Micellar Effects upon Nucleophilic Aromatic and Aliphatic Substitution[1]

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Abstract: The reaction between hydroxide ion and 2,4-dinitrochlorobenzene in water or aqueous alcohol is catalyzed by cationic micelles of cetyltrimethylammonium bromide (CTA) and retarded by anionic micelles of sodium lauryl sulfate (NaLS), but a nonionic micelle has no effect. The cationic micelles decrease the activation energy and the anionic micelles increase it. Added salts, especially arenesulfonates, inhibit the catalysis by CTA. The rate constant, in the presence of CTA, increases to a maximum, and then falls, and the kinetic form can be interpreted quantitatively in terms of incorporation of substrate and hydroxide ion into the cationic micelles. The binding constant between substrate and ionic micelles is 4600 for CTA and 2700 for NaLS in water at 25°. The kinetic effects of the ionic micelles are much larger in water than in ethanol-water 25:75 w/w or in *t*-butyl alcohol-water 18:82 w/w. The reaction between thiophenoxide ion and 2,4-dinitrochlorobenzene in ethanol-water 25:75 w/w is also assisted by cationic micelles of CTA, and inhibited by anionic micelles of NaLS. There is similar catalysis and retardation of the reaction between *n*-pentyl bromide and thiosulfate ion by CTA and NaLS in ethanol-water 25:75 w/w. However, these effects disappear in ethanol-water 44:56 w/w where CTA and NaLS display simple positive and negative kinetic salt effects.

We have observed specific kinetic effects of electrolytes which apparently depend upon the reaction mechanism and the charge density of the ions, *e.g.*, A1 hydrolyses of carboxylic esters are assisted much more by anions of low than of high charge density, and the opposite is true for the A2 hydrolyses.[2] We also observed specific electrolyte effects in the reaction between hydroxide ion and 2,4-dinitrochlorobenzene and found that a cation of low charge density, *e.g.*, tetramethylammonium, stabilizes the anionic transition state relative to the hydroxide ion, while the alkali metal cations of higher charge density have the opposite effect.[3]

These relations between reaction rate and charge density led us to examine the effect of ionic micelles upon the rates of some of these reactions. There are many recent investigations of the kinetic effects of micelles.[4-11] Generally they fit the simple rules put forth by Hartley for absorption of solutes into micelles,[12] and several workers have combined the kinetic study with a determination of the amounts of reactants incorporated into the micelle.[8,10] In particular, Richards and his coworkers have shown that detergents affect the rate of reaction between 2,4-dinitrofluorobenzene and amines, and have determined the rate inside the micelle.[8] The reaction between aryl fluorides and nucleophiles is a two-step reaction involving nucleophilic addition to give a tetrahedral intermediate whose decomposition may be slow.[13] Because of these possible complications with an aryl fluoride, we examined the reaction between hydroxide and thiophenoxide ion and 2,4-dinitrochlorobenzene, where the slow step is nucleophilic addition and the decomposition of the intermediate is fast.[13] We also determined the distribution of the aryl chloride between water and the micelle in order to estimate the rates of reaction in the two phases. The reaction of 2,4-dinitrochlorobenzene and hydroxide ion was carried out in both water, aqueous ethanol, and *t*-butyl alcohol, and that with thiophenoxide in aqueous ethanol. As an example of a simple S_N2 reaction of an alkyl halide we examined the reaction between *n*-pentyl bromide and sodium thiosulfate,[14] but the alkyl halide was so insoluble in water that we had to use aqueous ethanol as solvent.

Some of the earlier studies of micellar effects upon reactions between hydroxide ion and uncharged substrates were carried out using buffer solutions to control the pH. This procedure has the disadvantage that the hydrogen ion activity in the body of the solution as measured by a glass electrode, for example, may be different from that in the micelle, where much of the reaction is occurring. This problem is not present in our reactions where we control the concentration of the nucleophilic anion.

Experimental Section

Materials. Cetyltrimethylammonium bromide (CTA) was purified by the method of Duynstee and Grunwald,[4] as was sodium lauryl sulfate (NaLS) (City Chemical Corp.). The nonionic detergent, Igepal, was dinonylphenol condensed with 24 ethylene oxide units (General Aniline and Film Corp.) and is denoted as DNPE in the text. It was kindly supplied by Professor T. C. Bruice and was used without further purification. The purification of the other reagents has been described.[3]

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[1] Support of this work by the National Science Foundation is gratefully acknowledged.

[2] C. A. Bunton, J. Crabtree, and L. Robinson, *J. Am. Chem. Soc.*, **90**, 1258 (1968).

[3] C. A. Bunton and L. Robinson, *ibid.*, **90**, 5965 (1968).

[4] E. F. Duynstee and E. Grunwald, *ibid.*, **81**, 4540, 4542 (1959).

[5] M. T. A. Behme and E. H. Cordes, *ibid.*, **87**, 260 (1965).

[6] M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, **87**, 266 (1965).

[7] J. L. Kurz, *J. Phys. Chem.*, **66**, 2239 (1962).

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[9] K. G. van Senden and C. Koningsberger, *Tetrahedron*, **22**, 1301 (1966).

[10] F. M. Menger and C. E. Portnoy, *J. Am. Chem. Soc.*, **89**, 4698 (1967).

[11] (a) T. E. Wagner, C. Hsu, and C. S. Pratt, *ibid.*, **89**, 6366 (1967); (b) T. C. Bruice, J. Katzhendler, and L. R. Fedor, *ibid.*, **90**, 1333 (1968).

[12] G. S. Hartley, *Trans. Faraday Soc.*, **30**, 444 (1934).

[13] J. F. Bunnett, *Quart. Rev.* (London), **12**, 1 (1958); S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963); J. F. Bunnett and R. H. Garst, *J. Am. Chem. Soc.*, **87**, 3875, 3879 (1965).

[14] T. I. Crowell and L. P. Hammett, *ibid.*, **70**, 3444 (1948); P. M. Dunbar and L. P. Hammett, *ibid.*, **72**, 109 (1950).

