Kinetic Study and Analytical Application of the Hexadecyltrimethylammonium Bromide-Catalyzed Reaction of 1-Fluoro-2,4-dinitrobenzene with Amines

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Abstract□ Arylation of amines by reaction with 1-fluoro-2,4-dinitrobenzene is catalyzed by micelles of cetrimonium bromide. This catalysis has been exploited to reduce the analysis time in the spectrophotometric determination of amines as their dinitrophenyl derivatives. The kinetics of the catalysis were studied for the five amines: alanine, phenylalanine, aniline, 4-methylaniline, and 4-methoxyaniline. The dependence of rate constant on surfactant concentration can be quantitatively accounted for by Berezin's model, in which uptake of the amine and the 1-fluoro-2,4-dinitrobenzene by the micelle is described as a partitioning phenomenon for both species. An alternative model is developed in which one reactant partitions into the micellar phase and the other binds to the micelle with 1:1 stoichiometry; the two models are formally equivalent. Intrinsic catalytic rate constants and binding constants were evaluated. About one-third to one-half of the maximum observed micellar acceleration is attributed to a true micellar catalysis, the remainder being ascribed to an increase in local reactant concentrations in the micelle.

Keyphrases □ 1-Fluoro-2,4-dinitrobenzene—hexadecyltrimethylammonium bromide-catalyzed reaction with amines, kinetics, analytical application □ Hexadecyltrimethylammonium bromide-catalyzed reaction—1-fluoro-2,4-dinitrobenzene with amines, kinetics, analytical application □ Kinetics—hexadecyltrimethylammonium bromide-catalyzed reaction of 1-fluoro-2,4-dinitrobenzene with amines, analytical application

1-Fluoro-2,4-dinitrobenzene undergoes nucleophilic aromatic substitution by amines to give dinitrophenylamines, which are useful derivatives for the spectrophotometric analysis of amines (1–5). Typical reaction times are 10–20 min at 65°. The catalysis of this reaction by the surfactant cetrimonium bromide was previously described (6). It was later suggested (7, 8) that this catalysis could be applied to the analytical system to reduce the reaction times. A preliminary communication showed that this was practical, and described analytical conditions making use of the micellar catalysis (9). The present paper extends the investigation of this analytical application and reports kinetic studies, and their interpretation, of the cetrimonium bromide-catalyzed reaction of 1-fluoro-2,4-dinitrobenzene with five amines.

EXPERIMENTAL

Materials—Cetrimonium bromide[1] was purified by a previous procedure (10). 1-Fluoro-2,4-dinitrobenzene was distilled under reduced pressure. Aniline[2] was distilled; bp 181°. 4-Methylaniline[3] (*p*-toluidine) was distilled under reduced pressure; bp 61.5°/2 mm Hg, mp 44.5–45° [lit. mp 44.8° (11)]. 4-Methoxyaniline[3] (*p*-anisidine) was distilled under reduced pressure; bp 98°/2 mm Hg, mp 56.5–57° [lit. mp 57° (12)]. Other chemicals were used directly.

Product Identification—Alanine and 1-fluoro-2,4-dinitrobenzene were reacted in pH 9.2 borate buffer in the presence of cetrimonium bromide. The solution was acidified to below pH 3 with concentrated HCl and was extracted with diethyl ether. The ether layer was dried, redissolved in ether, and then spotted on silica gel TLC plates[4]. This was developed with a mixed solvent of ether-glacial acetic acid-water (100:3:3). The product (2,4-dinitrophenylalanine) isolated in this way was recrystallized from 50% ethanol, and its IR spectrum was determined in solid potassium bromide for comparison with the spectrum of an authentic sample of 2,4-dinitrophenylalanine[5]. UV spectra were also measured.

The hydrolysis of 1-fluoro-2,4-dinitrobenzene was studied in pH 9.2 borate buffer containing cetrimonium bromide, but no amine. After hydrolysis the solution was acidified, extracted with ethyl acetate, the extract was evaporated to dryness, and the residue was dissolved in methanol for spotting on TLC plates. The development solvent was chloroform–methanol-glacial acetic acid (40:10:0.5). The spot was scraped off, dissolved in methanol, and centrifuged. The supernatant was dried, and the residue was compressed with potassium bromide for IR spectroscopy[6]. An authentic sample of 2,4-dinitrophenol was carried through the same procedure.

