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Three-Phase Model of Micellar Reactions. Methylation of Thymidine by (Long-chain-alkyl)dimethylsulfonium Iodides[1]

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Abstract: Micellar methylation of thymidine to 3-methylthymidine was studied by using mainly *n*-octadecyldimethylsulfonium iodide at pH 7–12 and 60–75 °C. The reaction exhibited the presence of an induction period as long as 1 h, a bell-shaped pH dependence of the methylation rate with an optimum pH of ca. 10, and competitive inhibitory effects of added salts on the micellar reaction, etc. A three-phase model was proposed to analyze the micellar events, assuming that (i) the anions (dT^-) of thymidine, the active species of the nucleoside, diffuse from the aqueous bulk phase to the Stern layer across the Gouy–Chapman layer, (ii) dT^- ions concentrate in the Stern layer to obey the Langmuir adsorption isotherm theory, and (iii) the dT^- ions in the layer are methylated in a bimolecular fashion with the dimethylsulfonium ions, the head groups of the micelles. The model furnished apparent kinetic constants such as binding constants of counterions (dT^-, I^-, OH^-, etc.) to the micelle, a diffusion rate constant of dT^- to the Stern layer, and a bimolecular methylation rate constant as well as real kinetic constants such as desorption rate constants of dT^- and Me–dT from the Stern layer. The effects of temperature on these constants were studied carefully to estimate the respective thermodynamic constants. The three-phase model was compared with other micellar models reported. The micellar methylation was discussed briefly in connection to the enzymatic methylation that utilizes *S*-adenosylmethionine as a cofactor.

A micelle, especially an ionic one, provides a highly condensed polar region in the surface and often catalyzes various kinds of reactions.[2–4] The first quantitative study is the hydrolysis of esters by anionic surfactants,[5] and the kinetic scheme involved partitioning of the substrates between the aqueous bulk phase and the micellar phase. Although this "enzyme model" was applied successfully to many reactions, the assumptions made by the model were apparently oversimplified, viz., association of the substrate with the micelle with a 1:1 stoichiometry, and the binding of only one of reactants in a bimolecular reaction. Later, these drawbacks were corrected by using the partition coefficients for all reactants[6] or considering a volume element of the Stern layer and a ratio of the micellar bound substrate to the concentration of micellized surfactant.[7] In the "pseudophase model" the observed rate constant was expressed in terms of the aqueous and micellar rate constants.

In this paper we describe a "three-phase model" for micellar reactions. The new model is characterized by its treating separately the Gouy–Chapman layer, the Stern layer,[8,9] and the aqueous bulk phase as diffusion, reaction, and stock layers of substrates, respectively. Thus, the model does not take account only of the micellar reaction of the substrates; it deals also with the diffusion process of the substrates to the micelles.

Chart I

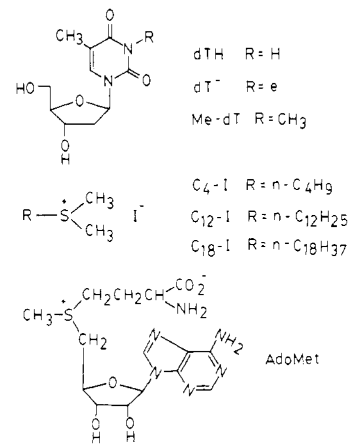

Table I. Conversion of dTH into Me–dT by Alkyldimethylsulfonium Iodides[a]

R in $R\text{-}S^+(CH_3)_2I^-$	C_D,[b] × 10^3 M	[dTH] × 10^3 M	react time, h	yield of Me–dT, %
$n\text{-}C_4H_9$	100	1.0	15	2
$n\text{-}C_{12}H_{25}$	69.0 (10.0)	6.9	6	>90
$n\text{-}C_{18}H_{37}$	0.09 (0.9)	0.03	3	0
$n\text{-}C_{18}H_{37}$	1.0 (10)	0.5	3	13
$n\text{-}C_{18}H_{37}$	15.0 (150)	0.5	1.5	86

[a] Reaction temperature 70 °C; pH 11. [b] The number in parentheses means C_D/cmc.

The reaction examined was the methylation of thymidine (dTH) to 3-methylthymidine (Me–dT) by functional micellar reagents such as *n*-octadecyldimethylsulfonium iodide (C_{18}–I) (Chart I). Being the simple system, the model could explain quantitatively the micellar events such as a bell-shaped pH dependence of the rate, inhibitory effects of added salts on the reaction, and the presence of an induction period (T_i). As described later, the T_i related directly to the diffusion of the substrates. Further, effects of temperature on the micellar events could be examined by means of the new model since it defined the regions of the micelles more explicitly than the previous models.

The kinetic equations of the three-phase model are derived in the following section. The results of the micellar methylation will

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(1) Notation: *A*, Avogadro's number; C_D, the concentration of a surfactant in the micellar solution; cmc, the critical micelle concentration of a surfactant; d_r, the thickness of the Gouy–Chapman layer; $[dT^-]_o$ and $[dTH]_o$, the overall concentrations of dT^- and dTH in the micellar solution, respectively; $[dTH]_t$, $[dT^-]_o + [dTH]_o$; *N*, aggregation number of the micelle; r_c, the radius of the core of the micelle; r_s, the radius of the micelle including the Stern layer; V_o, the total volume of the micellar solution; V_G and V_W, total volumes of the Gouy–Chapman layer and the aqueous bulk phase, respectively; v^e and v^t, methylation rates at equilibrium and at time *t*, respectively; $[X^-]_o$, the overall concentration of X^- ions ($X^- = dT^-$, I^-, and OH^-) in the micellar solution; $[X^-]_S$, $[X^-]_G$, and $[X^-]_W$, the concentrations of X^- in the Stern layer, the Gouy–Chapman layer, and the aqueous bulk phase, respectively, at equilibrium.

(2) Cordes, E. H.; Bull, H. G. *Chem. Rev.* **1974**, *74*, 581.

(3) Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecular Systems"; Academic Press: New York, 1975.

(4) Bunton, C. A. *Appl. Biochem. Syst. Org. Chem. Part 2* **1976**, *10*, 731.

(5) Menger, F. M.; Portnoy, C. E. *J. Am. Chem. Soc.* **1967**, *89*, 4698.

(6) Yatsimirski, A. K.; Martinek, K.; Berezin, I. V. *Tetrahedron* **1971**, *27*, 2855. Martinek, K.; Osipov, A. P.; Yatsimirski, A. K.; Berezin, I. V. *Ibid.* **1975**, *31*, 709.

(7) Bunton, C. A.; Romsted, L. S.; Savelli, G. *J. Am. Chem. Soc.* **1979**, *101*, 1253. Bunton, C. A.; Romsted, L. S.; Thamavit, C. *Ibid.* **1980**, *102*, 3900 and other references of the pseudophase model cited therein.

(8) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111.

(9) Stigter, D. *J. Phys. Chem.* **1964**, *68*, 3603.

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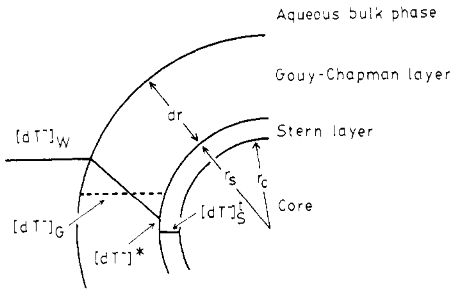

Figure 1. Schematic representation of a spherical cationic micelle and the concentrations of dT^- ions in the three phases.

then be discussed using the model and compared briefly with the enzymatic methylation which utilizes *S*-adenosylmethionine (AdoMet) as a cofactor.[10,11]

Kinetic Equations

Micelles of (long-chain-alkyl)dimethylsulfonium iodides were very reactive to transform dTH into Me–dT (Table I). The methylation, however, took place only at pH > ca. 8, indicating that an anion (dT^-) of dTH is a substrate of the reaction. Since dT^- should attack the methyl group of the cationic head group of the micelle, the Stern layer should be the region where the reaction takes place. Thus, one may have to consider first adsorption of dT^- to the Stern layer in order to derive kinetic equations.