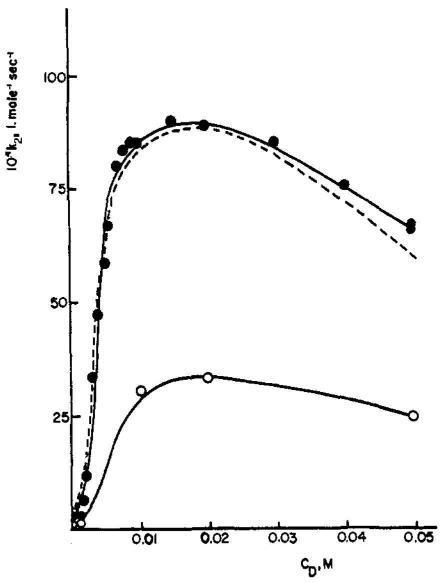

Figure 1. Second-order rate constants for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene in water in the presence of CTA: ○, at 15.0°; ●, at 25.0°; broken line is calculated.

Kinetics. The reaction of 2,4-dinitrochlorobenzene was followed spectrophotometrically and the reaction between thiosulfate ion and *n*-pentyl bromide was followed titrimetrically by methods already described.[8]

The concentration of 2,4-dinitrochlorobenzene was 10^{-4} *M* for reaction with sodium hydroxide and 5×10^{-5} *M* for reaction with sodium thiophenoxide, and the concentration of sodium thiosulfate and *n*-pentyl bromide was 0.02 *M*, except for the runs in ethanol-water 25:75 w/w where they were 10^{-3} *M*, because of the low solubility of the alkyl halide. For reactions of 2,4-dinitrochlorobenzene the concentration of hydroxide ion was much higher than that of the aryl chloride, and we calculated first-order rate constants graphically and converted them into second-order rate constants. The rapid reaction between thiophenoxide ion and 2,4-dinitrochlorobenzene in aqueous ethanol in the presence of CTA was followed by forcing a square Teflon plunger into the reaction solution contained in a conventional 1-cm cell. The plunger had small tapered holes into which the substrate in the reaction solution was held by capillary attraction, and the solutions were mixed very rapidly. For the fastest reactions only part of the reaction could be followed, but the plots of log *C* against time were linear for 2 half-lives of that part of the reaction which was followed. Because of the low solubility of sodium thiophenoxide we could not use this reagent in water. We used equal reagent concentrations for the reaction between *n*-pentyl bromide and sodium thiosulfate and calculated the second-order rate constants directly. There was some scatter in the rate constants for this reaction in ethanol-water 25:75 w/w where we had to use *ca.* 10^{-3} *M* reagents, and the detergents made it difficult to determine the end point for the titration with iodine using starch as indicator.

Solubility Measurements. The solubility of 2,4-dinitrochlorobenzene in the aqueous detergent solutions was determined after equilibration by hydrolyzing it to 2,4-dinitrophenol which was determined spectrophotometrically by methods already described.[8]

Determination of Critical Micelle Concentration. Two methods were used to determine the critical micelle concentrations. For neutral aqueous alcohol we measured the conductivity at 25.0° and by plotting Λ against $C^{1/2}$ obtained the usual break which indicates micelle formation.[15] This method could not be used in the presence of sodium hydroxide, or for DNPE, and here we used the dye method,[16,17] although it is known to be somewhat unreliable because incorporation of the dye may induce micellization.[18] The indicators used were bromophenol blue for CTA and DNPE and methylene blue for NaLS, and the absorbances were measured at 5900 Å for bromophenol blue and 6580 Å for methylene blue.

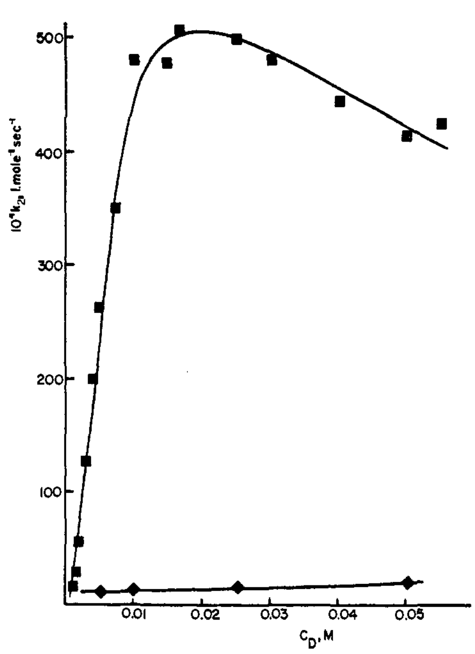

Figure 2. Second-order rate constants for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene in water in the presence of CTA and CNPE at 45.0°: ■, CTA; ◆, DNPE.

Results

Kinetics. The effect of a cationic detergent upon the second-order rate constant, k_2, for the reaction between hydroxide ion (0.05*M*) and 2,4-dinitrochlorobenzene in water is very simple. The reaction rate increases sharply with concentrations of CTA above the cmc to a maximum at a detergent concentration of *ca.* 0.015 *M* (Figures 1 and 2). The second-order rate constants for reaction between hydroxide ion and 2,4-dinitrochlorobenzene in water are, at 15.0°, 0.37×10^{-4}; at 25.0°, 1.42×10^{-4}; and at 45.0°, 13.5×10^{-4} l. mol^{-1} sec^{-1}. Increasing the hydroxide ion concentration decreases the second-order rate constant of the detergent-catalyzed hydrolysis (Table I), probably because sodium hydroxide affects the electrolyte properties of the ionic micelles. However, the effects are small by comparison with the over-all kinetic effects of the detergent. Changes in temperature do not affect the general relation between reaction rate and concentration of CTA. Added salts decrease the rate in the presence of CTA (Table II). For the most part they decrease, rather than suppress, the catalysis, but sodium toluene-*p*-sulfonate and naph-

Table I. Effect of Hydroxide Ion Concentration upon the Detergent-Catalyzed Hydrolysis of 2,4-Dinitrochlorobenzene[a]

	[CTA], *M*		
	0.01	0.02	0.05
[NaOH], *M*		10^4k_2, l. mol^{-1} sec^{-1}	
0.005	110	115	93
0.010	109	116	93
0.025	107	109	87
0.050	83	84	67

[a] In water at 25.0°.