Kinetic Studies—For reactions in which the reagent (1-fluoro-2,4-dinitrobenzene) concentration was higher than the amine concentration, typical initial conditions were: 5×10^{-4} *M* amine and 0.035 *M* cetrimonium bromide in 0.065 *M* pH 9.2 borate buffer; the reaction was initiated by adding 1.0 ml of 1.3% v/v 1-fluoro-2,4-dinitrobenzene (dissolved in acetone) to 19 ml of thermostated aqueous solution. Samples of 1.0 ml were removed at recorded times and were added to 9.0 ml of a 1:100 dilution of concentrated HCl in dioxane (4). The absorbance was measured[7] at the wavelength of maximum absorption (usually 350 nm) in a 1.0-cm cell against a reagent blank carried through the same procedure.

For reactions in which the amine concentration exceeded the 1-fluoro-2,4-dinitrobenzene concentration, the reaction was monitored directly in the thermostated spectrophotometer cell compartment.

Proposed Analytical Method—To a 25-ml volumetric flask 0.25 g of cetrimonium bromide and enough of the amine sample should be added so that its final concentration will be 10^{-4} *M*; the solution brought to 19 ml with 0.065 *M* pH 9.2 borate buffer; the flask brought to the desired reaction temperature (25–45°); and the reaction initiated by adding 1.0 ml of 1.3% v/v 1-fluoro-2,4-dinitrobenzene in acetone. After ~5 half-lives at the experimental temperature, a 1.0-ml portion should be added to 9.0 ml of a 1:100 dilution of concentrated hydrochloric acid in dioxane, and the absorbance immediately measured at the absorption maximum against a reagent blank carried through the same procedure. A standard curve should be prepared by subjecting known concentrations of the same amine to the procedure.

RESULTS

Analytical Method—Analytical conditions require that the concentration of reagent (1-fluoro-2,4-dinitrobenzene) should be greater than that of the amine. Under these conditions, light absorption by the 2,4-dinitrophenolate produced through concurrent hydrolysis of the reagent interferes with direct observation of the dinitrophenylated amine. It is, therefore, necessary to withdraw samples and to acidify them, which stops the reaction and concomitantly alters the spectrum of the phenol so that it does not interfere with the detection of the amine derivative (4).

Figure 1 shows the extent of the catalysis by cetrimonium bromide in the reaction of alanine with 1-fluoro-2,4-dinitrobenzene. The apparent first-order plots were linear for two or more half-lives in both the presence and absence of surfactant. Table I lists half-lives for numerous amines subjected to this procedure, and the rate enhancement produced by the surfactant is given in the final column. Rate enhancements for aliphatic amino acids and peptides are in the range of 10–20, whereas aromatic amino acids show much greater enhancements. The neutral aniline has

[1] Baker Analyzed Reagent.
[2] Mallinckrodt.
[3] Aldrich.
[4] Eastman Kodak.
[5] Sigma Chemical Co.
[6] Perkin-Elmer 599B IR spectrophotometer.
[7] Cary models 14 or 16, or Perkin-Elmer 559 spectrophotometers.

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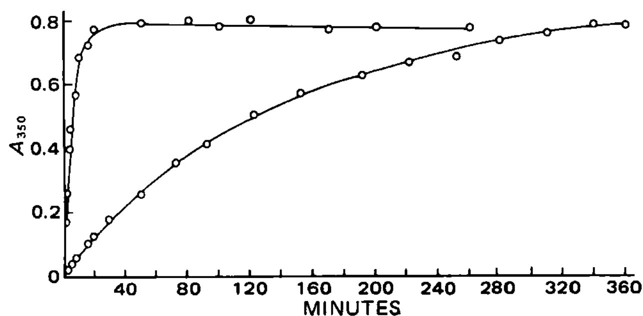


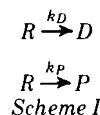
Figure 1—*Change of absorbance at 350 nm with time for the arylation of alanine at 23°: 5 × 10⁻⁴* M *alanine, 3.5 × 10⁻³* M *1-fluoro-2,4-dinitrobenzene, pH 9.2. Upper curve, 0.035* M *cetrimonium bromide; lower curve, no surfactant.*

the lowest relative rate in the table. These data suggest that the catalysis by the cationic micelle is assisted by anionic and hydrophobic sites on the amine. When both features are present, as in 11-aminoundecanoic acid, a very large rate enhancement can occur. The half-lives in Table I can guide the analyst in selecting appropriate reaction times.