1. Adsorption Equation at Equilibrium.[12] A micellar system of a (long-chain-alkyl)dimethylsulfonium iodide is illustrated in Figure 1, consisting of a core, the Stern and Gouy–Chapman layers, and an aqueous bulk phase. The counteranions are dT^-, I^-, and OH^-. The Gouy–Chapman layer is much larger in volume than the Stern layer and has the counterions in concentration considerably higher than the aqueous bulk phase. The three-phase model utilizes the Langmuir adsorption isotherm theory[13] in order to account for adsorption of the anions from the Gouy–Chapman layer to the Stern layer. Namely, the amounts of the anions adsorbed to the Stern layer after equilibrium is established will depend on the natures of the anions and the Stern layer (or the sulfonium ions), the concentrations of the anions in the Gouy–Chapman layer, and the temperature. Let $[dT^-]_G$, $[I^-]_G$, and $[OH^-]_G$ be the concentrations of the anions in the Gouy–Chapman layer at equilibrium and K_{dT}, K_I, and K_{OH} be the binding constants of the anions denoted in the subscripts. Here, it is assumed conveniently that the anions are distributed homogeneously within the Gouy–Chapman layer, as shown by a broken line for $[dT^-]_G$ in Figure 1. The fraction of the Stern layer that is occupied by dT^- is given by

$$\theta_{dT}{}^e = \frac{[dT^-]_G}{K_m + [dT^-]_G} \tag{1}$$

where

$$K_m = (1 + K_I[I^-]_G + K_{OH}[OH^-]_G)/K_{dT} \tag{2}$$

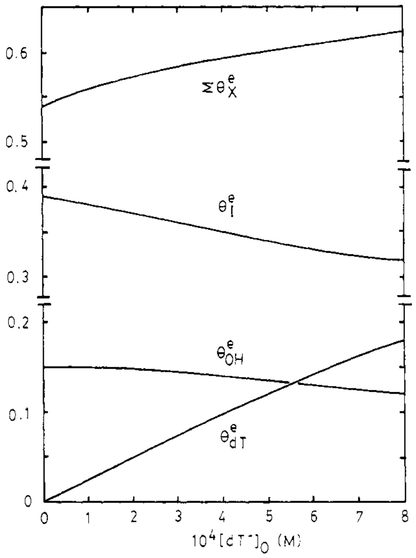

Figure 2. Variation of $\theta_X{}^e$ and $\sum\theta_X{}^e$ with $[dT^-]_o$ at C_D of C_{18}–I = 1.0 × 10^{-3} M, $[I^-]_W = 0.65 \times 10^{-3}$ M, $[OH^-]_W = 5.0 \times 10^{-4}$ M and 70 °C. The $\theta_X{}^e$ is given by $K_X'[X^-]/(1 + K_{dT}'[dT^-]_o + K_I'[I^-]_W + K_{OH}'[OH^-]_W)$, where $[X^-] = [dT^-]_o$, $[I^-]_W$, or $[OH^-]_W$, and K_{dT}', K_I', and K_{OH}' are 600, 1320, and 660 M^{-1}, respectively.

Of a variety of analytical methods for measuring the concentrations of ions, the simplest will be the use of a specific ion electrode, if any. The method, however, may permit evaluation of the concentration[14] in the bulk aqueous phase only, $[X^-]_W$ (X^- = dT^-, I^-, and OH^-). To deal with the problem, we defined the distribution coefficient, P_X, which is assumed independent of concentration, by

$$[dT^-]_W = P_{dT}[dT^-]_G$$
$$[I^-]_W = P_I[I^-]_G$$
$$[OH^-]_W = P_{OH}[OH^-]_G \tag{3}$$

The equations resemble Henry's equation[15] and will, of course, apply exactly to the solution infinitely dilute in X^- ions and the adsorbent which is a microcomponent of the system like a micelle.

Meanwhile, no electrode is available for dT^-, nor can other conventional methods permit one to evaluate $[dT^-]_W$. $[dT^-]_G$ is then correlated directly with $[dT^-]_o$, an overall concentration of dT^- in the micellar solution, by

$$[dT^-]_G = a[dT^-]_o \tag{4}$$

By the use of eq 3 and 4, eq 1 is transformed into

$$\theta_T{}^e = \frac{[dT^-]_o}{K_m' + [dT^-]_o} \tag{5}$$

where

$$K_m' = (1 + K_I'[I^-]_W + K_{OH}'[OH^-]_W)/K_{dT}' \tag{6}$$

and

$$K_{dT}' = aK_{dT}$$
$$K_I' = P_I^{-1}K_I$$
$$K_{OH}' = P_{OH}^{-1}K_{OH} \tag{7}$$

Now, note that a is expressed by

$$a = b\left(1 - \frac{C_D - \text{cmc}}{K_m' + [dT^-]_o}\right) \tag{8}$$

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(10) Kerr, S. J.; Borek, E. *Enzymes, 3rd Ed.* **1973**, p 167.

(11) Senoh, S.; Tokuyama, Y.; Witkop, B. *J. Am. Chem. Soc.* **1962**, *84*, 1719. Hegazi, M. F.; Borchardt, R. T.; Schowen, R. L. *Ibid.* **1976**, *98*, 3048; **1979**, *101*, 4359.

(12) It is unlikely that dTH and dT^- penetrate into the core of the micelle since they are insoluble in alkanes. Hence, the kinetics of the micellar methylation may be studied by changing $[dTH]_t$ keeping the C_D constant. By contrast, most micellar reactions reported to date dealt with substrates and products which were considerably hydrophobic. Incorporation of large amounts of such compounds into the core of micelles may change the physical properties of the micelles such as the cmc and *N*; the kinetics in most cases, therefore, were studied by changing the C_D and keeping the substrate concentration constant and low.

(13) Laidler, K. J. "Chemical Kinetics"; McGraw-Hill; New York, 1965; Chapter 6.

(14) The electrode method gives the activity of ions. In this text, however, no distinction is made between activity and concentration since the concentration of ions is very low in the micellar system.

(15) Moore, W. J. "Physical Chemistry", 3rd ed.; Prentice-Hall: New York, 1962; p 126.

where b is a positive constant (Appendix I), C_D is a concentration of the surfactant, and cmc is the critical micelle concentration.

Since eq 5 is valid only when a is positive and does not vary significantly, the kinetics must be studied under either of the next conditions: (i) $K_m' + [dT^-]_o \gg C_D - \text{cmc}$, or (ii) $K_m' \gg [dT^-]_o$ and $K_m' > C_D - \text{cmc}$. In Figure 2, variations of $\theta_X{}^e$ with $[dT^-]_o$ are shown under representative conditions employed for the micellar methylation.

2. Adsorption Equation at Preequilibrium. When an aqueous solution of dTH is mixed with the micellar solution, dT⁻ will begin to migrate to the Stern layer till the fraction of the layer that is occupied by dT⁻ approaches $\theta_{dT}{}^e$ from 0.[16] It would be difficult to set and solve kinetic equation for the preseady state since not only θ_{dT} but also fractions those covered by I⁻ and OH⁻ vary with time. We, therefore, apply an exchange adsorption theory by Boyd et al.[17] to the presteady state (Appendix III). That is, when $[dT^-]_W$ does not change significantly during the adsorption process, the fraction of the Stern layer that is covered by dT⁻ at time, t, is given by

$$\theta_{dT}{}^t = \theta_{dT}{}^e[1 - e^{-k_{+1}'(K_m' + [dT^-]_o)t}] \tag{9}$$

and

$$k_{+1}' = aP_{dT}k_{+1}$$

$$k_{+1} = \frac{4\pi(r_s)^2AD}{Nd_r} \tag{10}$$

where r_s is a radius of the micelle including the Stern layer, d_r is a thickness of the Gouy–Chapman layer, D is a diffusion constant of dT⁻ across the Gouy–Chapman layer, A is Avogadro number, and N is an aggregation number of the micelle. Note that k_{+1} and k_{+1}' are regarded as real and apparent rate constants of adsorption of dT⁻ to the Stern layer, respectively.