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(15) R. J. Williams, J. N. Phillips, and K. J. Mysels, *Trans. Faraday Soc.*, **51**, 728 (1955).

(16) G. S. Hartley, *J. Chem. Soc.*, 1968 (1938).

(17) M. L. Corrin, H. B. Klevens, and W. D. Harkins, *J. Chem. Phys.*, **14**, 480 (1946); M. L. Corrin and W. D. Harkins, *J. Am. Chem. Soc.*, **69**, 679, 683 (1947).

(18) P. Mukerjee and K. J. Mysels, *ibid.*, 77, 2937 (1955).

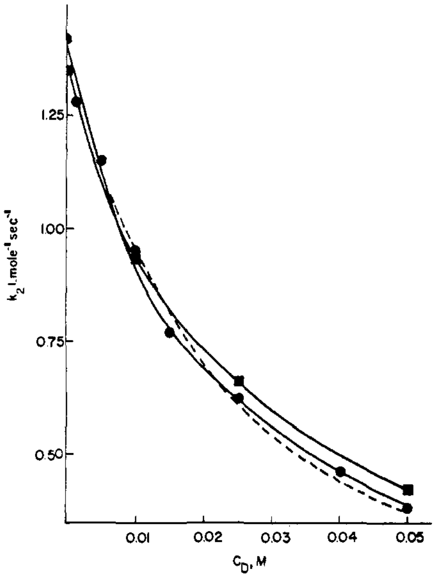

Figure 3. Second-order rate constants for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene in water in the presence of NaLS: ●, at 25.0°, 10^4k_2; the broken line is calculated; ■, at 45.0°, 10^3k_2.

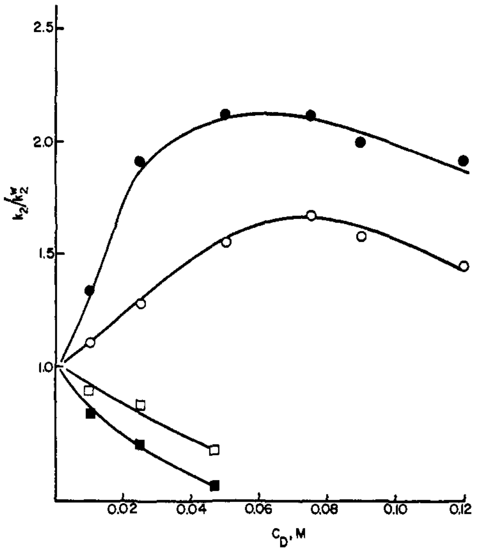

Figure 4. Relative second-order rate constants for the reaction between lyate ions and 2,4-dinitrochlorobenzene in ethanol-water 25:75 w/w: ●, CTA at 25.0°; ○, CTA at 45.0°; ■, NaLS at 25.0°; □, NaLS at 45.0°.

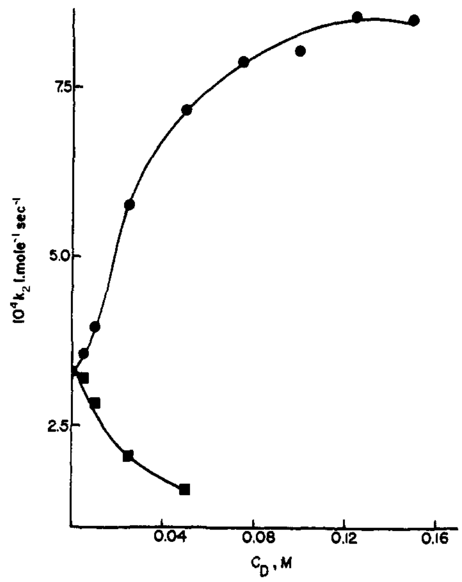

Figure 5. Second-order rate constants for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene in *t*-butyl alcohol-water 18:82 w/w at 25.0°: ●, CTA; ■, NaLS.

thalenesulfonate, when in concentration equal to or higher than that of the detergent, almost completely suppress the catalysis, and even when sodium naphthalenesulfonate is present at a concentration which is half that of the detergent it still sharply decreases the rate. Sodium β-naphthalenesulfonate could not be studied at high concentration, because then it gave a precipitate with the cationic detergent.

Added sodium lauryl sulfate decreases the reaction rate in water at both 25.0 and 45.0° (Figure 3), but the uncharged detergent has very little kinetic effect (Figure 2). The kinetic effects of detergents are smaller in ethanol-water 25:75 w/w than in water, as is shown in Figure 4 for the reaction between hydroxide ion (0.05 *M*) and 2,4-dinitrochlorobenzene where the rate constant, relative to that in the absence of detergent, is plotted against detergent concentration. With CTA the rate increases sharply to a maximum, but the over-all rate enhancement at the maximum is only twofold as compared with approximately 100-fold in water. The retardation by sodium lauryl sulfate is also much less in aqueous ethanol than in water. (In the absence of detergent, at 25.0°, $k_2 = 3.94 \times 10^{-4}$, and at 45.0°, 27.6×10^{-4} l. mol^{-1} sec^{-1} in this solvent.) Similar results were obtained in aqueous *t*-butyl alcohol (Figure 5).

Table II. Effect of Added Salts upon the Detergent-Catalyzed Hydrolysis of 2,4-Dinitrochlorobenzene[a]

		[CTAB], *M*		
		0.005	0.01	0.02
Salt	[Salt], *M*	10^4k_2, l. mol^{-1} sec^{-1}		
		73.3	109	116
NaCl	0.040		48.3	55.8
KCl	0.040		43.3	50.0
NaBr	0.040		25.8	34.6
Na_2SO_4	0.020		46.7	53.3
$NaCH_3SO_3$	0.040		50.0	57.5
$NaC_7H_7SO_3$	0.040		2.78	4.18
$NaC_{10}H_6SO_3$	0.005	4.82		
$NaC_{10}H_6SO_3$	0.010			33.8

[a] In aqueous 0.01 *M* NaOH at 25.0°. In these conditions with no detergent $k_2 = 1.42 \times 10^{-4}$ l. mol^{-1} sec^{-1}.