The effect of temperature on the reaction rate was studied in the presence and absence of 0.0175 *M* surfactant to learn the extent of the analytical advantage to be gained by working at a higher temperature. The reaction was studied at 15, 25, 35, and 45°; the Arrhenius plots were linear. In the absence of surfactant, the activation enthalpy $\Delta H^{\ddagger}$ was 16.1 (*SD* 0.5) Kcal/mole and the activation entropy $\Delta S^{\ddagger}$ was −11.2 (*SD* 0.5) EU (entropy units). In the presence of surfactant, $\Delta H^{\ddagger}$ was 13.7 (*SD* 0.4) Kcal/mole and $\Delta S^{\ddagger}$ was −14.6 (*SD* 1.3) EU. No mechanistic interpretation is given to these results, because they include several effects (the micellar rate effect and the uptake of the two reactants by the micelle). However, the analytical reaction time can be reduced by a factor of ~3 by raising the temperature from 25 to 45°. The slopes of the concentration-absorbance curves were identical for reactions run at 25 and 45°.

The product identification studies showed, by means of TLC, IR spectroscopy, and UV spectroscopy, that the products of the reaction of 1-fluoro-2,4-dinitrobenzene with alanine in the presence of cetrimonium bromide were 2,4-dinitrophenylalanine and 2,4-dinitrophenol.

Reaction Order—In the analytical studies the reagent was in excess by necessity, but for studying the reaction kinetics it is more convenient to have the amine in excess. This permits the reaction to be monitored directly in the spectrophotometer. However, 1-fluoro-2,4-dinitrobenzene undergoes two reactions in this system, yielding the two products, a 2,4-dinitrophenylamine and 2,4-dinitrophenol. The following kinetic treatment takes this into account. Scheme I is the kinetic scheme, where R represents 1-fluoro-2,4-dinitrobenzene, D is the dinitrophenylamine derivative, P is dinitrophenol, k_D is an apparent first-order rate constant for the production of D, and k_P is an apparent first-order rate constant for the production of P.



Scheme I

Then $-d[R]/dt = (k_D + k_P)[R] = k[R]$, where $k = k_D + k_P$; the loss of R is a first-order process, and $[R] = [R]_0 \exp(-kt)$. The rate of formation of D is $d[D]/dt = k_D[R] = k_D[R]_0 \exp(-kt)$. Integrating this with the initial condition $[D] = 0$ at $t = 0$ gives:

$$[D] = \frac{k_D[R]_0}{k}(1 - e^{-kt}) \quad \text{(Eq. 1)}$$

In the same way, Eq. 2 is obtained:

$$[P] = \frac{k_P[R]_0}{k}(1 - e^{-kt}) \quad \text{(Eq. 2)}$$

The absorbance of the solution (in a 1-cm cell) at any time is given by:

$$A = \epsilon_R[R] + \epsilon_D[D] + \epsilon_P[P] \quad \text{(Eq. 3)}$$

Combining Eqs. 1–3 gives:

$$A = \frac{[R]_0}{k}(\epsilon_D k_D + \epsilon_P k_P) + \frac{[R]_0}{k}(\epsilon_R k - \epsilon_D k_D - \epsilon_P k_P)e^{-kt} \quad \text{(Eq. 4)}$$

Table I—Micellar Catalysis of Amine-1-Fluoro-2,4-dinitrobenzene Reactions by Cetrimonium Bromide [a]

Amine	Half-life/min		Rate Enhancement
	No Surfactant	0.035 *M* Surfactant	
Glycine	36.0	2.0	18.0
Alanine	87.4	4.7	18.6
Phenylalanine	32.0	<0.3	>94
Tyrosine	22.0	<0.5	>44
Tryptophan	9.0	<0.1	>90
Glycylglycine	63.5	5.4	11.8
Glycylglycylglycine	94.0	7.5	12.5
Glutamic acid	72.0	<0.3	>240
p-Aminobenzoic acid	137.5	3.0	45.8
11-Aminoundecanoic acid	133.0	<0.1	>1330
Aniline	60.0	7.5	8.0

[a] At pH 9.2 and 23°; 0.0035 *M* 1-fluoro-2,4-dinitrobenzene.