3. Methylation Rate Equation. At any time, a rate of desorption of Me–dT from the Stern layer is expressed by $k_{+2}(C_D - \text{cmc})\theta_{dT}{}^t$, where k_{+2} is a rate constant of desorption of Me–dT from the layer. Since the neutral hydrophilic product will depart from the layer as soon as it is formed, k_{+2} may be also defined as the first-order methylation rate constant. On the other hand, a rate of methylation occurring in the aqueous bulk phase and the Gouy–Chapman layer may be expressed by $k_0([dT^-]_W + [dT^-]_G{}^t)\text{cmc}$, assuming that both phases are the same in the methylation rate constant (k_0) and in the surfactant concentration which is equal to the cmc. A combination of the above two rate equations gives an overall methylation rate, which, by use of eq 5 and 9, becomes

$$v^t = \frac{k_{+2}(C_D - \text{cmc})[dT^-]_o}{K_m' + [dT^-]_o}[1 - e^{-k_{+1}'(K_m' + [dT^-]_o)t}] + k_0([dT^-]_W + [dT^-]_G{}^t)\text{cmc} \tag{11}$$

It is important to note here that though the micelles themselves serve as electrophiles of dT⁻ ions adsorbed to the Stern layer, the C_D is considered to be constant in eq 11. This assumption will, of course, be applied only when the amount of Me–dT produced is much smaller than that of the surfactant initially used. Under the condition, the alkylmethyl sulfide coformed ($R\text{–}S\text{–}CH_3$, see Chart I for R) will also be small and thus will not perturb the micellar structure.

From the mathematical treatment of eq 11, an induction period is expressed by

$$T_i = \frac{1}{k_{+1}'(K_m' + [dT^-]_o)} \tag{12}$$

which is convenient to estimate k_{+1}' since T_i and K_m' can be determined easily from the kinetics.

By the way, when t is large, the exponential term of eq 11 can be neglected. Further, if C_D is considerably larger than cmc, the micellar methylation dominates the overall methylation (see Table I). Hence, eq 11 is reduced to

$$v^e = \frac{k_{+2}(C_D - \text{cmc})[dT^-]_o}{K_m' + [dT^-]_o} \tag{13}$$

When $[dT^-]_o$ is much smaller than K_m', eq 13 gives

$$k_m = \frac{k_{+2}}{K_m'} \tag{14}$$

as an apparent bimolecular methylation rate constant.

By contrast, if one permits very large $[dT^-]_o$, the Stern layer is occupied exclusively by dT⁻, and the maximum velocity, V_{max}, is attained. From eq 13,

$$V_{max} = k_{+2}(C_D - \text{cmc}) \tag{15}$$

Hence,

$$v^e = \frac{V_{max}[dT^-]_o}{K_m' + [dT^-]_o} \tag{16}$$

Equation 16 is formally similar to the Michaelis–Menten equation of enzyme reactions.[18] The terms K_m' and V_{max} are important values to characterize the micellar reaction, and are obtained by using the reciprocal form of eq 16:

$$\frac{1}{v^e} = \frac{K_m'}{V_{max}[dT^-]_o} + \frac{1}{V_{max}} \tag{17}$$

which is analogous to the Lineweaver–Burk equation. A double reciprocal plot with $1/v^e$ on the ordinate and $1/[dT^-]_o$ on the abscissa will give a straight line with $1/V_{max}$ and K_m'/V_{max} on the intercept and the slope, respectively.

Once K_T', k_{+1}', and k_{+2} are determined by kinetic experiments, a desorption rate constant (k_{-1}) of dT⁻ from the Stern layer is calculated from the following relationship between the constants.

$$K_{dT}' = \frac{k_{+1}'}{k_{-1} + k_{+2}} \tag{18}$$

Experiments and Results

Materials. The starting nucleoside (dTH), potassium hydroxide, and potassium halides were commercial products of the highest purity obtainable. The C_{18}–I was prepared as follows: a mixture of methyl n-octadecyl sulfide (6.8 g, 22.6 mmol) and methyl iodide (3.8 g, 26.8 mmol) in tetrahydrofuran (10 mL) was allowed to stand at 10 °C for 5 days. The resulting sulfonium iodide was filtered and recrystallized from acetone containing a small amount of water; 3.8 g (38%), mp 82–103 °C (turbid gel–liquid). Anal. ($C_{20}H_{43}I_1S_1$) C, H. Similarly prepared were [yield, mp] C_4–I [95%, 81–82 °C (lit.[19] mp 82 °C)] and C_{12}–I [71%, 85.5–86 °C (lit.[20] mp 87 °C)].

Product. The high-pressure liquid chromatography (HPLC) (vide infra) of micellar reaction mixtures showed Me–dT as a sole product in the reaction at pH 8–12. Both dTH and Me–dT were stable under the experimental conditions. Me–dT was isolated as follows: e.g. dTH (1.0

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[16] The ¹H NMR spectra of an aqueous solution of C_{18}–I (C_D = 1 – 10cmc) showed a single weight averaged band for the $(CH_3)_2S^+$ groups with no line broading under the conditions used in the methylation study. Thus, simple micelles were formed by the surfactant, and a mean residence time of the surfactant molecules or ions in the micelles was presumably less than 4 × 10^{-3} s which was calculated according to the literature (Muller, N. *J. Phys. Chem.* **1972**, *76*, 3017). This short residence time will reflect a rapid exchange of surfactant ions and counterions around an interface between the Stern layer and the Gouy–Chapman layer, and the ions will diffuse slowly as a mean process of successive rapid collisions or individual ions with like ions or other species such as solvent molecules of a nearby environment (ref 30; Chapter 2). Of course, this diffusion is balanced with retrodiffusion of the ions to keep the micelle structure. Similarly, migration of the added counterions (dT⁻) from the bulk phase to the Stern layer across the Gouy–Chapman layer may not take place instantaneously, but the traveling of the ions, hence the increase in the concentration of the exchange adsorbed ions in the Stern layer, will be diffusion controlled. A length of T_i is discussed in note 32.

[17] Boyd, G. E.; Adamson, A. W.; Myers, L. S., Jr. *J. Am. Chem. Soc.* **1947**, *69*, 2836. Boyd, G. E.; Soldano, B. A. *Ibid.* **1953**, *75*, 6091.

[18] Conn, E. E.; Stumpf, P. K. "Outlines of Biochemistry", 4th ed.; Wiley: New York, 1976; p 157.

[19] Ingold, C. K.; Jeesop, J. A.; Kuriyan, K. I.; Mandour, A. M. M. *J. Chem. Soc.* **1933**, 533.

[20] Yano, Y.; Okonogi, T.; Tagaki, W. *J. Org. Chem.* **1973**, *38*, 3912.

Table II. The cmc of C_{18}-I[a]

pH	*T*, °C	10^4cmc, M
6.5	60	0.98
6.5	65	1.02
6.5	70	1.05
6.5	80	1.08
10.0	70	0.98
11.6	70	0.90
10.5	70	0.98 (Cl^-)[b]
10.5	70	0.98 (Br^-)[b]
10.5	70	0.96 (I^-)[b]

[a] A dye (eosin) method was used for the measurement. Experimental error, $\pm 0.03 \times 10^{-4}$ M. [b] The cmc in the presence of the corresponding potassium halide (2×10^{-3} M).

g, 0.41 mmol) was treated with the C_{12}–I (0.66 g, 1.8 mmol) in water (0.30 dm^3) at pH 11 and 70 °C for 10 h. The reaction mixture was neutralized with 2 N hydrochloric acid and washed with chloroform. The resulting aqueous solution was concentrated to give the residue which was then applied to a silica gel column (Merck, type 7734, 1.5 × 20 cm). Elution with a mixture of chloroform and methanol (15–1 v/v) afforded Me–dT as crystals, 0.63 g (60%); mp 136.5–137 °C (from water) (lit.[21] mp 132–134 °C).

