Micelle-Enhanced Dissociation of a Ru Cation /DNA Complex†

R. A. Marcus*

Noyes Laboratory of Chemical Physics, California Institute of Technology, Pasadena, California 91125

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Anionic surfactant monomers have a large catalytic effect on the dissociation rate constant of a Ru_2^{4+}−DNA complex, an effect further enhanced upon exceeding the critical micelle concentration. Electrostatic estimates are made of this effect, the effect of salt and temperature on the binding constant, and of the binding constant itself. The effects are compared with the experiment, and the calculated salt effect on the binding constant is compared with condensation theory. The results indicate that the catalytic effect is primarily nonelectrostatic (hydrophobic) in nature.

I. Introduction

For decades micelles have been used to sequester drug cations dissociated from DNA. Recently Westerlund et al.[1] reported that not only do anionic micelles sequester cations but they also accelerate the rate of dissociation dramatically. The effect was first discovered when studying the extremely slow DNA binding kinetics of a rigid dimeric Ru complex.[2] It was subsequently studied for another flexible Ru dimer compound[3] in which each Ru was attached to two phenanthrolines and a phenazine. The two phenazines of the Ru^{2+} complexes were linked by a hydrocarbon chain and the dimeric complex threaded through DNA, a polyanion. In this complex, the phenazines were intercalated in the DNA stack, separated by two base pairs. The overall interpretation was based in part on the fluorescence behavior.[3]

The surfactant used to extract the Ru_2^{4+} complex from the DNA was sodium dodecyl sulfate (SDS). A plot of the rate of extraction of the Ru_2^{4+} complex versus the SDS concentration was linear and had a finite intercept at zero SDS concentration.[1] When the critical micelle concentration (CMC) was exceeded, the slope of the plot became much steeper. Dissociation rate constants for the various processes are obtained from these data. They differ in units and in size of collision partners. For any comparison, it is useful to place them first on the same basis, which we do as follows:

We denote by k_d the first-order rate constant for the unassisted dissociation of the Ru_2^{4+} complex from DNA, by k_d^m the second-order dissociation rate constant due to bimolecular interaction with a surfactant monomer below its CMC, and by k_d^M the corresponding quantity (slope) above the CMC. From the intercept of the plot, one finds[1] $k_d \cong 0.001\ s^{-1}$, and from the slope of the plot below the CMC one finds[1] $k_d^m = 0.6\ M^{-1}\ s^{-1}$. From the slope of the plot above the CMC, we estimate a rate constant of $1.42\ M^{-1}\ s^{-1}$. Since there are about 90 monomers per SDS micelle,[4−7] the result for k_d^M when expressed in terms of micelle concentration units is 90 times larger than the k_d^M calculated using monomeric SDS (i.e., it is 130 $M^{-1}\ s^{-1}$). In the present paper, we explore the possible sources of this catalysis by the monomer and by the micelle.

The paper is organized as follows: The various rate constants are placed on the same basis in section II A, and formal expressions for the rate constants are also given there. After an overview of electrostatic potentials and free energies in section II B, an equation is obtained in section II C for the electrostatic free energy of activation for the DNA−micelle interaction in the transition state, and in section II D for the Ru_2^{4+} complex−DNA and the Ru_2^{4+} complex−micelle interaction there. An equation for the dependence of the equilibrium constant K_{obs} for the DNA−Ru_2^{4+} complex on salt concentration is obtained in section II E and for the magnitude of K_{obs} itself in section II F. Numerical calculations are given and discussed in section III A for the surface charge densities, for the effect of temperature on K_{obs} in section III B, the effect of salt on K_{obs} in section III C, and the value of K_{obs} itself in section III D. The calculated salt effect on K_{obs} is compared in section III E with that calculated from condensation theory. The electrostatic catalytic salt effect is calculated for the surfactant monomer and micelle in sections III F and III G, respectively, and a nonelectrostatic (hydrophobic) effect is roughly estimated and discussed in section III H. Concluding remarks are made in section IV.