If the absorbance is measured at a wavelength where $\epsilon_D = \epsilon_P = \epsilon$, Eq. 4 simplifies to:

$$\epsilon[R]_0 - A = (\epsilon - \epsilon_R)[R]_0 e^{-kt} \quad \text{(Eq. 5)}$$

But $\epsilon[R]_0 = A_\infty$, the absorbance when reaction is complete. Therefore, a conventional plot of $\log(A_\infty - A)$ against t should be linear, the slope yielding $k = k_D + k_P$. Since k_P can be measured in a separate experiment in the absence of amine, the desired rate constant (k_D) is accessible. Absorbance measurements were made at 350 nm, where $\epsilon_D = \epsilon_P$, and the first-order plots were linear for over three half-lives.

At pH 9.2 with alanine serving as the amine substrate, the kinetic dependence on the amine and the reagent was established. In the presence of 0.035 *M* cetrimonium bromide, the rate was directly dependent on the concentrations of amine and 1-fluoro-2,4-dinitrobenzene, confirming the first-order dependence upon each of these reactants in the presence of the surfactant.

Kinetic Dependence on Surfactant Concentration—The kinetics of the reaction of five amines (alanine, phenylalanine, aniline, 4-methylaniline, and 4-methoxyaniline) were studied in the presence of varying concentrations of surfactant at 25° and pH 9.2; the amine concentrations were 0.001–0.1 *M*, and the 1-fluoro-2,4-dinitrobenzene concentration was 6.32×10^{-5} *M*. Figure 2 is a plot of the first-order rate constant (k_D) against the total surfactant concentration (C_T) for phenylalanine. The general pattern in Fig. 2 was seen with all amines, namely an increase in rate at low surfactant concentrations with a saturation-type effect setting in at high concentrations. However, instead of an invariant plateau level, a maximum is observed in the plot (13).

At very low surfactant concentrations, the rate constant depends linearly on surfactant concentration, as shown in Fig. 3 for three concentrations of alanine. The discontinuity in the plot marks the effective critical micelle concentration (*CMC*); below this concentration the surfactant exists solely as the monomer.

DISCUSSION

The Partitioning–Partitioning Model—The kinetic dependence of micellar catalysis on surfactant concentration is often described by means of a kinetic scheme analogous to the Michaelis–Menten model of enzyme kinetics (14). This description is appropriate for a first-order reaction (*i.e.*, one in which a single substrate is taken up by the micelle), for which it predicts a saturation curve with an invariant plateau value at high surfactant concentrations. Evidently, the Michaelis–Menten model cannot provide a quantitative treatment of a reaction like the nucleophilic substitution described here, for the concentration dependence of the rate reveals a maximum. It is necessary to take into account the uptake of two reactants by the micelle in this second-order reaction, and this leads to a quantitative description of the experimental curve. This was accomplished previously (15–18) by workers who investigated (among other systems) the acceleration of the aminolysis of 1-fluoro-2,4-dinitrobenzene with *N*-benzoyl-L-histidine methyl ester in the presence of cetrimonium bromide. To account for the dependence of rate on surfactant concentration they proposed a model in which both the 1-fluoro-2,4-dinitrobenzene (designated R) and the amine (S) are distributed between the micellar (M) and aqueous (W) phases in conformity with the simple distribution law. This model is referred to here as the partitioning–partitioning model, since it postulates a partitioning mechanism for the uptake of both solutes.

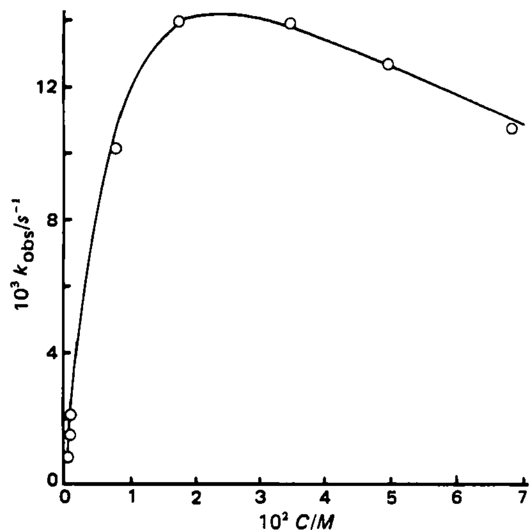


Figure 2—*Plot of first-order rate constant for the phenylalanine-1-fluoro-2,4-dinitrobenzene system at 25° and pH 9.2 as a function of surfactant concentration. The phenylalanine concentration is 1.04 × 10^{-3}* M. *The smooth line was drawn with Eq. 33.*