Quantitative Determination of Me–dT. HPLC was run by means of a high-pressure liquid chromatograph (Toyo-Soda Model 803) with an UV flow cell detector, using an ODS-silica gel column (Toyo-Soda, LS-410-ODS, stainless steel, 0.4 × 30 cm), and a mixture of water, methanol, triethylamine and acetic acid (800–200–6–3 v/v) as a solvent. Flow rate and column pressure were 1.67 mL/min and 185 kg/cm^2, respectively. Both dTH and Me–dT were monitored at 265 nm, giving sharp peaks with 4.7 and 8.7 mL as the retention volumes, respectively. The yield (%) of Me–dT was obtained by inserting the peak-height (h_1) of dTH and that (h_2) of Me–dT to the equation, $100 \times h_2/(h_1 c + h_2)$, where *c* was a slope of a straight calibration line which was always obtained upon plotting h_2/h_1 on the ordinate and a mole ratio of Me–dT to dTH on the abscissa. The *c* varied from 0.43 to 0.48 depending on the column temperature (room temperature), so that *c* was determined in each series of kinetic experiments. The yield determined by the method was reproducible within ±0.5%.

Measurement of $[I^-]_W$ and $[OH^-]_W$. The concentration of iodide ions was measured with a Horiba Model 2535A-06T double-junction reference electrode and a Horiba 8004-06T specific iodide ion electrode. The pH was determined with a Horiba Model 6326-06C combination electrode. All measurements were recorded with a Hitachi Model H-7LD pH/mv meter. The procedure was essentially the same as that used by Larsen and Magid.[22] Prior to the measurements, the micellar solution was warmed at the temperature employed in the kinetics for about 1 h. Readings on the micellar solutions were frequently checked with readings on standard solutions because of the problem of electrode drift toward constant values with time; a waiting period of ca. 10 min was necessary to get reliable results. Reproducibility to within ±1 mv and ±0.02 pH unit were generally possible for the micellar samples.

Determination of cmc. Since C_{18}–I was a key surfactant in the present study, its cmc was examined in detail under various conditions. The value was measured by titrating of the C_{18}–I solution (1.5×10^{-4} M), which was prepared by dissolving the surfactant in an eosin solution (0.4×10^{-4} M) with the same dye solution according to the literature.[23] The typical results are shown in Table II, indicating that the cmc was not affected significantly by salts, pH, and temperature. The cmc of C_{12}–I was measured similarly to be 6.89×10^{-3} M at pH 10.5 and 65 °C, which agreed well with the values obtained by means of conductometric and vapor pressure osmometric methods (7.2 and 7×10^{-3} M, respectively). Both methods, however, did not give the reliable cmc of C_{18}–I owing to the relatively large experimental errors.

Methylation Reaction. A. Kinetic Conditions. The following precautions were taken for the kinetic study. The C_D was adjusted to 7–10 times the cmc of the micellar reagent to ensure the spherical micelles.[8,24] The $[dT^-]_0$ was chosen so as to satisfy conditions i and ii of section 1 (Adsorption Equation at Equilibrium). The concentrations of added potassium halides were varied within two holds of C_D to minimize the effect of the salts on *N*, P_X, and *a*. Buffers were not utilized in order to keep the pH and the ionic strength of the micellar solution constant; it is useless to employ unknown salts for testing the three-phase model. The kinetic study was terminated when the conversion of dTH to Me–dT reached 10–13% in order to apply the initial C_D to the rate eq 13.

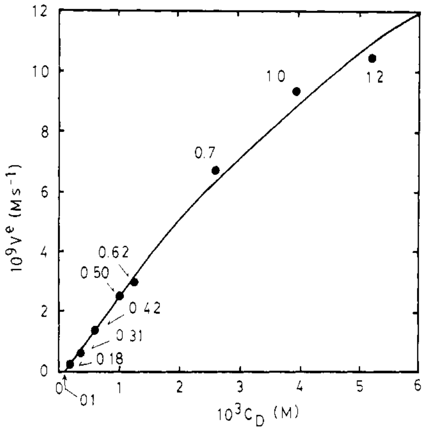

Figure 3. Variation of methylation rate (v^e) with C_D of C_{18}–I at $[dTH]_t = 0.62 \times 10^{-3}$ M, pH 10.5 and 70 °C. The line is calculated by use of eq 13 [$k_{+2} = 1.82 \times 10^{-5}$ s^{-1}, cmc = 0.1×10^{-3} M, and the K_m', which is obtained by substituting K_X' values (see the caption of Figure 2) to eq 6]. The $[I^-]_W$ values observed are indicated along with the line (10^{-3} M unit).

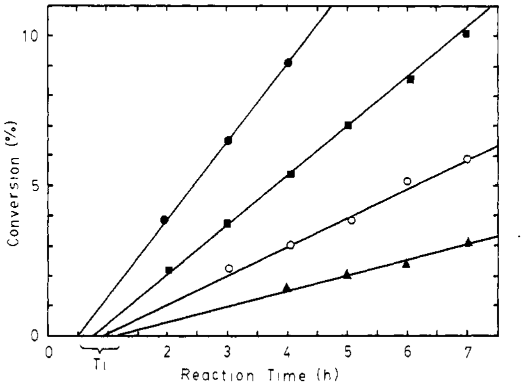

Figure 4. Conversion of dTH to Me–dT by C_{18}–I at pH 10.3: $[dTH]_t = 0.51 \times 10^{-3}$ M, $C_D = 1.0 \times 10^{-3}$ M; (▲) 60 °C, (○) 65 °C, (■) 70 °C, (●) 75 °C. The lines are calculated. The T_i are estimated to be ca. 4300, 3300, 2700, and 1800 s at 60, 65, 70, and 75 °C, respectively.

B. Kinetic Procedure. A surfactant was dissolved in degassed water, and the pH of the resulting solution was adjusted by concentrated aqueous potassium hydroxide. Similarly prepared were the aqueous solutions of dTH and of a potassium halide having the same pH. These three kinds of solutions were then mixed in a glass tube to give a micellar solution with appropriate concentrations of the surfactant, dTH, and the salt. The tube was sealed tightly with a polyethylene cap and shaken in a water bath thermostated at the reaction temperature, which was controlled within ±0.25 °C. At suitable time intervals the aliquots were subjected to HPLC analysis to determine the degree of conversion of dTH to Me–dT. It was found that the decrease in the pH of the micellar reaction mixtures was very small; the results were checked independently on the micellar solutions of the larger size by means of the pH meter.

C. Induction Period (T_i). The rate of the micellar methylation reached a steady state only after a considerably long T_i, as displayed in Figure 4. The T_i was read directly, as seen in the figure. Examples of the T_i under various conditions are shown in Table III. Increasng temperature reduced considerably the induction period.

D. v^e, V_{max}, and K_X'. The degree of conversion of dTH to Me–dT was plotted against reaction time, as shown in Figure 4, in order to determine v^e. Then, a double reciprocal plot was made between $1/v^e$ and $1/[dT^-]_0$ according to eq 17. Usually a good straight line was obtained, as shown in Figure 5, from which K_m' and V_{max} were evaluated.

The K_m' was then plotted against $[I^-]_W$ and $[OH^-]_W$ as demonstrated in Figures 6 and 7, respectively. The slope and the intercept in Figure 6 were read as K_I'/K_{dT}' and $(1 + K_{OH}'[OH^-]_W)/K_{dT}'$, respectively. Similarly, K_{OH}'/K_{dT}' and $(1 + K_I'[I^-]_W)/K_{dT}'$ were evaluated from Figure 7. A set of K_{dT}', K_I', and K_{OH}' was calculated by solving any three of these four simultaneous equations. The Arrhenius plots of log K_X' vs. T^{-1} (K) are shown in Figure 9 to estimate the corresponding thermodynamic constants (Table IV). Each spot is an average of three runs. The

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(21) Miles, H. T. *J. Am. Chem. Soc.* **1957**, *79*, 2565.
(22) Larsen, J. W.; Magid, L. J. *J. Am. Chem. Soc.* **1974**, *96*, 5774.
(23) Corrin, M. L.; Harkins, W. D. *J. Am. Chem. Soc.* **1947**, *69*, 679.
(24) Ahmad, S. I.; Friberg, S. *J. Am. Chem. Soc.* **1972**, *94*, 5196.