II. Theory

A. Overall Kinetic Considerations and Reduction of Rate Constants to the Same Basis. To gain insight into the catalytic effect, we first remove the effect of differences in units and in molecular size. One can do so by comparing the values of k_d/ν, k_d^m/Z_m, and k_d^M/Z_M, where ν is a frequency for the dissociation coordinate leading to the "transition state" (TS) of the process, and Z_m and Z_M are collisional frequencies of the relevant anion m or M with the nearest Ru^{2+} moiety in the Ru_2^{4+} complex. For ν we take ca. $10^{13}\ s^{-1}$ (corresponding to some low-frequency vibration), and for Z_m we use a typical value of the order of $10^{11}\ M^{-1}\ s^{-1}$. (We note that for this system it may be lower[8] by a factor of 2 and similarly for Z_m.) Since a molecular cross-section varies as the 2/3 power of a molecular volume, we take $Z_M \sim Z_m(90)^{2/3}$ (i.e., $Z_M = 2 \times 10^{12}\ s^{-1}$). We thus compare the values of $0.001/10^{12} = 10^{-15}$, $0.5/10^{11} = 5 \times 10^{-12}$, and $160/2 \times 10^{12} = 8 \times 10^{-11}$. On such a basis there is a very large catalytic effect by the monomer, a factor of 50 000, with a further increase of a factor of ∼15 when the bimolecular partner is a micelle instead of a monomer.

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* E-mail address: Ram@caltech.edu.

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To obtain some insight into the principal factors affecting the catalytic effect of the factor of 15 of the micelle relative to that of the monomer unassisted dissociation, it is also necessary to understand the even more dramatic catalytic effect of the factor of about 50 000 of the monomer relative to the unassisted dissociation. Can electrostatic factors alone account for such effects, or to what extent is it necessary to invoke non-electrostatic influences? There are two separate issues, the catalytic effect of the monomer relative to unassisted dissociation and the catalytic effect of the micelle relative to the monomer.

The electrostatic interactions include the attraction of the dissociating Ru_2^{4+} to the anionic DNA in which it is threaded, the attraction of the nearest Ru^{2+} to the incoming anionic micelle or monomer, and the repulsion between the DNA and the micelle or monomer. There is also the non-electrostatic interaction between the Ru complex and the DNA and the micelle or monomer, and the entropic effect due to the small probability of finding a micelle or monomer close to a Ru_2^{4+} in the DNA. This last entropic effect was accounted for by introducing in the previous section a comparison of rate constants reduced to the same basis by introducing collision frequencies Z and the vibration frequency ν. The collision frequencies contain the small probability of finding the collision partners near each other instead of being in the body of the solution.

One expects the Ru_2^{4+} to be more strongly attracted electrostatically to the micelle than to the monomer, and so the extra catalytic effect of the micelle becomes qualitatively understandable. In particular, the electrostatic potential of an anion (surfactant monomer or micelle) varies approximately as the charge divided by the separation distance, multiplied by a "shielding factor" due to the ionic atmosphere. The intrinsic negative charge of the micelle is roughly proportional to the number of monomers it contains and so varies as the cube of the radius. On the other hand, the separation distance from the nearest Ru^{2+} in the Ru_2^{4+} complex is proportional to inverse first power of the radius plus a constant. So, the net electrostatic attraction to Ru_2^{4+} increases somewhat faster than the square of the radius and is therefore expected to be substantially larger for micelles than for monomers. This feature is borne out in more detailed calculations. The effect is partly offset by the larger repulsion between the DNA and the micelle relative to DNA and the monomer and by the hydrophobic attraction of the exposed hydrocarbon chain of the monomer to the aromatic ligands of the Ru^{2+}.

There are several components of the reaction coordinate in the transition state (TS) for the dissociation of a Ru_2^{4+} complex from the DNA: a DNA$-Ru^{2+}$ distance and, in a monomer or micelle assisted dissociation, also the distance between the monomer or micelle and the nearest Ru^{2+} in the complex. There is a contribution from each change to the free energy of activation.

