligible. Then eq 8 becomes

$$k_{exp} = \frac{(\bar{k}_M K_A K_B + k_M' K_A) C}{1 + (K_A + K_B)C + K_A K_B C^2} \quad (9)$$

and $\bar{k}_M = k_M/\bar{V}$ because the partition coefficients are much higher than unity. In eq 9 subscript A then refers to **2a** or **2b** and subscript B to **1.** At sufficiently high concentration of surfactant the unity in the denominator of eq 9 becomes redundant and the equation can be transformed into

$$1/k_{exp} = (K_A + K_B)/\phi_M + K_A K_B C/\phi_M \quad (10)$$

where

$$\phi_M = (\bar{k}_M K_A K_B + k_M' K_A) \quad (11)$$

As shown in Figures 4 and 5, plots of $1/k_{exp}$ vs. CTAB concentration give fairly good straight lines for both reactions. This provides further support for the applicability of Berezin's equation.[24] From these plots the ratio of slope to intercept should produce a value for the ratio $K_A K_B/(K_A + K_B)$. However, it is known that the surface potential of the micelles decreases exponentially as the gegenion concentration is increased.[23] Thus for ionic surfactants the cmc is decreased by the addition of an inert electrolyte or gegenion common electrolyte.[7,23,38] In the case of anionic dodecyl sulfate micelles in the absence of added electrolyte it appears that at about twice the cmc the surface potential on the micelles practically approaches a limiting value. By contrast, for cationic dodecylpyridinium micelles limiting values are not reached even if much higher concentrations are employed.[39] In the light of these results, it is obvious that the assignment of the cmc to CTAB for obtaining the ratio $K_A K_B/(K_A + K_B)$ from Figures 4 and 5 is not straightforward. For a semiquantitative analysis we proceed as follows. If the reasonable assumption is made that the binding constants for **3** and **1** are about the same, the ratio $K_A K_B/(K_A + K_B)$ would be approximately equal to K_B since $K_A \gg K_B$ (vide infra). On the other hand, if the surface potential of CTAB is much less than 150 mV, implying that

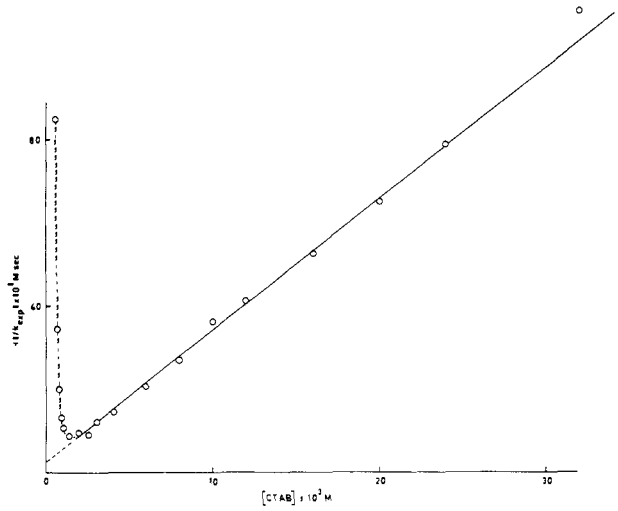

Figure 4. Plot of $1/k_{exp}$ vs. concentration of CTAB for the reduction of **1** by **2a.**

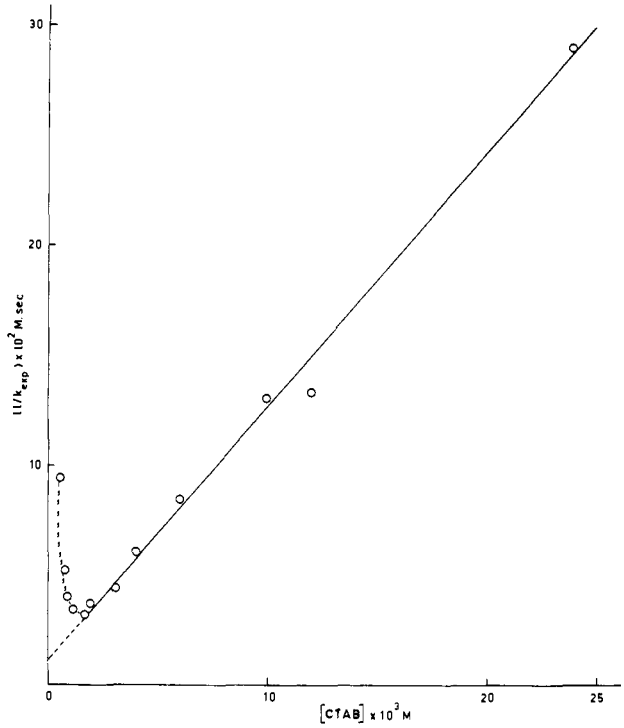

Figure 5. Plot of $1/k_{exp}$ vs. concentration of CTAB for the reduction of **1** by **2b.**