If V_T, V_M, and V_W represent the total volume of the system, the volume of the micellar phase, and the volume of the aqueous phase, respectively, then $V_T = V_M + V_W$, and:

$$\frac{V_W}{V_T} = 1 - \frac{V_M}{V_T} \quad \text{(Eq. 6)}$$

A mass balance on R yields:

$$[R]_T V_T = [R]_M V_M + [R]_W V_W \quad \text{(Eq. 7)}$$

and similarly for S. Substituting into Eq. 2 from Eq. 1:

$$[R]_T = [R]_M \frac{V_M}{V_T} + [R]_W \left(1 - \frac{V_M}{V_T}\right) \quad \text{(Eq. 8)}$$

The molar concentration of surfactant present as micelles, C, is defined:

$$C = C_T - (CMC) \quad \text{(Eq. 9)}$$

Letting V be the molar volume of surfactant, it follows that the product CV is the liters of surfactant present as micelles per liter of solution, or the volume fraction of the micellar phase, hence:

$$CV = V_M/V_T \quad \text{(Eq. 10)}$$

which, combined with Eq. 8, gives:

$$[R]_T = [R]_M CV + [R]_W(1 - CV) \quad \text{(Eq. 11)}$$

The distribution equilibria, according to this model, are:

$$R_W \rightleftarrows R_M$$

$$S_W \rightleftarrows S_M$$

Scheme II

The partition coefficient for R is defined:

$$P_R = \frac{[R]_M}{[R]_W} \quad \text{(Eq. 12)}$$

and similarly for S. Eqs. 11 and 12 are combined to yield:

$$\frac{[R]_T}{[R]_W} = 1 + (P_R - 1)CV \quad \text{(Eq. 13)}$$

The quantity K_R is defined:

$$K_R = (P_R - 1)V \quad \text{(Eq. 14)}$$

Then Eq. 15 is written for R, and Eq. 16 is the analogous equation for S:

$$\frac{[R]_T}{[R]_W} = 1 + K_R C \quad \text{(Eq. 15)}$$

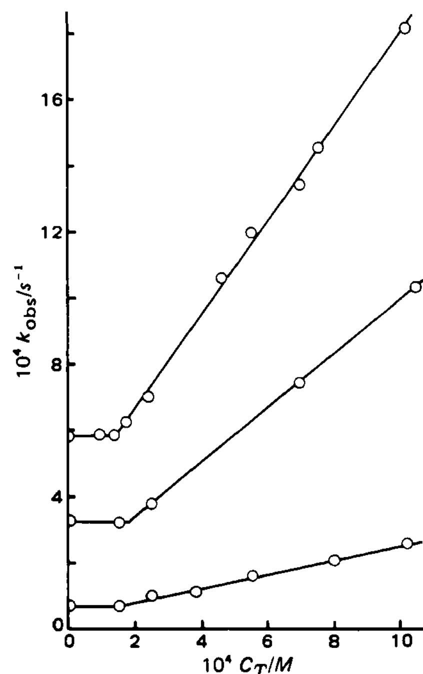


Figure 3—*Plot of first-order rate constant for the alanine-1-fluoro-2,4-dinitrobenzene system as a function of total surfactant concentration. Alanine concentrations, top to bottom: 0.025* M, *0.0125* M, *0.00267* M.

$$\frac{[S]_T}{[S]_W} = 1 + K_S C \quad \text{(Eq. 16)}$$

In these equations K_R and K_S have the units of M^{-1}; *i.e.*, they have the character of 1:1 binding constants.

The bimolecular reaction between R and S can occur in both phases, with corresponding rate equations:

$$v_M = k_M[R]_M[S]_M \quad \text{(Eq. 17)}$$

$$v_W = k_W[R]_W[S]_W \quad \text{(Eq. 18)}$$

The observed velocity (v) is equal to the sum of the products of the velocities in the individual phases and the volume fractions of the phases:

$$v = v_M CV + v_W(1 - CV) \quad \text{(Eq. 19)}$$

An experimentally observed second-order rate constant can be defined:

$$v = k_{\text{exp}}[R]_T[S]_T \quad \text{(Eq. 20)}$$

Equations 19 and 20 are combined with 15 and 16 and the partition coefficient definitions:

$$k_{\text{exp}} = \frac{k_M P_R P_S CV + k_W(1 - CV)}{(1 + K_R C)(1 + K_S C)} \quad \text{(Eq. 21)}$$