Table III. Excerpts of Kinetic Data of the Methylation of dTH by C_{18}-I under Various Conditions[a]

T, °C	$[dT^-]_0$[b]	$[OH^-]_W$[b]	$[I^-]_W$[b]	$10^3 T_i$, s	K_m'[b]	$10^9 V_{max}$, M s^{-1}	θ_{dT}[e]	a[c]	P_I[d]
60	0.35	0.10	0.37	4.6-5.1	2.6	5.5	0.12	0.69b	0.16
65	0.35	0.10	0.42	3.5-3.9	2.6	9.1	0.12	0.69b	0.16
70	0.36	0.10	0.48	2.9-3.1	2.8	18.8	0.11	0.71b	0.18
75	0.37	0.10	0.52	1.9-2.1	3.1	25.0	0.10	0.73b	0.18

[a] $C_D = 1.0 \times 10^{-3}$ M. [b] 10^{-3} M. [c] See eq 8 and 20 for a and b. [d] $P_I = [I^-]_W/[I^-]_G$, where $[I^-]_G = (V_0/V_G)\{([I^-]_0 - \theta_I{}^e(C_D - \text{cmc}) - [I^-]_W)\} - [I^-]_W$, an equation analogous to 19. Here, V_G was set tentatively to 0.1 V_0 in the temperature range examined: $V_G = (4/3)\pi\{(r_s + d_r)^3 - r_s{}^3\}(C_D - \text{cmc})V_0 A/N$, where r_s, d_r and N were assumed to be 30×10^{-9} dm (ref 34), 135×10^{-9} dm, and 80-100 (light-scattering measurement at 65 °C), respectively; $\theta_I{}^e$ was calculated from the equation described in the caption of Figure 2, using K_X' values plotted in Figure 9.

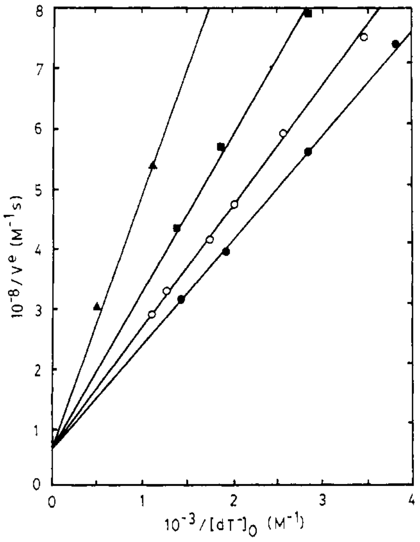

Figure 5. Double reciprocal plot of the methylation rate (v^e) as a function of $[dT^-]_0$ at C_D of C_{18}-I = 1.0×10^{-3} M and 70 °C: (●) pH 10.0, $[I^-]_W = 0.48 \times 10^{-3}$ M; (○) pH 10.5, $[I^-]_W = 0.5 \times 10^{-3}$ M; (■) pH 10.0, $[I^-]_W = 1.16 \times 10^{-3}$ M; (▲) pH 11.5, $[I^-]_W = (0.6\text{-}0.7) \times 10^{-3}$ M.

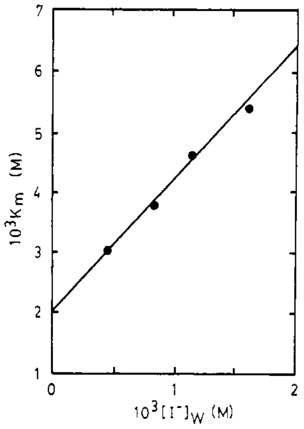

Figure 6. Effect of $[I^-]_W$ on K_m' at C_D of C_{18}-I = 1.0×10^{-3} M, pH 10.5 and 70 °C.

least-squares method was used to draw the lines (see Discussion section also for P_X and a, etc.).

Determination of Apparent Dissociation Constant of dTH, pK_a'. The pH of the micellar solution containing C_{18}-I (1.0×10^{-3} M) and dTH (0.6×10^{-4} M) was adjusted by aqueous potassium hydroxide (0.05-2 N) to an appropriate value. After the solution was kept at 60-75 °C for at least 30 min and the pH value read accurately, the absorbance was measured at 265 nm. Both dTH and dT^- exhibited the maximum absorption at the wavelength. Taking the pH which corresponded to a half-difference between the lowest and the highest adsorbances, the pK_a' was determined as follows: 9.05, 9.00, 8.93, and 8.83 at 60, 65, 70, and 75 °C, respectively.

Discussion

Previously, trimethylsulfonium salts, $(CH_3)_3S^+ X^-$ ($X^- = F^-$, I^-, and OH^-) were shown to methylate various compounds in aprotic organic solvents but to lose completely their activity in water.[25,26] They, however, can be brought into active micellar

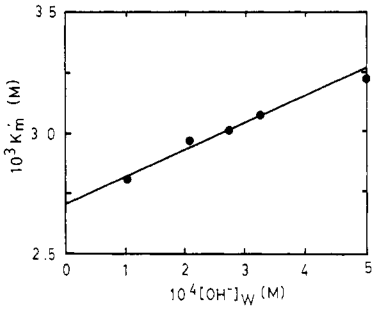

Figure 7. Effect of $[OH^-]_W$ on K_m' at C_D of C_{18}-I = 1.0×10^{-3} M and 70 °C. $[I^-]_W$ at pH 10-10.5 = ca. $0.47\text{-}0.50 \times 10^{-3}$ M.

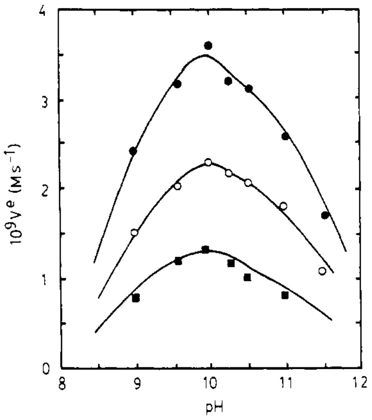

Figure 8. Variation of methylation rate (v^e) with pH: $[dTH]_t = 0.50 \times 10^{-3}$ M, C_D of C_{18}-I = 1.0×10^{-3} M; (■) 65 °C, (○) 70 °C, (●) 75 °C. The lines are calculated.

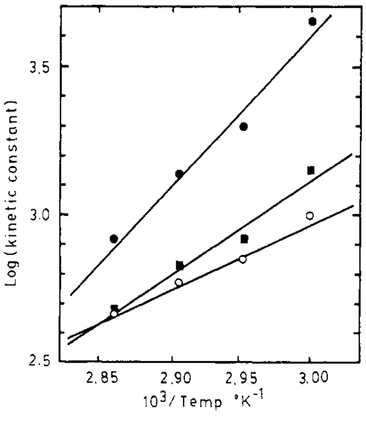

Figure 9. Arrhenius plots of binding constants: (●) K_I'; (■) K_{OH}'; (○) K_{dT}'.

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(25) Yamauchi, K.; Tanabe, T.; Kinoshita, M. *J. Org. Chem.* **1979**, *44*, 638. Yamauchi, K.; Nakajima, T.; Kinoshita, M. *Ibid.* **1980**, *45*, 3865. Yamauchi, K.; Hisanaga, Y.; Kinoshita, M. *Synthesis* **1980**, 852.