Although the detergent effects do not change markedly with temperature the activation enthalpy is affected by ionic detergents. For reaction in water CTA decreases the activation enthalpy (Table III), and when reaction is taking place almost wholly on the micelle the activation enthalpy is *ca.* 4 kcal mol^{-1} sec^{-1} lower than for reaction in water, because of the favorable electrostatic interactions. The activation entropy is, however, less favorable for reaction on a CTA micelle, presumably because of the decrease in the mobility of the substrate. Addition of micelles of the anionic detergent, NaLS, leads to an increase in the activation enthalpy because of unfavorable electrostatic interactions, and there is a slight decrease in the activation entropy.

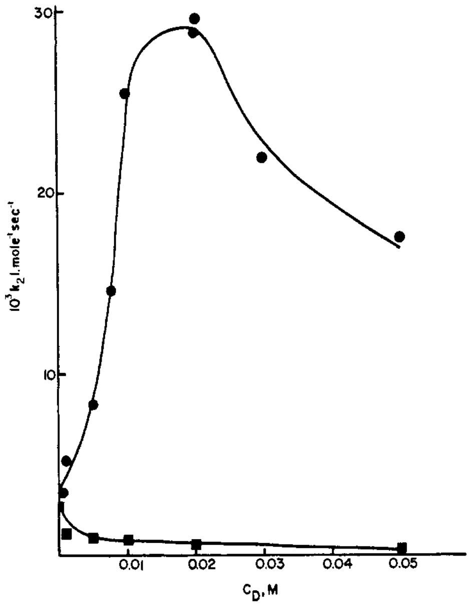

Figure 6. Second-order rate constants for the reaction between thiosulfate ion and *n*-pentyl bromide in ethanol-water 25:75 w/w at 25.0° with 0.001 *M* reagents: ●, CTA; ■, NaLS.

The effects of micelles upon the activation parameters are smaller in aqueous ethanol than in water, as are their effects upon rates. These values of ΔS^* and ΔH^* are based on measurements at two temperatures only, and are less reliable than in water, but the main effects are upon the activation enthalpy, which is decreased by CTA and increased by NaLS.

Table III. Variation of Activation Parameters for Reaction between Hydroxide Ion in the Presence of Ionic Detergents[a]

Detergent	C_D, *M*	ΔH^*, kcal mol^{-1}	ΔS^*, eu
		21.3	−5.2
CTA	0.001	18.3	−13.8
CTA	0.010	16.4	−13.4
CTA	0.020	16.5	−14.3
CTA	0.050	16.6	−14.3
NaLS	0.010	21.3	−5.6
NaLS	0.025	21.9	−6.5
NaLS	0.050	22.3	−7.5
		17.8[b]	−2.9[b]
CTA	0.010	16.1[b]	−2.4[b]
CTA	0.050	15.0[b]	−1.5[b]
NaLS	0.010	19.1[b]	−3.3[b]
NaLS	0.050	20.5[b]	−4.7[b]

[a] Taking 1 *M* reagents at 25.0° as the standard state, and in water unless specified. [b] Ethanol-water 25:75 w/w.

The relation between reaction rate and detergent concentration for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene is very similar in *t*-butyl alcohol-water 18:82 w/w (Figure 5) and is very similar to that observed in aqueous ethanol (Figure 4) although the catalysis is slightly larger, but less than that observed in water. Similar micellar effects are observed for the reaction between thiophenoxide ion and 2,4-dinitrochlorobenzene (Table IV). Although this reaction is so fast that the rate constants cannot be measured accurately for higher concentrations of CTA, there again appears to be a rate maximum at *ca.* 0.05 *M* CTA.

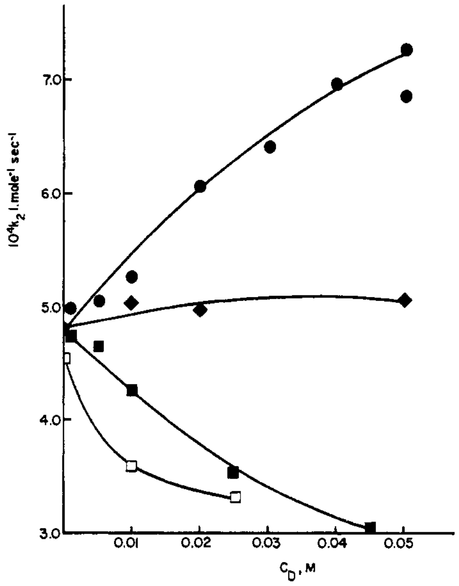

Figure 7. Second-order rate constants for the reaction between thiosulfate ion and *n*-pentyl bromide in aqueous ethanol at 25.0° with 0.02 *M* reagents: ●, CTA in ethanol-water 44:56 w/w; ■, NaLS in ethanol-water 44:56 w/w; ◆, DNPE in ethanol-water 44:56 w/w; □, NaLS in ethanol-water 55:45 w/w.

Because of solubility and analytical problems, the reaction between *n*-pentyl bromide and sodium thiosulfate was followed only in aqueous alcohol (Figures 6 and 7). For ethanol-water 25:75 w/w the general effects of the detergents were similar to those found for the reaction between lyate ions and 2,4-dinitrochlorobenzene (Figure 6). However, with the less aqueous solvent, ethanol-water 44:56 w/w, the pattern changes (Figure 7), and the effects become similar to those of simple electrolytes.