$(K_A + K_B)$ cannot be approximated to K_A, we will obtain $K_AK_B/(K_A + K_B) < K_B$. Now if we assign values between 2×10^{-3} and 2.5×10^{-3} M to the cmc of CTAB, the slope to intercept ratios for the plots shown in Figure 4 and 5 would range from 290 to 350 and are about equal for the same concentration of CTAB. Lower values for the cmc lead to much higher values of the slope to intercept ratio. The value of the binding constant obtained from gel filtration chromatography is 325 M^{-1}, and this in conjunction with a value of 150 mV for the surface potential of CTAB micelles would predict the cmc to be between 2×10^{-3} and 2.5×10^{-3} M. If the surface potential of CTAB would be much less than 150 mV, a much higher value for the cmc would be expected. This, however, is not plausible, since beyond 2×10^{-3} M CTAB the surface potential appears to be practically constant because Berezin's equation is followed (cf. Figures 4 and 5). Therefore, we suggest that the cmc for the present case should be taken as 2.2×10^{-3} M. We infer that this rather high value is not the concentration of CTAB where the concentration of micelles would become zero while approaching from the higher concentration side. It only means that if CTAB micelles were to appear with a surface potential corresponding to that of aggregates which exist beyond 2.5×10^{-3} M CTAB in the present systems, it will do so just above 2.2×10^{-3} M CTAB. Normally, micelles would appear at appreciably lower concentrations but with higher surface potential.

We now like to comment shortly on the observed cmc on the Sephadex G-25 column (see Experimental Section). For nonionic solutes it was previously observed that on Sephadex G-25 in conjunction with CTAB, one obtains cmc values for CTAB which are three times higher[40] than that determined in water.[41] Apparently, Sephadex gels put some constraint on the surface potential of CTAB micelles leading to the appearance of aggregates of much lower surface potential and a concomitant high cmc. Although we also assume a higher cmc for CTAB on Sephadex G-25, our value is not as high as those reported previously,[40] most likely because of a normal salt effect of the ionic solute on the cmc on the gel column.

From eq 10 and the condition $K_A + K_B \approx K_A$, the slope and intercept of the plots of Figure 4 and 5 are given by

$$\text{intercept} = 1/(\bar{k}_M k_B + k_M') \quad (12)$$

$$\text{slope} = K_B/(\bar{k}_M K_B + k_M') \quad (13)$$

Substituting $K_B = 325$ M^{-1} and cmc $= 2.2 \times 10^{-3}$ M, the factor $(\bar{k}_M K_B + k_M')$ becomes 100 and 30 M^{-1} s^{-1} for the oxidation of **2a** and **2b,** respectively. In aqueous solutions **2b** is oxidized by **1** predominantly via an inner-sphere mechanism.[16] Further, we note that since the bivalent ion **2b** is strongly bound to micelles in aqueous media (vide infra), it is fair to presume that it will be in a fashion such that the hydrophobic cyclohexane ring of the ligand penetrates to some extent beyond the Stern layer into the micellar core. Since the water molecule in the first coordination sphere of the central metal ion is located perpendicularly to the cyclohexane ring, the situation arises that in the preferred orientation of the complex bound to the micelle, the water molecule will be oriented parallel to the micellar surface. This will then effectively hamper the operation of an inner-sphere path in the interphase process. If a micelle-induced operation of an outer-sphere path is ruled out in the interphase process, then k_M' for oxidation of **2b** can be equated to zero. With these assumptions, the rate constant for encounters in the micellar phase, k_M $(= 3.3 \times 10^{-2}$ M^{-1} $s^{-1})$, can be evaluated using $\bar{V} = 0.363$ M^{-1} and $K_B = 325$ M^{-1}. Interestingly, this rate constant is about six times *less* than that in bulk aqueous solution. On the other hand, in the oxidation of **2a** by **1** in aqueous solutions under weakly acidic conditions outer-sphere as well as inner-sphere mechanisms are operative, the former being the more favorable.[16,18] Unfortunately, the contributions of outer-sphere and inner-sphere mechanisms to k_M and k_M' are not estimable at the moment. But in contrast to the reaction of **2b,** for **2a** no restriction on the operation of an inner-sphere path in the interphase reaction can be imposed on geometric grounds, because of the absence of specific sites for hydrophobic bonding. The $Coedta^{2-}$ complex is about spherically symmetrical from the electrostatic point of view, leading to nonpreferential binding including situations in which the pivot water molecule lies perpendicular to the micellar surface as demanded for an inner-sphere interphase reaction. Interphase reactions via an outer-sphere path are also conceivable since it has recently been demonstrated[8a,42] that electronic interactions between electron donor and acceptor pairs can range over distances considerably larger than collision diameters. In addition, it can be shown[30] that Co(II) aminocarboxylate complexes will behave as stronger reductants on the micellar surface as a result of its