Table IV. Thermodynamic Constants in the Methylation of dTH by C_{18}-I[a,b]

K_{dT}'	adsorption energy of dT^- to the Stern layer	11.0 kcal mol^{-1}
K_I'	adsorption energy of I^- to the Stern layer	24.5 kcal mol^{-1}
K_{OH}'	adsorption energy of OH^- to the Stern layer	16.0 kcal mol^{-1}
k_{+1}'	E of diffusion of dT^- to the Stern layer, E^d	11.9 kcal mol^{-1}
k_{-1}	E of desorption of dT^- from the Stern layer	21.1 kcal mol^{-1}
k_{+2}	desorption of Me–dT from the Stern layer, or the first-order methylation of dT^- in the layer:	
	E	25.0 kcal mol^{-1}
	$\Delta S^‡$	−5.6 eu[d]
	$\Delta H^‡$	25.7 kcal mol^{-1} [d]
k_0,[c]	methylation of dT^- occurring in the aqueous bulk phase:	
	E	27.5 kcal mol^{-1}
	$\Delta S^‡$	−5.2 eu[d]
	$\Delta H^‡$	26.9 kcal mol^{-1} [d]

[a] The kinetic constants in the left column were used to calculate the thermodynamic constants. [b] E refers to the Arrhenius activation energy. [c] The k_0 was estimated from the nonmicellar methylation of dT^- by C_4-I. [d] At 65 °C.

methylating agents by replacing one of three methyl groups with a long-chain-alkyl group. The methylation of dTH with C_{12}–I and C_{18}–I was typical (Table I). Recently $C_{16}H_{33}N^+(CH_3)_2CH_2CH_2S^+(CH_3)_2 \cdot 2CF_3SO_3^-$ was also designed as a methylating surfactant for thiophenol.[27]

Since the micellar reactions may take place on the substrates that are incorporated in a special environment of a micelle–water interface, we studied the kinetics of the present micellar reaction in detail. Although the known micellar models were considerably successful in interpreting, and sometimes quantitatively, the micellar reactions,[2-7] they could not deal with the presence of an induction period (T_i). Further, the models were intended primarily for the micellar reactions of hydrophobic compounds and were not suitable to analyze the present micellar methylation of hydrophilic dTH.

The three-phase model may be featured by its assignment of the Stern layer and Gouy–Chapman layer to reaction and diffuse layers, respectively. Accordingly, $[X^-]_W$ and $[dT^-]_o$ were correlated to $[X^-]_G$ and $[dT^-]_G$ by means of P_X and a, respectively (X^-: counterions such as dT^-, I^-, and OH^-). The kinetic equations were then contrived by coupling the Boyd exchange adsorption theory with the Langmuir adsorption isotherm theory. In the following sections we describe the validity of the model and the kinetic constants of the micellar methylation.

Validity of the Three-Phase Model. The model may be applied to any bimolecular reactions using functional micelles and hydrophilic substrates. But when a substrate concentration in the aqueous phase cannot be measured as was not $[dT^-]_W$, the model becomes valid under conditions i and ii of section 1 (Adsorption Equation at Equilibrium). In such a case, the smaller is the cmc of the surfactant, the better the model fits for the kinetics. Namely, in the methylation by C_{12}–I at $C_D = 6.9 \times 10^{-2}$ M (10 times the cmc), pH 10.5 and 60 °C, the estimated K_m' was (1–2) $\times 10^{-2}$ M. Hence, in order to meet condition i, $[dT^-]_o$ must be larger than at least 0.5 M. Obviously, such a high concentration of dT^- will make the rate measurement difficult and also perturb significantly the micellar structure to give erroneous results. By contrast, C_{18}–I has a small cmc (0.1×10^{-3} M), and the C_D used ((0.7–1.0) $\times 10^{-3}$ M) was considerably smaller than the K_m' ((2.5–10) $\times 10^{-3}$ M). Thus, the kinetics using C_{18}–I would be studied safely at various concentrations of dTH ($[dT^-]_o$ used in the experiments was (0.1–1.0) $\times 10^{-3}$ M and therefore constitutes the main contents in the present text.

On the other hand, the reactant of the micellar reaction must be as hydrophilic as dTH since the model assumes adsorption of the substrate to the Stern layer only and hence prefers the compounds or ions which cannot be incorporated into the hydrophobic core of the micelles.[12] Some other cautions for carrying out the kinetics are mentioned in the Experimental Section under Methylation Reaction.

Kinetic Conditions. K_X' and Effects of pH. It was found that the added salts such as KI, KBr, and KCl as well as pH of the micellar solution did not affect V_{max} but only K_m', as shown in Figure 5. Apparently, the corresponding anions behave as competitive inhibitors to the methylation of dT^-. The leveling off of the rate with increasing C_D (Figure 3) thus can be attributed to the increasing K_m' or to an inhibitory action of I^- of the micellar reagent per se. Such a phenomenon is common to micellar reactions.[28]

The effects of pH on the methylation rate (v^e) are displayed in Figure 8. Obviously, the increasing rate with increasing pH (up to ca. 10) arises from enhanced dissociation of dTH to dT^-, while the decreasing rate in the higher pH is ascribed to the rapidly increasing K_m'; namely, the Stern layer is occupied mainly by OH^- rather than dT^-. Indeed, the v^e vs. pH profile of Figure 8 was simulated well by rate eq 13, where K_m' was calculated from eq 6, and $[dT^-]_o$ was estimated from the Henderson–Hasselbalch equation[29] by using the experimental pK_a' of dTH in the micellar solution.

It is not easy to determine P_X and a since the volume of the Gouy–Chapman layer (V_G) is unknown. The V_G, however, may change little in the temperature range examined.[30] Accordingly, calculations were made for P_I and a upon setting an arbitrary value for V_G (see Appendix I) to reveal that temperature was quite insensitive to both parameters (see Table III for P_I and a when $V_o/V_G = 10$, where V_o is a total volume of the micellar solution), and perhaps this could also be so for P_{OH} and P_{dT}. Though the calculations depend on the unconfirmed assumption of V_G, these results accord with the small effect of temperature generally observed on partition coefficients in multiliquid phase systems.[31] Thus, K_X may parallel closely K_X' in the temperature characteristics (see eq 7). Figure 9 displays the plot of log K_X' vs. T^{-1} (K), giving fairly good straight lines. From the above discussion, the apparent adsorption energy will represent for the most part the real adsorption energy; the order of increasing energy was $dT^- < OH^- < I^-$ (Table IV).

By the way, Br^- and Cl^- were also found to inhibit competitively the methylation reaction. The apparent binding constants of all counterions examined were as follows at 70 °C (M^{-1}): Cl^- (80), Br^- (250), dT^- (600), OH^- (660), and I^- (1320). The increasing order of the constants seemed to agree with the lyotropic series of the ions for the cationic micelles.[22]

Induction Period (T_i) and k_{+1}. The micellar methylation exhibited a considerably long T_i as shown in Figure 4 and Table III. The three-phase model explains the T_i as the time to be spent till θ_{dT} grows from 0 to the equilibrium value (θ_{dT}^e) or the concentration of dT^- in the Stern layer reaches its maximum value ($[dT^-]_S^e$, eq 23, Appendix II). T_i and K_m' were put into eq 12 to determine k_{+1}', which is proportional to $(aP_{dT}/Nd_r)D$ as shown in eq 10; here, a, P_{dT}, and d_r are considered to be insensitive to temperature as aforementioned, and the varietion of N may be also negligible in the small temperature range examined (Δ 15 °C). Thus, the effect of temperature on k_{+1}' will be reflected in that on D to furnish an activation energy of diffusion (E^d) of dT^- across the Gouy–Chapman layer. A plot of log k_{+1}' vs. T^{-1} (K)

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(26) Yamauchi, K.; Nakajima, T.; Kinoshita, M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2787.

(27) Moss, R. A.; Sanders, W. J. *Tetrahedron Lett.* **1979**, 1669.

(28) Dunlap, R. B.; Cordes, E. H. *J. Am. Chem. Soc.* **1968**, *90*, 4395. Other examples are cited in ref 2–4.

(29) Reference 18, p 12.

(30) A small change in temperature (Δ 15 °C) will affect hardly V_G since it has been considered that d_r is proportional to $T^{1/2}$(K) according to the Debye–Huckel theory. Jirgensons, B.; Straumanis, M. E. "A Short Textbook of Colloid Chemistry", 2nd ed.; Pergamon Press: London, 1962; Chapter 7.