Table IV. Micellar Effects upon the Reaction between Thiophenoxide Ion and 2,4-Dinitrochlorobenzene[a]

C_D, *M*	CTA	NaLS
0.001	82	
0.0025	1.1 × 10^2	
0.005	1.9 × 10^2	80.1
0.010		75.2
0.0125	6.9 × 10^2	
0.025	1.0 × 10^3	67.0
0.050	1.3 × 10^3	52.2
0.075	1.2 × 10^3	
0.100	1.0 × 10^3	

[a] Values of k_2, l. mol^{-1} sec^{-1}, at 25.0°, in ethanol-water 25:75 w/w, and 5 × 10^{-4} *M* sodium thiophenoxide and 5 × 10^{-3} *M* NaOH. In the absence of detergent k_2 = 81.8 with 5 × 10^{-4} *M* sodium thiophenoxide and 82.8 with 10^{-3} *M* sodium thiophenoxide.

Critical Micelle Concentrations. Addition of sodium hydroxide decreases the cmc of both CTA and NaLS in water, as shown in Table V. The cmc's of these detergents are also much lower in aqueous ethanol than in water. These results are in agreement with the general observation that addition of electrolytes and organic solvents to water decreases the cmc of ionic detergents.[19]

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(19) K. Shinoda in "Colloidal Surfactants," K. Shinoda, T. Nagagawa, B.-I. Tamamushi, and T. Isenura, Ed., Academic Press, New York, N. Y., 1963, Chapter I.

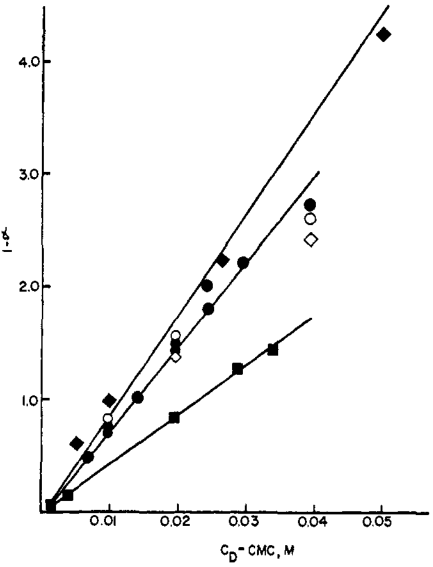

Figure 8. Effects of detergents on the solubility of 2,4-dinitrochlorobenzene in water at 25.0°: ●, CTA; ○, CTA + 0.04 M NaCl; ◇, CTA + 0.04 M $C_7H_7 \cdot SO_3Na$; ■, NaLS; ◆, DNPE.

Incorporation of Substrate. We used solubility measurements to determine the amount of 2,4-dinitrochlorobenzene which was taken up by the micelles. If we consider only concentrations of detergent well above the cmc, and also assume that incorporation of the substrate into the micelle does not change the cmc, we can assume an equilibrium between the substrate in solution, S, and that in the micelle, SD_n[20]

Table V. Critical Micelle Concentrations[a]

Detergent	Solvent	Cmc, M
CTA	H_2O	7.8×10^{-4} [b]
CTA	H_2O[d]	3.2×10^{-4} [e]
CTA	EtOH-H_2O 25 wt %	9×10^{-5} [f]
NaLS	H_2O	6.4×10^{-3} [c]
NaLS	H_2O[d]	2.5×10^{-3} [e]
NaLS	EtOH-H_2O 25 wt %	7×10^{-5} [f]
Igepal	H_2O[d]	4.7×10^{-4} [e]

[a] At 25.0°. [b] *Cf.* ref 21. [c] M. L. Corrin and W. D. Harkins, *J. Am. Chem. Soc.*, **69**, 679 (1947); J. N. Phillips and K. J. Mysels, *J. Phys. Chem.*, **59**, 325 (1955). [d] 0.05 M NaOH. [e] Determined spectrally. [f] Determined conductometrically.

$$D_n + S \overset{K}{\rightleftharpoons} SD_n$$

where C_m, the concentration of micelles, is given by eq 1

$$C_m = \frac{C_D - \text{cmc}}{N} \tag{1}$$

where C_D is the total concentration of detergent, and N the aggregation number.

If we assume that the increase in solubility of the substrate in the presence of the detergent is caused wholly by its incorporation into the micelles, we can then calculate the amount, α, of substrate present in the micelle from the relative solubilities in detergent solution and water, and calculate K/N, using eq 2.

$$\frac{K}{N} = \frac{\alpha}{(1 - \alpha)(C_D - \text{cmc})} \tag{2}$$

Figure 8 shows plots of $\alpha/(1 - \alpha)$ against C_D − cmc for CTA and NaLS in water at 25.0°.

The values of K/N obtained from Figure 8 are 75 for CTA, 44 for NaLS, and 88 for the nonionic detergent, DNPE. For CTA, $N \approx 61$,[21] and for NaLS, $N \approx 62$,[22] and therefore, for the incorporation of 2,4-dinitrochlorobenzene into CTA, $K \approx 4600$, and into NaLS, $K \approx 2700$. The aggregation number is not known for DNPE, but it, and therefore K, is probably of the order found for the ionic detergents.

These results show that the failure of the uncharged detergent to catalyze the reaction is not due to its inability to incorporate the substrate. They also show that there is strong binding between substrate and micelle, and as has been noted these binding constants may be as large as some of those found for enzyme–substrate interactions.[10] The results in Figure 8 show that added sodium chloride or tosylate does not markedly affect the incorporation of 2,4-dinitrochlorobenzene into the CTA micelle.

Discussion

Kinetics in Water. The qualitative picture is very simple, and consistent with other work.[4,10] The substrate, *e.g.*, 2,4-dinitrochlorobenzene, when incorporated into a cationic micelle, *e.g.*, CTA, is more readily attacked by an anion, because of the electrostatic attraction, but the opposite is true for incorporation into an anionic micelle, *e.g.*, NaLS, and incorporation into a nonionic micelle has no kinetic significance.