For the unassisted dissociation, the free energy to reach the TS is the sum of that required to decrease the non-electrostatic part of the bonding of the Ru_2^{4+} complex with the DNA ($\Delta G_{np}^{\dagger}$) and the change in electrostatic free energy of interaction of the two Ru^{2+} moieties with the DNA ($\Delta G_{D-Ru}^{\dagger}$). For a micelle or monomer assisted dissociation the $\Delta G_{np}^{\dagger}$ also contains a non-electrostatic binding of the Ru_2^{4+} complex to m or M. There is, in addition, the electrostatic free energy of interaction of the outer Ru^{2+} with the micelle ($\Delta G_{Ru-M}^{\dagger}$) and the electrostatic free energy of repulsion of DNA and the micelle ($\Delta G_{D-M}^{\dagger}$). For the dissociation assisted by the monomer, the same symbols are used but with M replaced by m. The $\Delta G_{np}^{\dagger}$ and $\Delta G_{D-Ru}^{\dagger}$ have same meaning as before, but their values can differ from before since the position of the TS along the reaction coordinate can differ.

An approximate TS theory description of the unassisted and assisted dissociation of the Ru_2^{4+} complex from DNA yields expressions for the various rate constants. By evaluating several of the partition functions approximately, we have[8]

$$k_d = \nu e^{-(\Delta G_{np}^{\dagger}+\Delta G_{D-Ru}^{\dagger})/kT} \quad \text{(unassisted dissociation)} \quad (1)$$

$$k_d^M = Z_M e^{-(\Delta G_{np}^{\dagger}+\Delta G_{D-Ru}^{\dagger}+\Delta G_{Ru-M}^{\dagger}+\Delta G_{D-M}^{\dagger})/kT} \quad \text{(dissociation by micelle)} \quad (2)$$

$$k_d^m = Z_m e^{-(\Delta G_{np}^{\dagger}+\Delta G_{D-Ru}^{\dagger}+\Delta G_{Ru-m}^{\dagger}++\Delta G_{D-m}^{\dagger})/kT} \quad \text{(dissociation by monomer)} \quad (3)$$

B. Electrostatic Potentials and Free Energies: General Remarks. For the electrostatic contributions, we use approximate solutions of the nonlinear Poisson−Boltzmann (PB) equation for the electrostatic potential in systems of spherical and cylindrical geometry but without linearization. The PB equation is a mean-field treatment of electrostatic interaction. Its solution has been the subject of numerous studies, as discussed in two recent brief surveys.[9,10] Approximate solutions have been compared with computer-based solutions and with more molecular approaches (e.g., refs 11−19). The relationship between the PB solution and "condensation theory"[20−22] for cylindrical macro ions and their atmospheres has been discussed.[17−19] In particular, the results become the same only when the radius of the rod is assumed to be extremely small, for example, 0.001 nm[19] (i.e., when the rod is a line charge). The condensation behavior for spherical macro ions[23] and for liquid crystals[24] has also been studied. The related topic of renormalization of bare to effective charges of macro ions has been treated (e.g., refs 25−27).

C. DNA−Micelle Electrostatic Free Energy of Activation to Form the TS. For $\Delta G_{D-M}^{\dagger}$ in eq 2, we use Derjaguin's method,[28,29] which applies when the radii (a values) of D and of M are large relative to the thickness of the electrical double layer ($1/\kappa$), but even when $\kappa a \sim 1$ the results are found to be reasonably good. The Derjaguin approximation is based on the solution of the PB equation for two parallel planes. The PB equation for the potential ψ near a single plane is[30]

$$\frac{d^2\psi}{dx^2} = \frac{2cze}{\epsilon}\sinh\frac{ze\psi}{kT} \quad (4)$$

where ze is the ionic charge of a z:z electrolyte; c is the salt concentration at infinite distance; and ϵ denotes ϵ_o and ϵ_r, with ϵ_o being the permittivity of a vacuum and ϵ_r being the permittivity (dielectric constant) of the solution relative to that of a vacuum. We use SI units.