(31) For instance, Johnson, S. M.; Bangham, A. D. *Biochim. Biophys. Acta* **1969**, *193*, 92. Saito, S.; Aburai, K. *J. Chem. Soc. Jpn.* **1960**, *81*, 351.

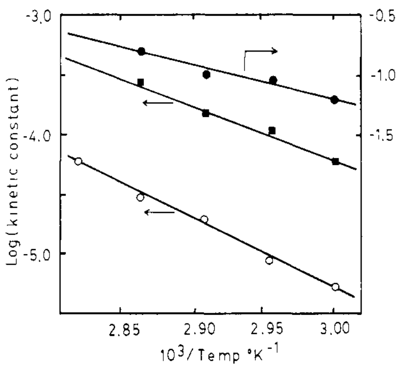

Figure 10. Arrhenius plots of kinetic constants: (●) k_{+1}'; (■) k_{-1}; (○) k_{+2}.

was displayed in Figure 10 to give ca. 12 kcal mol^{-1} as E^d. It has been shown that E^d for OH$^-$ and halide ions in anion-exchange resins was 6–10 kcal mol^{-1} [17] and that free diffusion of electrolyte in aqueous solutions was about 5 kcal mol^{-1}. The larger E^d in the present micellar reaction may be rationalized by the bulkiness of dT$^-$ and the low charge density of the sulfonium ion in comparison to that of the ammonium ions of the ion-exchange resins. The missing induction period in the previous micellar reactions, which were carried out with surfactants of ammonium ion or sulfate ion types, will be attributed most likely to the large D values of the substrates (ions).[32]

Methylation Rate Constants (k_0, k_m, and k_{+2}). When the concentration of C_{18}–I was below the cmc, the methylation rate was too slow to be followed accurately. Accordingly, the bimolecular methylation rate constant, k_0, in the aqueous bulk phase was estimated from a nonmicellar methylation of dTH using *n*-butyldimethylsulfonium iodide (C_4–I); the reaction conditions were identical with those employed in the micellar reaction except the concentration of C_4–I which was 100-fold that of cmc of C_{18}–I. The k_0 thus determined were: 1.17, 2.33, 3.61, and 7.1 ($\times 10^{-6}$) M^{-1} s^{-1} at 60, 65, 70, and 75 °C, respectively. The apparent bimolecular methylation rate constant, k_m, on the other hand, was calculated to be (2–9) $\times$ 10^{-3} M^{-1} s^{-1} in the temperature range. It is remarkable that k_m was larger than k_0 by a factor of (1–1.5) $\times$ 10^3, though the difference decreased with the increasing temperature.

Meanwhile, the three-phase model indicates that k_{+2} is not affected by the micellar structure but only by temperature. As aforementioned, the constant can be treated as the first-order methylation rate constant of dT$^-$ as well as the desorption rate constant of Me–dT from the Stern layer. Hence, it is interesting to find that the thermodynamic constants estimated from k_{+2} were similar to those from k_0, though an activation energy from the former was somewhat smaller (Table IV).

It has been known that an enzymatic methylation using *S*-adenosylmethionine (AdoMet) transferred directly the methyl group to a substrate via a SN2 transition state[11] and was inhibited by various anions such as Cl$^-$, Br$^-$, and ClO$_4^-$ with increasing effect in that order.[33] In various points, the present micellar reaction resembled the enzymatic reaction; they were the acceleration of the methylation rate by the concentration of dT$^-$ ions in the active site (the Stern layer) or the large k_m in comparison to k_0, the bell-shaped profile of the methylation rate vs. pH, and inhibition of the rate by the coanions aforementioned. The micelles, however, cannot catch the substrates as well as enzymes, and the efficiency depends on a simple diffusion of the substrates which is a function of the D value, and the nature of the micelles which is represented by r_s, d_r, N, etc. (see eq 10).

Appendix I

Although the Stern layer cannot be covered completely by counteranions ($\sum\theta_X^e < 1$; see Figure 2) because of electrostatic repulsion between anions adsorbed side by side, a CPK model of the micelle indicates that one cationic head group can match easily one dT$^-$ in the layer from a steric viewpoint. The θ_{dT}^e was simulated to be very small (Figure 2 and Table III) to suggest that dT$^-$ ions are distributed sporadically in the Stern layer. Thus, the molar amount of dT$^-$ ions which are adsorbed to the layer may be given by $(C_D - \text{cmc})\theta_{dT}^eV_o$. Hence, the concentrations of dT$^-$ ions in the three phases are related by

$$[\text{dT}^-]_oV_o = (C_D - \text{cmc})\theta_{dT}^eV_o + [\text{dT}^-]_GV_G + [\text{dT}^-]_WV_W$$

Since $V_W = V_o - V_G$ (the volume of the micelles is neglected),

$$V_oV_G^{-1}([\text{dT}^-]_o - (C_D - \text{cmc})\theta_{dT}^e - [\text{dT}^-]_W) + [\text{dT}^-]_W = [\text{dT}^-]_G \quad (19)$$

which, by use of eq 3 and 5 for $[\text{dT}^-]_W$ and θ_{dT}^e, respectively, is transformed to

$$a = \frac{[\text{dT}^-]_G}{[\text{dT}^-]_o} = \frac{V_o}{V_G + P_{dT}(V_o - V_G)}\left(1 - \frac{C_D - \text{cmc}}{K_m' + [\text{dT}^-]_o}\right) \quad (20)$$

Since P_{dT} and V_G are considered to be constant at a given temperature (see Discussion section), eq 20 becomes equivalent to eq 8.

Appendix II

A total amount of dT$^-$ stored in the Stern layer at any time is written as $(C_D - \text{cmc})\theta_{dT}^tV_o$. A number of micelles is $(C_D - \text{cmc})V_oAN^{-1}$. A total volume of the Stern layer is $(^4/_3)\pi(r_s^3 - r_c^3)(C_D - \text{cmc})V_oAN^{-1}$. Hence, an amount of adsorbed dT$^-$ ions per a micelle is

$$Q^t = \theta_{dT}^tNA^{-1} \quad (21)$$

The concentrations of dT$^-$ in the Stern layer at time t and at equilibrium are given, respectively, by

$$[\text{dT}^-]_S^t = \frac{3\theta_{dT}^tN}{4\pi(r_s^3 - r_c^3)A} \quad (22)$$

$$[\text{dT}^-]_S^e = \frac{3N[\text{dT}^-]_o}{4\pi(r_s^3 - r_c^3)(K_m' + [\text{dT}^-]_o)A} \quad (23)$$

Appendix III

The exchange adsorption theory by Boyd et al.[17] was modified to deal with the adsorption of dT$^-$ ions to the cationic micelles as follows. The dT$^-$ ions must cross the diffuse layer, which may be equivalent to the Gouy–Chapman layer, in order to be adsorbed to the Stern layer (see Figure 1). The exchange flow of dT$^-$ ions across the Gouy–Chapman layer per micelle is given by

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(32) Most of previous micellar reactions were carried out by using ammonium ion and sulfate ion type surfactants, and, therefore, the counterions examined such as OH$^-$, halide ions, and small organic ions would have the D values in the magnitude similar to those measured by using ion-exchange resins which were functioned by the similar hard ionic groups; e.g., D = 10^{-7}–10^{-10} cm^2 s^{-1} (ref 17) [the diffusion constants of various surfactant ions and counterions have also been estimated to be <10^{-7} cm^2 s^{-1} at the surfactant concentrations employed usually in the micellar reactions, though the constants were determined under no concentration gradients of any species existed in the systems: Lindman, B.; Brun, B. *J. Colloid Interface Sci.* **1973**, *42*, 388. Brady, A. P.; Salley, D. J. *J. Am. Chem. Soc.* **1948**, *70*, 914. Stigter, D.; Williams, R. J.; Mysels, K. J. *J. Phys. Chem.* **1955**, *59*, 330]. When these D values are substituted into eq 10, assuming that all parameters except d_r and r_s are the same as those of C_{18}–I micelles, and when the resulting k_{+1}' was used in eq 12, the T_i is calculated to be only a few milliseconds or a few seconds indicating rapid equilibration of added counterions in the micellar systems. This length of T_i would correspond to that of previous micellar reactions and is too short to be detected by conventional kinetic techniques but special methods like a stopped-flow measurement. In the present study, D of dT$^-$ was calculated to be ca. 10^{-13} cm^2 s^{-1} at 70 °C when d_r = (100–300) $\times$ 10^{-9} dm, k_{+1}' = 0.2 M^{-1} s^{-1}, and P_{dT} (= [dT]$_W$/[dT$^-$]$_o$) = 0.7–0.85, which was estimated by the ultrafiltration method.