Anticatalysis. The rate retardation of the reaction between hydroxide ion and NaLS can be analyzed very simply using the treatment that has been applied to similar systems.[10] We assume reaction of the hydroxide ion with the substrate in the water or on the micelle

$$\begin{tikzcd} D_n + S \arrow[r, shift left] \arrow[d, "OH^-"', "k_2^w"] & SD_n \arrow[l, shift left] \arrow[dl, "OH^-"', "k_2^m"] \\ \text{products} & \end{tikzcd}$$

and following the usual approximations,[10] we can write

$$\frac{1}{k_2^w - k_2} = \frac{1}{k_2^w - k_2^m} + \frac{1}{(k_2^w - k_2^m)} \frac{N}{K(C_D - \text{cmc})} \tag{3}$$

where k_2 is the observed second-order rate constant.

Equation 3 fits the results reasonably well (Figure 9) except at low detergent concentrations where there is some curvature in the plot, as is to be expected because of the approximations made in the derivation of eq 3.[10] The value of K/N determined kinetically using eq 3 is 58, which is reasonably close to the value of 45 calculated from the enhanced solubility of 2,4-dinitrochlorobenzene in aqueous NaLS in the absence of hy-

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[20] See ref 10 for a discussion of the validity of these approximations as applied to kinetic effects of detergents.

[21] E. W. Anacker, R. M. Rush, and J. S. Johnson, *J. Phys. Chem.*, **68**, 81 (1964).

[22] K. J. Mysels and L. H. Princen, *ibid.*, **63**, 1696 (1959); *cf.* R. W. Mattoon, R. S. Stearns, and W. D. Harkins, *J. Chem. Phys.*, **16**, 644 (1948); D. Stigter, *Rec. Trav. Chim.*, **73**, 611 (1954).

droxide ion (Figure 8). Exact agreement between these two independent methods is not to be expected, because the hydroxide ion may change both the aggregation number of the detergent and the equilibrium constant for incorporation of 2,4-dinitrochlorobenzene into the micelle. In addition, the anionic detergent may indirectly affect the rate of that part of the reaction which continues in the water, but this effect appears to be relatively unimportant because the experimental results fit the predictions of 3 reasonably well.

The intercept of the plot in Figure 9 gives $k_2^{\mathrm{w}} - k_2 = -1.4 \times 10^{-4}$ l. mol^{-1} sec^{-1}, which is very close to the value of $k_2 = 1.42 \times 10^{-4}$ l. mol^{-1} sec^{-1} in the absence of detergent,[3] showing that, as expected, the reaction between 2,4-dinitrochlorobenzene and hydroxide ion is very slow when the substrate is incorporated into the anionic micelle. As another indication of the applicability of eq 3, the broken line plotted in Figure 3 was calculated using $K/N = 58$ and fits the experimental points at 25.0° reasonably well.

Catalysis. For reaction in the presence of CTA, the general form of plots of k_2 against detergent concentration (Figures 1 and 2), and anticatalysis by added salts, are qualitatively understandable from electrostatic considerations. For an increase in the ionic strength of 0.04, sulfate, mesylate, or chloride has similar effects (Table III), but sodium bromide has a larger effect. Sodium tosylate (0.04 M) almost suppresses the catalysis by CTA, and sodium β-naphthalenesulfonate, even at very low concentration, is still more effective, although these salts do not stop the incorporation of 2,4-dinitrochlorobenzene into the micelle (Figure 8). Therefore, it seems that an arenesulfonate ion binds very strongly to the cationic micelle and by decreasing its net positive charge so reduces the electrostatic attraction of hydroxide ion that the catalysis is suppressed. The strong inhibition by the arenesulfonate ions shows the extent to which physical forces can assist suppression of catalysis of a condensed-phase reaction at an interface.

Rearrangement of eq 3 gives eq 3a. The results (Figures 1 and 2) clearly do not fit this equation because

$$k_2 = \frac{k_2^{\mathrm{w}} + k_2^{\mathrm{m}} K C_{\mathrm{m}}}{1 + K C_{\mathrm{m}}} \tag{3a}$$

the rate constant does not level off at a value of k_2^{m} when $KC_{\mathrm{m}} \gg 1$ and $k_2^{\mathrm{m}} K C_{\mathrm{m}} \gg k_2^{\mathrm{w}}$. These requirements should be satisfied when the concentration of CTA is greater than 0.02 M. In order to fit the results we have introduced an additional term into eq 3a to give

$$k_2 = \frac{k_2^{\mathrm{w}} + k_2^{\mathrm{m}} K C_{\mathrm{m}}}{1 + K C_{\mathrm{m}} + a C_{\mathrm{m}}^2} \tag{4}$$

A rationalization for the addition of this term is that when the number of micelles is large, and virtually all the substrate is in the micellar phase, additional micelles will take up hydroxide ions, which will thereby be deactivated because of the low probability of a substrate molecule in one micelle reacting with a hydroxide ion in another. We suggest that these rate maxima may be quite common for anion–molecule reactions catalyzed by micelles, and they have been observed for hydrolyses of mono-p-nitrophenyl dodecanedioate and p-nitrophenyl octanoate, but not p-nitrophenyl acetate, at pH 10.49, catalyzed by n-dodecyltrimethylammonium bromide.[10] Another example of such a rate maximum is the alkaline hydrolysis of benzylideneacetophenone catalyzed by cetyltrimethylammonium bromide.[9,22a]

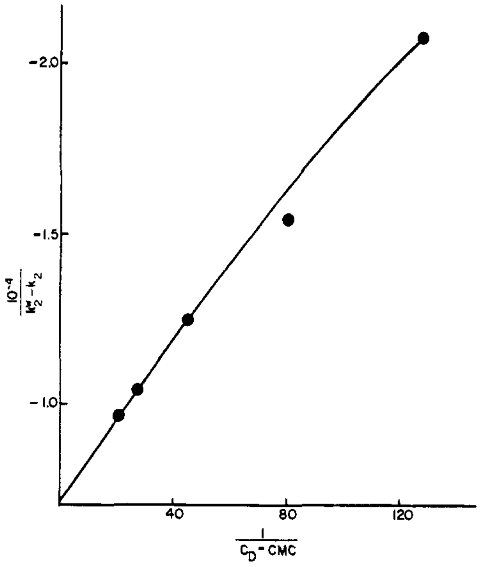

Figure 9. Inhibition of the reaction between hydroxide ion and 2,4-dinitrochlorobenzene by NaLS in water at 25.0°.