The charge density σ_s at a plane surface is related to the electrostatic potential at that surface ψ_s by[30]

$$\sigma_s = (4cze/\kappa)\sinh(ze\psi_s/2kT) \quad (5)$$

where κ is the Debye length, $(2z^2e^2c/\epsilon kT)^{1/2}$ for a z:z electrolyte.

The potential ψ at any point x is related to that at the surface ψ_s by[30]

$$\tanh(ze\psi(x)/4kT) = e^{-\kappa x}\tanh(ze\psi_s/4kT) \quad (6)$$

Since $ze\psi_s/4kT$ and $ze\psi/4kT$ are large, each tanh is close to unity, and so eq 6 makes $ze\psi/4kT$ ultrasensitive to κx. Such a

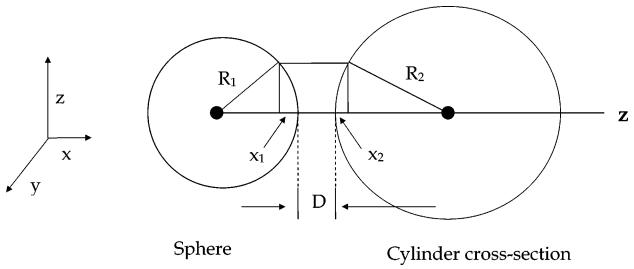

Figure 1. Cross-section of a sphere of radius R_1 (SDS) and of a cylinder of radius R_2 (DNA), with an edge to edge separation distance of D. The x_is denote the distances between the foot of a perpendicular and the edge of the sphere (x_1) or of the cylinder (x_2).

solution should ultimately be replaced by one that takes into account the discrete nature of the phosphate, Ru^{2+}, and other ionic charges.

For the interaction of two parallel planes of charge densities, σ_1 and σ_2 are needed. The electrostatic free energy of interaction per unit area (W) in the approximation of weak overlap of the two electrical double layers is given by[31]

$$W \cong (64kTc/\kappa)\gamma_1\gamma_2 e^{-\kappa d} \tag{7}$$

where d is the distance between the two parallel surfaces, and

$$\gamma_i = \tanh\,(e\psi_s^i/4kT) \tag{8}$$

($i = 1, 2$). To obtain $\Delta G^{\dagger}_{D-M}$ using Derjaguin's method, the interaction energy W in eq 7 is integrated (Figure 1) over the coordinates of the sphere $dy_1\ dz_1$ from $-\infty$ to ∞ for each coordinate:

$$W = 64kTc\gamma_1\gamma_2 \int\int e^{-\kappa d}\, dy_1\, dz_1 \tag{9}$$

where the geometric relations between d, y_1, and z_1 are given in ref 32. This W is the term denoted in eq 2 by $\Delta G^{\dagger}_{D-M}$:

$$\Delta G^{\dagger}_{D-M} = 64kTc\gamma_1\gamma_2(2\pi/\kappa^2)\left(\frac{R_2}{R_1+R_2}\right)^{1/2} R_1 e^{-\kappa D} \tag{10}$$

for the interaction of a sphere of radius R_1 with a cylinder of radius R_2. When $R_2 \rightarrow \infty$, eq 10 reduces to the expression[29,30] for the interaction of the sphere 1 with a plane 2.

D. Ru Complex−DNA and Ru Complex−Micelle: Electrostatic Free Energy of Activation To Form the TS. For the other electrostatic-based $\Delta G^{\dagger}$ values in eqs 1−3, we need electrostatic potential ψ at the position r_{Ru} of the relevant Ru^{2+} in each case. If $\psi_{D-Ru}(r_{Ru})$ is the potential at r_{Ru} due to the DNA, then if the Ru^{2+} were treated as a probe charge so providing an upper limit, we would have

$$\Delta G^{\dagger}_{D-Ru} = \Delta(2e\psi_D(r_{Ru})) \tag{11}$$

where Δ denotes the change due to extending the distance of Ru^{2+} from the DNA in order to reach the TS. For ΔG^{+}_{Ru-M} we have

$$\Delta G^{\dagger}_{Ru-M} = 2e\psi_M(r_{Ru}) \tag{12}$$

where $\psi_M(r_{Ru})$ is the potential due to the micelle at the point r_{Ru} occupied by this Ru^{2+}.