Equation 21 can be simplified for the present purpose. When partitioning into the micelle is favored, as with anionic and hydrophobic species, P is much larger than unity, and the binding constants from Eq. 14 can be written as $K_R = P_R V$ and $K_S = P_S V$. Moreover, when $CV \ll 1$, Eq. 21 becomes:

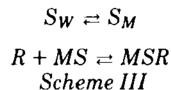
$$k_{\text{exp}} = \frac{k'_M K_R K_S C + k_W}{(1 + K_R C)(1 + K_S C)} \quad \text{(Eq. 22)}$$

where $k'_M = k_M/V$.

This model can account for the appearance of a maximum in the dependence of k_{exp} on C. As Berezin points out (17), to account for this maximum it is necessary to describe the uptake of both solutes, making the model, and the corresponding equation, qualitatively different from the Michaelis-Menten model.

A Binding-Partitioning Model—It is now shown that a result formally equivalent to the Berezin partitioning-partitioning model can be obtained with a different physical picture of the process. It is postulated that one of the reactants, the one in large excess (S in this case) partitions

between the micellar and aqueous phases, whereas the other reactant binds to the micelle with 1:1 stoichiometry. These equilibria are:



Scheme III

In this formulation, $[S]_M$ is the concentration of S in the micellar phase, and $[MS]$ is the solution concentration of S-containing micelles. There are no micelles without S, but there can be micelles without R. This is physically reasonable when $[S]_T >$ [micelles] $> [R]_T$. By arguments given above, Eq. 16 applies to S, whereas Eq. 23 defines the binding constant for R.

$$K'_M = \frac{[MSR]}{[R]_W[MS]} \quad \text{(Eq. 23)}$$

The rate equation for loss of R is given by:

$$-\frac{d[R]}{dt} = k_W[R]_W[S]_W + k_M[MSR][S]_M \quad \text{(Eq. 24)}$$

The mass balance on surfactant is:

$$C_T = [CMC] + n[MS] + n[MSR] \quad \text{(Eq. 25)}$$

where n is the micelle aggregation number. Combining Eqs. 9, 23, and 25:

$$[MS] = \frac{C}{n + nK'_M[R]_W} \quad \text{(Eq. 26)}$$

The mass balance on R is:

$$[R]_T = [R]_W + [MSR] \quad \text{(Eq. 27)}$$

since $[MSR]$ is the concentration of micelles each containing an R. This leads to:

$$[R]_W = \frac{[R]_T}{1 + K'_M[MS]} \quad \text{(Eq. 28)}$$

Combining the partition coefficient $P_S = [S]_M/[S]_W$ with Eqs. 23, 24, and 28 gives the rate equation:

$$-\frac{d[R]_T}{dt} = \left[\frac{k_M K'_M P_S[MS] + k_W}{1 + K'_M[MS]}\right][S]_W[R]_T \quad \text{(Eq. 29)}$$

This is first-order in $[R]_T$, with the apparent first-order rate constant k_{obs}:

$$k_{obs} = \left[\frac{k_M K'_M P_S[MS] + k_W}{1 + K'_M[MS]}\right][S]_W \quad \text{(Eq. 30)}$$

Eq. 26 is combined with Eq. 30 to give:

$$k_{obs} = \left[\frac{\dfrac{k_M K'_M P_S C}{n + nK'_M[R]_W} + k_W}{1 + \dfrac{K'_M C}{n + nK'_M[R]_W}}\right][S]_W \quad \text{(Eq. 31)}$$

Equation 31 is simplified by using the reasonable assumption $K'_M[R]_W \ll 1$, substituting $K_S = P_S V$, and replacing $[S]_W$ from Eq. 16 to give:

$$k_{exp} = \frac{k'_M K_M K_S C + k_W}{(1 + K_M C)(1 + K_S C)} \quad \text{(Eq. 32)}$$

where $k'_M = k_M/V$, $K_M = K'_M/n$, and $k_{exp} = k_{obs}/[S]_T$. Equation 32 for the binding–partitioning model is identical in form with Eq. 22 for the partitioning–partitioning model. In these equations the quantity K_S has the same significance, but K_R in Eq. 22 is interpreted as K'_M/n in Eq. 32 as a consequence of the different assumptions concerning the uptake of R into the micelle.