Alternatively we could assume that the size of the micelles increases with increasing detergent concentration, and that the substrate can then become buried deeply in the micelle. There is some evidence that hydrolysis would not occur so readily in such an environment.[10,23] However, we know of no evidence that the sizes of the micelles change in this way, and we regard this explanation as less probable than the other. Also nmr evidence suggests that polar aromatic compounds tend not to be absorbed into the interior of a CTA micelle, but stay near the surface in a water-rich area.[24]

In order to calculate the parameters in eq 4, we rewrite it as

$$k_2 = \frac{k_2^{\mathrm{w}} + k_2^{\mathrm{m}}(K/N)(C_{\mathrm{D}} + \mathrm{cmc})}{1 + (K/N)(C_{\mathrm{D}} - \mathrm{cmc}) + (a/N^2)(C_{\mathrm{D}} - \mathrm{cmc})^2} \tag{4a}$$

At the rate maximum we can neglect the rate constant k_2^{w} for the uncatalyzed reaction, and by inverting eq 4a and differentiating it we obtain

$$a = N^2/(C_{\mathrm{D}} - \mathrm{cmc})^2 \tag{5}$$

The aggregation number, N, = 61 for cetyltrimethylammonium bromide,[21] and $K/N = 75$, from partitioning experiments (Results), and therefore we obtain

$$k_2 = \frac{k_2^{\mathrm{w}} + k_2^{\mathrm{m}} 75(C_{\mathrm{D}} - \mathrm{cmc})}{1 + 75(C_{\mathrm{D}} - \mathrm{cmc}) + 4.4 \times 10^3 (C_{\mathrm{D}} - \mathrm{cmc})^2} \tag{6}$$

Under the conditions of our experiments cmc = 3.2×10^{-4} M for CTA (Table IV), and from the value of k_2

(22a) Note Added in Proof. Romsted and Cordes [L. R. Romsted and E. H. Cordes, *J. Am. Chem. Soc.*, **90**, 4404 (1968)] have recently suggested that inhibition by the counterion of the cationic micelle is responsible for these rate maxima.

[23] E. F. J. Duynstee and E. Grunwald, *Tetrahedron*, **21**, 2401 (1965).

[24] J. C. Eriksson and G. Gilberg, *Acta Chem. Scand.*, **20**, 2019 (1966).

at 25.0° in 0.05 *M* sodium hydroxide and 0.015 *M* detergent we calculate $k_2^{\mathrm{m}} = 248 \times 10^{-4}$ sec^{-1} mol^{-1} l., and, with $k_2^{\mathrm{w}} = 1.42 \times 10^{-4}$ sec^{-1} mol^{-1} l., eq 6 gives

$$10^4 k_2 = \frac{1.42 + 248[75(C_{\mathrm{D}} - 0.00032)]}{1 + 75(C_{\mathrm{D}} - 0.00032) + 4.4 \times 10^3(C_{\mathrm{D}} - 0.00032)^2} \tag{6a}$$

Equation 6a fits the results reasonably well, as can be seen from the broken line in Figure 1. However, it includes two parameters, k_2^{m} and *a*, which are not directly measured, and it is probable that they could be varied without impairing the fit between the calculated and experimental values; also in calculating these parameters we had to assume that the value of *K*/*N* obtained by solubility measurements in the absence of hydroxide ion could be applied to the kinetic system.

We did not apply this treatment to the experiments at 45°, because the necessary data were not available, but the similarity of the experimental plots of k_2 against detergent concentration at 25.0 and 45.0° suggests that the relation between these quantities is not strongly dependent upon temperature.

The satisfactory agreement between the parameters derived kinetically and those derived by measurements of the solubilization of the substrate makes it clear that the detergents are affecting the reaction rate by incorporating the substrate into the micellar aggregate, rather than by changing the solvent properties of the water. These conclusions accord with the results that other workers have obtained kinetically[4-11] and by direct studies of the incorporation of organic molecules into micelles.[8,12,16-18,24]

Effect of Nonoionic Detergent. The kinetic effect of the nonionic detergent is very small (Figure 2) although it is very effective at incorporating the substrate (Figure 8), suggesting that 2,4-dinitrochlorobenzene is just as reactive toward hydroxide ion when it is in the micelles of the uncharged detergent as in water. If the substrate were buried deeply in the interior of the micelle it would be protected from the hydroxide ion, and therefore we conclude that any substrate which is incorporated into micelles of the nonionic detergent must be in a water-rich region close to the surface of the micelle.

Reactions in Aqueous Alcohol. Micellar effects upon the reaction between 2,4-dinitrochlorobenzene and lyate ion are qualitatively similar in water and aqueous ethanol (Figures 1-5). The rate increases to a maximum in the presence of CTA and decreases steadily in the presence of NaLS but the effects are much less in aqueous ethanol than in water. Several factors may be involved. The cmc of CTA and NaLS are decreased by addition of ethanol or other organic solvents to water[19] (Table V), and the micelles will be smaller in the aqueous organic solvents. This effect, as well as the sign in the solvent itself, will reduce their ability to incorporate the substrate and therefore their kinetic effects.

Because of the high solubility of 2,4-dinitrochlorobenzene in aqueous ethanol, we cannot determine the extent to which it is incorporated into the micelles in this solvent. However, the retardation of the reaction by NaLS can be treated using eq 3, and a plot of $1/(k_2^{\mathrm{w}} - k_2)$ against $1/(C_{\mathrm{D}} - \mathrm{cmc})$ is linear with some scatter, and falls off at low detergent concentrations, because of the relatively small changes in the rate constants, and gives $K/N \sim 20$. This value is considerably lower than that found in water, and because the aggregation number, *N*, for NaLS is almost certainly lower in aqueous ethanol than in water, it follows that the association constant, *K*, between the anionic micelle and 2,4-dinitrochlorobenzene must also be lower than in water.