An expression relating the potential ψ_s at the surface of a sphere to the change density σ_s on a sphere or on a cylinder, correct to first order in $1/\kappa a$, where a is the radius, is[15,16]

$$\sigma_s = \frac{4zec}{\kappa}\left[\sinh\frac{ze\psi_s}{2kT} + \frac{K}{\kappa a}\tanh\frac{ze\psi_s}{4kT}\right] \tag{13a}$$

where $K = 0$, 1, and 2 for the plane, the cylinder, and the sphere, respectively. This expression reduces to eq 5 when $\kappa a \rightarrow \infty$. A simple and, for our purposes, accurate approximation for solving eq 13a for ψ_s is as follows: If ψ_s^o is the value of ψ_s, which satisfies eq 5, then we have

$$\sinh\frac{ze\psi_s}{2kT} \cong \sinh\frac{ze\psi_s^o}{2kT} - \frac{K}{\kappa a}\tanh\frac{ze\psi_s^o}{4kT} \tag{13b}$$

obtained by substituting ψ_s^o for ψ_s in the last term in eq 13a, which is a small perturbation term.

The potential ψ at any point distant r from the center of the body is, to this order in $1/\kappa a$,[15,16]

$$\psi(r) \cong \psi_o(r) + \frac{\psi_1(r)}{\kappa r} \tag{14}$$

where $\psi_o(r)$ is the $\psi(x)$ satisfying eq 6. The first-order correction $\psi_1(r)$ in eq 14 is given by[15,16]

$$\psi_1(r) = \frac{K}{2}\left(\sinh\frac{ze\psi_o}{2kT}\right)\left[\left(\tanh^2\frac{ze\psi_s}{4kT}\right)(1 - e^{-2\kappa}(r-a)) - 2\kappa(r-a)\right] \tag{15}$$

where K appeared also in eq 13.

If a Ru^{2+} were treated as a probe charge, then for $\Delta G^{\dagger}_{Ru-M}$ we would have

$$\Delta G^{\dagger}_{Ru-M} = 2e\left(\psi_o + \frac{\psi_1}{\kappa r}\right) \tag{16}$$

where ψ_o and ψ_1 are evaluated at the point occupied by this Ru^{2+} and satisfy eqs 6 and 15, respectively, with $K = 2$ (spherical SDS). For $\Delta G^{\dagger}_{Ru-D}$, eq 16 applies, but now $K = 1$ (cylindrical DNA).

E. Dependence of K_{obs} on Salt Concentration. It is useful to apply first some of the above expressions to a simpler problem to see the limitations or constraints. We give the equations here and their numerical application in the next section. We consider first the effect of salt concentration c on the equilibrium constant for forming the bound Ru_2^{4+} complex. If the two +2 charges were close to the surface of the DNA, then the equilibrium constant K_{obs} for the formation of the complex would be proportional to $\exp(-4e\psi_s/kT)$, where ψ_s is negative. The dependence of $\ln K_{obs}$ on $\ln c$ would be

$$\frac{\partial \ln K_{obs}}{\partial \ln c} = \frac{\partial(4e\psi_s/kT)}{\partial \ln c} \tag{17}$$