Estimation of the Model Parameters—Equations 22 and 32 can be written in the equivalent form:

$$k_{obs} = \left[\frac{k'_M K_M K_S C + k_W}{(1 + K_M C)(1 + K_S C)}\right][S]_T \quad \text{(Eq. 33)}$$

The parameters can be estimated in several ways from the dependence of k_{obs} on C.

A plot of k_{obs} against C_T, at very low C_T, will give $k_W[S]_T$ as the value of k_{obs} below the CMC. Above the CMC, the slope of the straight line is equal to $k'_M K_M K_S[S]_T$, from which the product $k'_M K_M K_S$ is found. The intersection of the straight line segments marks the CMC. Figure 3 shows plots of this type.

A plot of k_{obs} against C over the full range of C, as shown in Figure 2, exhibits a maximum if Eq. 33 describes the system. The concentration C_{max} corresponding to this maximum is found by setting the derivative dk_{obs}/dC equal to zero:

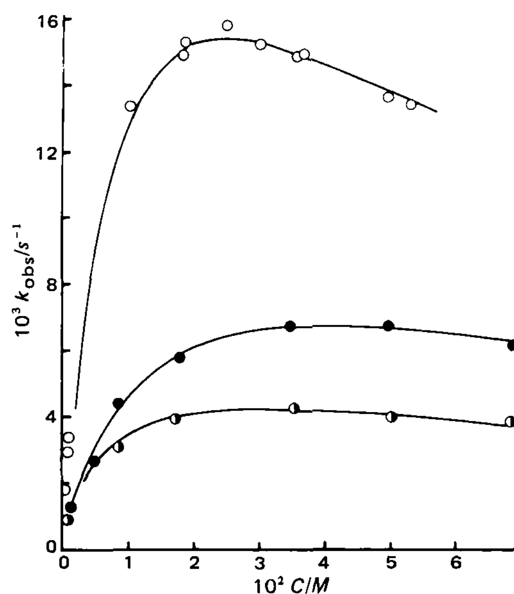


Figure 4—*Dependence of* k_{obs} *on surfactant concentration for aniline (○), 4-methylaniline (●), and 4-methoxyaniline (◑). The smooth curves were drawn with Eq. 33 and the parameters in Table II. The amine concentrations were: aniline, 0.0988* M; *4-methylaniline, 0.00807* M; *4-methoxyaniline, 0.0243* M.

$$C_{max} = (K_M K_S)^{-1/2} \quad \text{(Eq. 34)}$$

This result yields the product $K_M K_S$, and k'_M is obtained from this and the estimate of $k'_M K_M K_S$.

Inserting Eq. 34 into Eq. 32, and neglecting k_W, leads to Eq. 35, where k_{exp}^{max} is the value of k_{exp} when $C = C_{max}$:

$$\left[\frac{k_{max}^{exp}}{k'_M}\right]^{-1/2} = K_M{}^{-1/2} + K_S{}^{-1/2} \quad \text{(Eq. 35)}$$

With these relationships, the four parameters k_W, k'_M, K_M, and K_S can be evaluated. Because Eq. 33 is symmetrical in K_M and K_S, it is not possible to assign these quantities unambiguously.

Another approach is a modification of a method described previously (18). Eq. 32 can be rearranged to:

$$k_{exp} - k_W = \left[\frac{K_M C}{1 + K_M C}\right]\left[\frac{k'_M K_S}{1 + K_S C} - k_W\right] \quad \text{(Eq. 36)}$$

From this, Eq. 37 is obtained:

$$\frac{C}{k_{exp} - k_W} = \frac{1}{A} + \frac{(K_M + K_S)}{A}C + \frac{K_M K_S}{A}C^2 \quad \text{(Eq. 37)}$$

where $A = k'_M K_M K_S - k_W K_M(1 + K_S C)$. A plot of $C/(k_{exp} - k_W)$ against C is a curve, whose intercept at $C = 0$ is $1/(k'_M K_M K_S - k_W K_M)$. If the k_W term is negligible, this gives an estimate of $k'_M K_M K_S$.

Equation 32 is then rearranged to:

$$\frac{k'_M K_M K_S C + k_W - k_{exp}}{k_{exp} C} = K_M K_S C + (K_M + K_S) \quad \text{(Eq. 38)}$$

A plot of the left side against C yields $K_M K_S$ and $(K_M + K_S)$ from the slope and intercept.