(33) Young, D. V.; Srinivasan, P. R. *Biochim. Biophys. Acta* **1971**, *238*, 447.

(34) According to the literature, the radius of the core and the thickness of the Stern layer of the micelle of C_{18}–I were estimated to be 24.5 and 5.7 $\times$ 10^{-9} dm, respectively, making r_s to be 30.2 $\times$ 10^{-9} dm: Tanford, C. *J. Phys. Chem.* **1972**, *76*, 3020. Reference 22, p 5782. See also Zuccaro, D. E.; McCullough, J. D. *Z. Kristallogr.* **1959**, *112*, 401.

$$\frac{\mathrm{d}Q^t}{\mathrm{d}t} = 4\pi r_s^2 D \frac{\mathrm{d}[\mathrm{dT}^-]_\mathrm{G}}{\mathrm{d}r} \tag{24}$$

where Q^t is an amount of dT^- ions stored in the Stern layer, and $[\mathrm{dT}^-]_\mathrm{G}$, the concentration in the Gouy–Chapman layer, is assumed to vary linearly from $[\mathrm{dT}^-]_\mathrm{W}$ to $[\mathrm{dT}^-]^*$, the concentration adjacent to and hence equilibrium with the Stern layer. The distribution coefficient, k, which is independent of concentration, is defined by $[\mathrm{dT}^-]_\mathrm{S}^\mathrm{e} = k[\mathrm{dT}^-]_\mathrm{W}$. Using eq 7, $[\mathrm{dT}^-]_\mathrm{S}^\mathrm{e} = kP_\mathrm{dT}[\mathrm{dT}^-]_\mathrm{G}$, which also resembles Henry's equation.[15] Thus, the assumption will, of course, be applied exactly only to the solution infinitely dilute in dT^-.

Now, equilibrium at the surface of the adsorbing Stern layer is assumed for all times of contact, so that $[\mathrm{dT}^-]^* = k^{-1}[\mathrm{dT}^-]_\mathrm{S}^t$; hence

$$\frac{\mathrm{d}[\mathrm{dT}^-]_\mathrm{G}}{\mathrm{d}r} = \frac{[\mathrm{dT}^-]_\mathrm{W} - k^{-1}[\mathrm{dT}^-]_\mathrm{S}^t}{d_\mathrm{r}} = \frac{[\mathrm{dT}^-]_\mathrm{S}^\mathrm{e} - [\mathrm{dT}^-]_\mathrm{S}^t}{kd_\mathrm{r}}$$

which by use of eq 22 becomes

$$\frac{\mathrm{d}[\mathrm{dT}^-]_\mathrm{G}}{\mathrm{d}t} = \frac{3N}{4\pi(r_s^3 - r_c^3)kd_\mathrm{r}A}(\theta_\mathrm{dT}^\mathrm{e} - \theta_\mathrm{dT}^t)$$

Hence, eq 24 is written as

$$\frac{\mathrm{d}Q^t}{\mathrm{d}t} = \frac{3r_s^2 DN}{(r_s^3 - r_c^3)kd_\mathrm{r}A}(\theta_\mathrm{dT}^\mathrm{e} - \theta_\mathrm{dT}^t)$$

Since $\mathrm{d}Q^t/\mathrm{d}t = ((N/A)\mathrm{d}\theta_\mathrm{dT}^t)/\mathrm{d}t$ from eq 21,

$$\frac{\mathrm{d}\theta_\mathrm{dT}^t}{\mathrm{d}t} = \frac{3r_s^2 D}{(r_s^3 - r_c^3)kd_\mathrm{r}}(\theta_\mathrm{dT}^\mathrm{e} - \theta_\mathrm{dT}^t)$$

which upon integration for the condition that $\theta_\mathrm{dT}^t = 0$ when $t = 0$, becomes

$$\theta_\mathrm{dT}^\mathrm{e} = \theta_\mathrm{dT}^\mathrm{e}[1 - e^{-\{3r_s^2D/[(r_s^3-r_c^3)kd_r]\}t}] \tag{25}$$

Now, by substitution of k with $[\mathrm{dT}^-]_\mathrm{S}^\mathrm{e}/[\mathrm{dT}^-]_\mathrm{W}$ and expression of the $[\mathrm{dT}^-]_\mathrm{S}^\mathrm{e}$ by eq 23, eq 25 is written as

$$\theta_\mathrm{dT}^t = \theta_\mathrm{dT}^\mathrm{e}[1 - e^{-[4\pi r_s^2 AaP_\mathrm{dT}D/d_\mathrm{r}N](K_\mathrm{m}'+[\mathrm{dT}^-]_\mathrm{o})t}] \tag{26}$$

which is equivalent to eq 9.

Registry No. dTH, 50-89-5; Me-dT, 958-74-7; $(n\text{-}C_4H_9)S^+(CH_3)_2I^-$, 37127-44-9; $(n\text{-}C_{12}H_{25})S^+(CH_3)_2I^-$, 18412-81-2; $(n\text{-}C_{18}H_{37})S^+(CH_3)_2I^-$, 84040-81-3.

Photocycloaddition of 9,10-Dichloroanthracene to 1,3-Cyclohexadiene[1]

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Abstract: Irradiation of 9,10-dichloroanthracene (DCA) in the presence of 1,3-cyclohexadiene (CHD) gives three major adducts corresponding to [2 + 2] addition of CHD to the 1,2-positions of DCA and to [4 + 4] additions of CHD to the 9,10- and 1,4-positions of DCA. The previously undetected [2 + 2] adduct is the major primary photoproduct in toluene, benzene, acetonitrile, or pyridine, provided that it is protected from shorter wavelength exciting light. The dependence of emission and product quantum yields on [CHD] demonstrates that interaction between the first excited singlet state of DCA with CHD is the first step in these reactions. The product distributions are not entirely consistent with a recently proposed algorithm for prediction of reactivity in allowed [2 + 2] and [4 + 4] photocycloadditions. DCA·CHD exciplex emission was not detected, but involvement of a singlet exciplex in the cycloadditions is strongly suggested by (a) the inverse temperature dependence of Stern–Volmer plot slopes for CHD quenching of DCA fluorescence and (b) the marked decrease of adduct quantum yields in the presence of pyridine, a known exciplex-specific quencher.

Interaction of electronically excited arenes, notably anthracenes, with 1,3-dienes has been shown to lead to [4 + 4], [4 + 2], and [2 + 2] cycloadducts.[2-10] The preferred cycloaddition mode is very sensitive to substituents on either reactant. For example, anthracene gives only [4 + 4] adduct with 2,5-dimethyl-2,4-hexadiene,[2,4] both [4 + 4] and [4 + 2] adduct with 1,3-butadiene,[8] and only [4 + 2] adduct with dimethyl muconate.[7] The mode and location of the addition are influenced by substituents at the 9,10-positions of anthracene. Thus, chlorine and bromine substitutions lead to enhanced reactivity of the terminal anthracene rings.[2,9] The striking substituent dependence on the mode of addition is illustrated by 2,5-dimethyl-2,4-hexadiene, which, as stated above, gives mainly [4 + 4] addition with anthracene, [4 + 4] and [4 + 2] addition with 9-fluoroanthracene, and only [4 + 2] addition with 9,10-dichloro- or 9,10-dicyanoanthracene.[2,4]

The formation of arene/diene singlet exciplexes was suggested to account for the quenching of arene fluorescence by 1,3-dienes[11] and later confirmed in specific cases by the observation of exciplex

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