F. Magnitude of K_{obs}. We consider next the magnitude K_{obs} itself. If the ΔH_{obs} for the equilibrium constant K_{obs} is essentially zero, then the association equilibrium constant is

$$K_{obs} = e^{\Delta S_{obs}/k} \tag{18}$$

where

$$\Delta S_{obs}/k = 4e\psi_s/kT + \Delta S_{trans} \tag{19}$$

since it is seen later in the numerical section that the ΔH_{obs} associated with the electrostatic term is zero. The ΔS_{trans} in eq 19 is the entropy associated with transferring the Ru_2^{4+} complex

from the body of the solution (for a standard state of 1 M, i.e., units of M^{-1} for K_{obs}) to a threaded position in the DNA. While this $\Delta S_{obs}/k$ can be estimated from detailed statistical mechanical calculations, we can obtain a quick rough estimate of it as follows: the entropy of vaporization of a normal liquid to a gas of 1 atm pressure at 25 °C is 21.7 e.u. Since 1 atm. corresponds to 1/22.4 M, the $\Delta S_{trans}/k$ is approximately $-(21.7 \div 1.98 - \ln 22.4) = -9.3$. We thus have

$$\Delta S_{obs}/k = -4e\psi_s/kT - 9.3 \qquad (20)$$

(ψ_s is negative). We investigate the results based on eqs 17−20 in the next section.

III. Numerical Calculations

A. Surface Charge Densities. The surface charge densities of the DNA and of the micelle are readily estimated. For the DNA there is a unit charge e every 0.17 nm of axial length b, and so $\sigma = e/2\pi Rb$,[21,22] with the radius $R = 0.9$ nm,[33] with $b = 0.17$ nm, and so $\sigma/e = 1.0 \times 10^{14}$cm^{-2}. For the micelle we have $\sigma = -q/4\pi R^2$, where q is the charge. For SDS an R of 1.69 nm[34] and a micelle composed of ~90 SDS molecules[4] have been estimated. Thus, $\sigma/e = -1.0 \times 10^{15}$ cm^{-2}, and so the micelle has a σ/e some 10-fold greater than that of DNA. The experiments in ref 1 were performed at 50 °C, and so the values for ϵ and κ appropriate to that T are used.[35]

B. Effect of *T* on K_{obs}. It is also instructive to consider the effect of T on K_{obs}. When one introduces the dependence of κ on T via $\epsilon(T)$ and kT, one finds that κ is essentially independent of T (in the range examined, 25−75 °C). Thus, $e\psi_s/kT$ calculated from eq 13 is independent of T in this approximation. Accordingly, the calculated K_{obs} is also then independent of T. Since $\Delta G_{obs} = -kT \ln K_{obs}$, we have that the calculated $\Delta G_{obs}/T$ is independent of T (i.e., $\Delta H_{obs}[= \partial(\Delta G_{obs}/T)/\partial(1/T)]$ is zero, in the approximation of this theory). This observation agrees with the measured ΔH_{obs} values, which are small or close to zero for the intercalation into DNA of ethidium and propidium[36] and also for the intercalation of the Ru complex.[37] In condensation theory there is also the consequence, on different grounds, that the theoretical ΔH_{obs} is zero.

C. Effect of Salt on K_{obs}. We consider next the magnitude of the salt effect, $\partial \ln K_{obs}/\partial c$. For the very simple case of large ψ_s and large κa, eq 13 becomes $\sigma_s \cong (2ec/\kappa) \exp(e\psi_s/2kT)$. Noting that κ is proportional to $\sqrt{c}$, $\partial \ln K_{obs}/\partial \ln c = -\partial(4e\psi_s/kT)/\partial \ln c = -4$ for the limiting case of a very large magnitude of ψ_s.

Although $e\psi_s/2kT$ is large for DNA, it is not extremely large, and although κa is close to unity, it is not much greater than unity. So one expects some deviation of this limiting slope of −4. To avoid these two approximations, we consider eq 13 and a range of salt concentrations, 0.05−0.20 M, for which data have been obtained. For $c = 0.05$, 0.10, and 0.20 M one finds from eq 13 that the correction term (the last term in eq 13b makes a negligible contribution, and so eq 5 suffices. One finds that $\partial \ln K_{obs}/\partial \ln c$ is −4.0. The observed slope for *ct* DNA was −3.7 and for (poly dA−dT)$_2$ it was −3.3.[38]