apparent higher standard redox potential. Therefore, the deduction that k_M' is larger than k_M because $[k_M(K_B/\overline{V}) + k_M'] \approx 100\ M^{-1}\ s^{-1}$ and $(K_B/\overline{V}) \approx 9 \times 10^2$ is understandable. The value of k_M for the reaction of **2a** would then also be *less* than the rate constant for the reaction in aqueous solution regardless of the precise mechanism of the electron transfer process. The increase in free energy of activation for the reduction of **1** by **2a** and **2b** on the micellar surface as revealed in the lower k_M values is most likely primarily a consequence of the decrease in freedom of the reactants **1**, **2a**, and **2b** upon binding to the micellar surface. This binding process will be accompanied by a constraint on the encounters between the reactants on the surface of the micelle.

It is worth emphasizing that the kinetic parameters of the micelle-induced electron transfer processes are affected by a mélange of physical interactions, some of which may, at least in principle, partially compensate the rate-retarding effect described above. For instance, it is conceivable that owing to the lower dielectric constant in the vicinity of the micellar surface and also owing to some loss in solvation of the reactants, the outer-sphere reorganization energy of the outer-sphere path will be reduced as compared with that in bulk water. Furthermore, it may be anticipated that the better charge neutralization of the anionic reactants near the cationic head groups of the surfactant molecules within the micelle will also facilitate the redox reaction. Finally, it is possible that a micelle-induced change of the pK_A of **1** will affect the propensity of this complex to participate in inner-sphere electron transfer processes. In aqueous solutions, **1** behaves as a weak acid[11,43] (pK_A = 8.1) and the complex is heptacoordinated with the seventh coordination position occupied by a water molecule.[16,43] Now the pK_A values of weak acids may be either increased[32] (leading to a slower inner-sphere reaction) or decreased[44,45] (faster inner-sphere reaction) as compared with those in water. Two major causes for the micellar effect involve the dielectric constant of the medium near the micellar surface[45,46] and the electric potential at the micellar surface.[45]

In summary, we conclude that the rate enhancements observed up to 1.5×10^{-3} M CTAB may be attributed to the increase in the concentration of the reactants in the micellar phase with increasing concentration of CTAB. Because of the salt effect of the reactants under the employed reaction conditions, the cmc of CTAB micelles[47] may be lowered appreciably. In the concentration range between the cmc and 1.5×10^{-3} M CTAB the apparent second-order rate constant further increases despite the fact that the binding constant of the reactants continues to decrease with increasing concentration of CTAB because of the lowering of the surface potential of the micelles caused by the increase in gegenion concentration.[23,24] Above 1.5×10^{-3} M CTAB the lowering of the surface potential as well as the dilution of the reactants in the micellar pseudophase leads to a sharp decrease in rate.

Our present results show that the rates of simple electron transfer processes may be considerably enhanced in micellar environments and support the notion that for electron transfer in living systems the appropriate positioning of the electron donor and acceptor species in cell membranes may be one of the crucial factors in determining the efficiency of these processes. A quantitative elucidation of the intimate details of the catalytic effects constitutes a considerable challenge for further studies of electron transfer reactions in bioaggregates.

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Supplementary Material Available: Tables I (gel filtration parameters for Co(cydta)$^-$ with CTAB) and II (second-order rate constants for the oxidation of Co(edta)$^{2-}$ and Co(cydta)$^{2-}$ by Mn(cydta)$^-$) and Appendix A (3 pages). Ordering information is given on any current masthead page.

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Preparation and Kinetic Properties of Cysteine Surfactants

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Abstract: A cysteine surfactant (IV, AS-Cys) was synthesized by coupling cysteine to *N*-cetyl-*N*,*N*-dimethyl-*N*-β-aminoethylammonium chloride. Under micellar conditions at pH 8.0, excess AS-Cys cleaved *p*-nitrophenyl acetate (PNPA) with $k_\psi^{max} = 1.04\ s^{-1}$ (corresponding to $k_{cat} = 26.0$ L/mol·s), and the formation of *S*-acetyl-AS-Cys. The latter surfactant underwent intramolecular S → N transfer ($k^{max} = 0.44\ s^{-1}$ for nonmicellar conditions at pH 8.0, $k = 0.01\ s^{-1}$ in 5.5×10^{-3} M micellar cetyltrimethylammonium chloride) affording *N*-acetyl-AS-Cys. A second mole of PNPA could be cleaved by the free SH group of micellar *N*-acetyl-AS-Cys ($k_\psi^{max} = 1.45\ s^{-1}$ at pH 8.0, corresponding to $k_{cat} = 36.3$ L/mol·s) yielding *N*,*S*-diacetyl-AS-Cys. S-Deacetylation of the latter was slow ($k_\psi \sim 5 \times 10^{-5}\ s^{-1}$) under micellar conditions at pH 8, but could be accelerated by comicellization with imidazole-functionalized surfactants (e.g., $k_\psi = 9.2 \times 10^{-4}\ s^{-1}$). Various mechanistic aspects of these reactions are discussed in detail.