By either of these methods K_M and K_S are found by solving the quadratic formula. In some instances the solution is indeterminate—that is, the estimates $K_M K_S$ and $(K_M + K_S)$ are mutually inconsistent, because of experimental error. The individual constants are then evaluated by a curve-fitting method, in which Eq. 33 is fitted to the experimental points. This is a straightforward process, because the quantities $k'_M K_M K_S$ and $K_M K_S$ serve as constraints. Figures 2 and 4 show some of these curves.

Interpretation of the Micellar Catalysis—Table II gives the values of K_M, K_S, k_W, k'_M, and k_M for the cetrimonium bromide-catalyzed reaction of 1-fluoro-2,4-dinitrobenzene with five amines. The second-order rate constant k_M was obtained from the relationship $k_M = k'_M/V$, where V is the molar volume of surfactant; in this calculation V was taken as 0.35 liter/mole, as estimated by Berezin and coworkers (15, 18), who have

Table II—Parameters for the Cetrimonium Bromide-Catalyzed Reaction of 1-Fluoro-2,4-dinitrobenzene with Some Amines at 25° [a,b]

Amine	K_S, M^{-1}	K_M, M^{-1}	k'_M, s^{-1}	k_M, $M^{-1}s^{-1}$	k_W, $M^{-1}s^{-1}$	k_M/k_{exp}^{max}
Alanine	9.5 (0.7)	70. (5.2)	0.091 (0.012)	0.26	0.025	0.56
Phenylalanine	25.9 (1.1)	66. (2.8)	1.39 (0.19)	3.98	0.093	0.29
Aniline	9.2 (0.4)	113. (4.3)	0.0075 (0.0018)	0.0213	0.005	0.50
4-Methylaniline	27.0 (1.8)	55.5 (3.6)	0.20 (0.024)	0.57	0.143	0.30
4-Methoxyaniline	13.7 (1.0)	43.8 (3.3)	0.048 (0.0063)	0.138	0.0223	0.50

[a] Symbols refer to Eq. 33. [b] Standard deviations in parentheses.

also discussed the uncertainty involved in estimating V (17). The assignment of K_M and K_S to the binding constant estimates is based on two chemical factors: (a) it is expected that phenylalanine will be taken up by the micelle more extensively than will alanine; (b) the K_S values for the three anilines vary roughly as their partition coefficients in the octanol–water system (19). K_M represents binding of 1-fluoro-2,4-dinitrobenzene to the micelle; the variation in this quantity is greater than expected, indicating that the nature of the amine taken up by the micelle influences binding of the second reactant.

The uncertainties assigned to the K_S, K_M, and k'_M values in Table II are based upon the uncertainties in the products $k'_M K_M K_S$ and $K_M K_S$, which are the quantities directly evaluated from the data. Division of the uncertainty in $K_M K_S$ between K_M and K_S was based on the assumption that the uncertainty was weighted by the value of the constant, according to the relationship $s_{K_M}/s_{K_S} = K_M/K_S$, where s represents standard deviation.

Table II includes the k_W values, and it is seen that the ratio of k_M/k_W is substantially greater than unity for all of the amines. The last column of the table gives the ratio of k_M to k_{exp}^{max}, the maximum value of the observed second-order rate constant. This ratio is a measure of the fraction of true *micellar catalysis* contributing to the total micellar acceleration effect, as suggested:

$$\frac{k_M}{k_{exp}^{max}} = \frac{k_M/k_W}{k_{exp}^{max}/k_W}$$

That is, approximately one-third to one-half of the maximum observed acceleration is a consequence of catalysis by the micelle, the remainder being a concentration effect, through which the micelle increases the local concentrations of the reactants.

A previous study (18) carried out a similar analysis for the cetrimonium bromide-catalyzed reaction of 1-fluoro-2,4-dinitrobenzene with *N*-benzoyl-L-histidine methyl ester. These authors found that k_M/k_W was in the range of 1–2, and they concluded that most of the micellar acceleration was a result of the concentration of the reactants in the micellar phase. They also measured the binding constants by an independent solubility method, finding the value of 27 M^{-1} at 18° for 1-fluoro-2,4-dinitrobenzene. This value will be smaller at 25° because the heat of binding is negative. This result is not in good agreement with the K_M assignment in Table II, and this assignment is therefore in some doubt[8].

[8] One factor that may influence the binding constants is the composition of the solvent, which in the present studies contained 5% acetone. Another possible factor may be the buffer species.

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