Shielding by counterions will modify the calculated value of $\partial \ln K_{obs}/\partial \ln c$. In that case, the $\partial(4e\psi_s/kT)/\partial \ln c$ is replaced by $\partial(4e\psi/kT)/\partial \ln c$, where ψ is related to ψ_s by eqs 6 or 14−15. Qualitatively the effect is in the correct direction to explain the difference between −4.0 and the experimental values. Use of eq 6 and, for concreteness, an $x = 0.2$ nm, yields a slope of −3.6, for example. However, because of the sensitivity of eq 6 to the continuum approximation noted earlier, this quantitative result has to be regarded with caution.

D. Estimate of K_{obs}. A K_{obs} can also be estimated and compared with experiment: From the $e\psi_s/kT$ of −7.8 at 0.1. M salt, we find from eqs 18−20 that the calculated K_{obs} is $\exp(4 \times 7.8-9.3)$ (i.e., 3×10^9 M^{-1}). The experimental values at 0.1 M and 20 °C are $7.7 \pm 3 \times 10^8$, $8.0 \pm 2.4 \times 10^8$, and $4.8 \pm 4 \times 10^7$ for the Λ−Λ and Δ−Λ enantiomers of the Ru_2^{4+} complex in *ct* DNA and for the Δ−Δ enantiomer in (poly dA−dT)$_2$ DNA, respectively, in moderate agreement with the above "back of the envelope" calculation. Not included, for example, was any hydrophobic entropic change accompanying the association of the Ru_2^{4+} complex with the DNA.

E. Comparison with Condensation Theory for the Salt Effect on K_{obs}. The above calculated value of $\partial \ln K_{obs}/\partial \ln c$ is close with the calculated result of condensation theory. In the latter an expression has been given for $\partial \ln K_{obs}/\partial \ln c$:[39]

$$\frac{\partial \ln K_{obs}}{\partial \ln c} = -2\left(1 - \frac{1}{2\xi}\right) \qquad (21)$$

where

$$\xi = e^2/4\pi\epsilon kTb \qquad (22)$$

and b, the average distance between charges along the rod, is 0.17 nm for DNA, yielding $\xi = 4.2$. One notes that in eqs 21−22, the radius of the cylinder does not appear, only the line charge density. One finds $\partial \ln K_{obs}/\partial \ln c = -3.5$. This value is close to the experiment, as noted previously in ref 32. The experimental value of K_{obs} was obtained from the binding data after an analysis based on the McGhee−von Hippel treatment[40] of the effect of ligands that occupy multiple sites on the DNA. (It was assumed[41] that four sites are made inaccessible by the Ru_2^{4+} complex.) In the limit of very large ξ (large charge density), eqs 18 and 19 yield −4 for the answer, just as does the treatment based on eq 17.

F. Kinetic Salt Effect. In addition to the equilibrium studies of salt effects there are also kinetic studies. The reaction rates were biexponential and the ratio of forward (k_f) and reverse (k_r) rates of the faster components agreed well with the equilibrium constant. To the extent that in the TS the Ru_2^{4+} moiety is not situated at infinity, the dependence of $\ln k_f$ on $\ln c$ will not be as large as that of $\ln K_{obs}$ on $\ln c$. For example, if in the transition state one Ru^{2+} were at a fairly large distance from the DNA but the other was still near the surface, $\partial \ln k_f/\partial \ln c$ would be about half of the value for $\partial \ln K_{obs}/\partial \ln c$, namely, about −1.7. The observed value for $\partial \ln k_f/\partial \ln c$ for the Δ−Δ enantiomers is larger, about −2.4, indicating, in this view, that in the TS the other Ru^{2+} ion is also somewhat removed from the surface. It is clear that any detailed analysis will require structural calculations of the positions of each Ru^{2+} in the TS. The approximate theory provides only a rough qualitative guide.