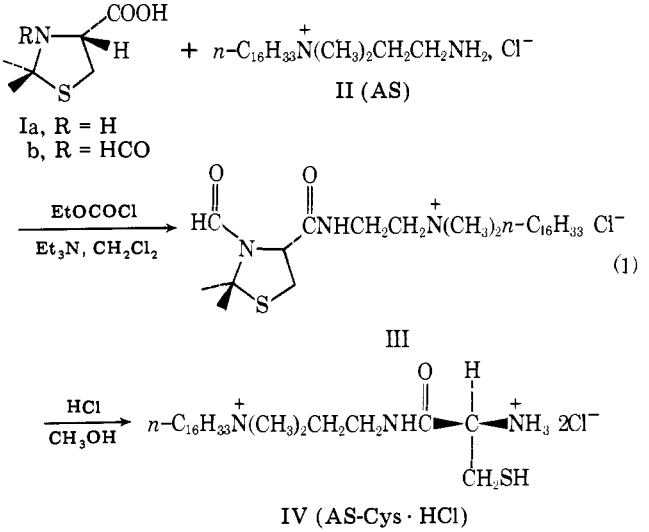
Continued interest in refining the analogy between micellar and enzymic catalysis has greatly stimulated the development of functional micellar reagents.[2-5] Although sulfhydryl surfactants are inherently attractive targets because of the key nucleophilic role played by the SH moiety in the cysteine proteinases papain, ficin, and stem-bromelain,[6] the facile oxidative dimerization of thiols, particularly under micellar conditions,[7] presents synthetic and mechanistic difficulties, and few relevant studies have appeared.

N-Dodecanoyl-DL-cysteine,[8] alkane thiols,[9] coenzyme A,[10] and glutathione,[10] each solubilized in micellar cetyltrimethylammonium[8,10] (CTA) or stearyltrimethylammonium bromides, were shown to accelerate the cleavage of *p*-nitrophenyl acetate (PNPA). Recently, Chaimovitch et al. investigated the effect of micelles on the rate of the *S*- to *N*-acetyl transfer of *S*-octanoyl-β-mercaptoethylamine.[11] In none of these cases, however, have *self-contained* thiol-functionalized surfactants been examined.

Recently, we prepared the first SH-functionalized surfactant catalyst, and offered a preliminary report of its nucleophilic properties toward PNPA.[12] Here, we present full details of the previous work, additional studies of mechanistically relevant comicellar systems, and an examination of the reaction sequence which ensues subsequent to the initial attack of the surfactant on PNPA.

Results

Synthesis. Using the procedure of Sheehan and Yang,[13] L-cysteine hydrochloride was condensed with acetone, affording thiazolidine Ia. The latter, upon formylation, gave Ib, which was converted to the mixed anhydride with ethyl chloroformate, and then coupled to amino surfactant II[14] (AS), yielding protected surfactant III. Deprotection with 1 N HCl in 50% aqueous methanol, followed by trituration with dry ether, gave crystalline surfactant IV (AS-Cys) as the hydrochloride. These reactions are summarized in eq 1.



(1)

IV (AS-Cys · HCl)

AS-Cys is sensitive to air; consequently, it was stored under high vacuum and manipulated under nitrogen. A satisfactory elemental analysis was obtained for immediate precursor III, but was not attempted for AS-Cys itself. The NMR spectrum of the surfactant, however, was definitive ($\delta_{D_2O}^{DSS}$): 0.83, crude "t", $CH_3(CH_2)_{15}$; 1.27, "s", $(CH_2)_{14}$; 3.17, s, $N^+(CH_3)_2$; 3.1-3.9, m, ($N^+CH_2CH_2NHCO + (CH_2)_{14}CH_2N^+ + CH_2SH$); 4.27, t, $J = 6$ Hz, methine. The integral areas appeared in the appropriate ratio. Moreover, an assay with Ellman's reagent[15] at pH 8.0 indicated that AS-Cys possessed 0.99 free SH group per molecule.

Owing to its propensity for oxidation, we did not determine the critical micelle concentration (cmc) of AS-Cys, but we estimate this value to be 5×10^{-4} M (0.02 M phosphate buffer, $\mu = 0.05$ (KCl), 25 °C), based on the cmc's of the related alanine and histidine surfactants under these conditions.[14]

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