G. Catalytic Effect of Surfactant. We turn next to the effect of the surfactant on the dissociation rate. In the transition state we denote the distance of the outer Ru^{2+} ion from the center of the SDS sphere by r_1 and from the axis of the DNA by r_2. Their values would be chosen so as to minimize the free energy of the transition state of the D-Ru-M system. The interaction in eqs 2 and 3 is more than "electrostatic". In particular, the interaction of the monomer and the outer Ru^{2+} is enhanced by a hydrophobic interaction of the hydrocarbon chain in the SDS monomer with the organic ligands of Ru^{2+}. When ion pair constants for such an interaction become available, this contri-

bution to ΔG^{κ}_{el}(Ru−m) can be added. In the meanwhile, we focus on comparing the $\Delta G^{\dagger}$ values in eqs 2 and 3.

A couple of iterations of eq 13 yields ψ_s in terms of σ_s, using eq 5 (i.e., $\kappa a = \infty$ for the zeroth order value of ψ). One finds that for a 1:1 electrolyte $e\psi_s/4kT = 0.97$ for the DNA (cylinder) and 0.59 for the micelle (sphere). We need the value of $2e\psi/kT$ for the calculation of $\Delta G^{\dagger}_{D-Ru}$ and $\Delta G^{\dagger}_{Ru-M}$ in eqs 11 and 12. In each case, it is related to $2e\psi_s/kT$ by eq 6. Since κ^{-1} is quite large (0.96 nm at 0.1 M NaCl) the attenuation of ψ from its magnitude, ψ_s, even at 0.5 nm is relatively small.

One finds that even if the change in $\Delta G^{\dagger}_{D-Ru}$ and the repulsion term $\Delta G^{\dagger}_{D-M}$ were neglected, the maximum catalytic effect of the micelle, namely, the value of $\Delta G^{\dagger}_{Ru-M}$ at $x = 0$ in eq 16 would only be exp $2e\psi_s/kT$ (i.e., exp($2 \times 0.59 \times 4$)), namely, a factor of 100, which is far below the desired factor of 15 000. Although the present equations are approximate, it seems unlikely that they could be that much in error.

H. Hydrophobic Effect. A natural inference from such results is that in the monomer-induced and micelle-induced dissociation of the Ru_2^{4+} complex from the DNA much of any catalytic effect on the dissociation rate is due to non-electrostatic effects. In the case of the micelle, the TS for the dissociation would have a penetration of the largely organic complex into the micelle and hence with organic−organic interactions. The factor of 15 difference between the monomer and micelle assisted dissociation rate constants can easily be accommodated by a difference in electrostatic interactions, but for the huge catalytic factors it appears that the effect may be largely non-electrostatic. We address this aspect next.

Thermodynamic measurements have shown that there is a very large hydrophobic entropic effect associated with the solution of SDS in water. Instead of the entropy of solution being in the neighborhood of a Trouton's rule type value, namely, the −9.3 given earlier for $\Delta S_{trans}/k$, it is +0.4.[42] If this hydrophobic contribution were fully present in the transition state (i.e., if the monomer were entropically in an environment in the TS close to what it is in the solid), the monomer would enhance the rate of extraction by a factor of exp($\Delta S_{trans}/k$) (i.e., exp(9.7) or 16 000, which compares with the observed ∼50 000). To the extent that the surfactant molecule that associates with the Ru complex in the TS is not fully shielded from the solvent the figure of 16 000 is an upper limit for this effect. More elaborate calculations of the interactions of the monomer and the DNA−Ru complex in the TS will add to our understanding of the huge catalytic effects uncovered by Nordén and coworkers.

IV. Concluding Remarks

Various electrostatic contributions to equilibrium (K_{obs}) and kinetic precursor in these systems have been estimated. The salt concentration effect on Ru_2^{4+} complex−DNA species is reasonably well-reproduced, as is the temperature behavior. The difference in catalytic effect of the surfactant monomer and micelle induced dissociation can be qualitatively consistent with electrostatic effect, but the very large catalytic effect of each on the dissociation rate appears to be primarily due to hydrophobic interactions.

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