There is an additional effect which must be considered for the reaction between lyate ions and 2,4-dinitrochlorobenzene in aqueous ethanol, where the reagent can either be hydroxide ion or the more nucleophilic ethoxide ion.[25-27] Addition of a detergent may change the position of this equilibrium, and therefore adventitiously affect the rate. However, in ethanol–water 25:75 w/w the equilibrium is almost wholly in favor of the hydroxide ion,[27] and therefore the effects of the detergents upon it should not be of major importance.

$$\mathrm{O\bar{H}} + \mathrm{C_2H_5OH} \rightleftharpoons \mathrm{C_2H_5\bar{O}} + \mathrm{H_2O}$$

This ambiguity is absent when the nucleophile is not a lyate ion, as in reactions of thiophenoxide ion with 2,4-dinitrochlorobenzene or thiosulfate ion with *n*-pentyl bromide, and the lyate ion should be present largely as hydroxide for reactions in aqueous *t*-butyl alcohol. These observations confirm our assumption that changes in the nature of the lyate ion are unimportant.

For the reactions between hydroxide or thiophenoxide ion and 2,4-dinitrochlorobenzene in ethanol–water 25:75 w/w or aqueous *t*-butyl alcohol, the rate maximum is at lower CTA concentrations than in water. This result is probably related to the decrease of the cmc of the detergent on addition of alcohol to water (Table V and ref 19), because this decrease should also decrease the aggregation number of the micelle.

For reaction between thiosulfate ion and *n*-pentyl bromide in ethanol–water 25:75 w/w, the rate decreases sharply on addition of NaLS. The rate maximum which we observe with CTA is probably caused by a deactivation of the nucleophilic thiosulfate ion by the cationic detergent, as in the reaction between hydroxide ion and 2,4-dinitrochlorobenzene. However, in the present system we cannot attempt to give any quantitative treatment of the CTA catalysis, because we are unable to measure the distribution of *n*-pentyl bromide between solvent and micelle.

For the reaction between *n*-pentyl bromide and sodium thiosulfate in ethanol–water 25:75 w/w, a plot of $1/(k_2^{\mathrm{w}} - k_2)$ against $1/(C_{\mathrm{D}} - \mathrm{cmc})$ is linear for NaLS concentrations above 0.01 *M*, but at lower concentrations the plot is curved. From the slope of this plot we calculate $K/N \sim 2$. The aggregation number, *N*, is probably lower in aqueous ethanol than in water, where it is ~62,[22] and therefore our value of *K*/*N* suggests that the association constant, *K*, is small for *n*-pentyl bromide in aqueous ethanol, although in the absence of a good value of *N*, we cannot estimate *K*.

With a decrease in the water content of the solvent, there is a change in the relation between rate constant and concentration of the cationic detergent (Figure 7), and in ethanol–water 44:56 w/w there is a small, but steady, rate increase with CTA, with no sign of a rate

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(25) J. Koskikallio, *Suomen Kemistilehti*, B30, 111 (1957).

(26) M. L. Bender and W. A. Glasson, *J. Am. Chem. Soc.*, 81, 1590 (1959).

(27) R. G. Burns and B. D. England, *Tetrahedron Letters*, 1 (1960).

maximum, or plateau. The nonionic detergent has almost no effect, as for the reaction between 2,4-dinitrochlorobenzene and hydroxide ion in water (Figure 2), and an anionic detergent, NaLS, decreases the rate smoothly and steadily (Figure 7).

These detergent effects in ethanol-water 44:56 w/w are very much like those of monomeric solutes, *e.g.*, the rate effects of the ionic detergents are very similar to those of simple electrolytes.[3] For example, the effect of NaLS upon the rate constant for reaction between *n*-pentyl bromide and sodium thiosulfate fits eq 7 with a

$$\log k_2/k_2^{\mathrm{W}} = aC_{\mathrm{D}} \qquad (7)$$

~ -9, and for the positive salt effect of CTA $a \sim 4$.

This linear relationship between the logarithm of the rate constant and electrolyte concentration is typical of electrolyte effects at concentrations above the Debye–Hückel region, although the values of "a" are much less for most electrolytes; *e.g.*, for KCl it is ~ -1.5, and for tetramethylammonium chloride it is ~ 0.4,[3] reflecting the differences in the charge densities of the ions.

We have already noted that the micelles affect the reaction rate by incorporating the substrate rather than by affecting the solvent properties of water. This conclusion is strengthened by comparing the micellar effects for reactions in water, aqueous ethanol, and aqueous *t*-butyl alcohol, because ethanol and *t*-butyl alcohol have quite different effects upon the structure of water.[28] Detergents have very marked effects upon water,[19] but this particular effect is not of major importance when the reaction is taking place almost wholly in the micelles, as it is with CTA, and it appears to be of relatively minor kinetic importance even with the anionic detergent, NaLS, which is an anticatalyst, and the nonionic detergent, DNPE, which has very little effect upon reaction rate. With aqueous ethanol of relatively low water content, *e.g.*, ethanol–water 44:56 w/w, the effects of the ionic detergents represent their effects as electrolytes in affecting the relative free energies of reactants and transition state, either directly or indirectly.

Relation between Kinetic Salt and Micellar Effects. The kinetic salt effects must be interpreted in terms of a differential effect upon the free energies of the initial and transition states of the reaction.[3,29] For reaction between hydroxide ion and 2,4-dinitrochlorobenzene we can separate these salt effects into those upon the free energy of the organic substrate and the differential effects upon the free energies of the small hydroxide ion and the transition state, which is an anion of low charge density.[3]

The simplest description of the effects of micelles is that the organic substrate is incorporated into the micelle, and is then in an environment which electrostatically attracts or repels the anionic nucleophile. However, another description is equally useful. A cationic micelle could decrease the free energy of a bulky anionic transition state relative to that of the initial state, which is an uncharged molecule plus a small anion, and an anionic micelle could have the opposite effect.

The micelles which we have examined all decrease the free energy of 2,4-dinitrochlorobenzene, and this effect of itself always retards reaction, but a cationic micelle should stabilize a bulky anion, such as the transition state, more than a small anion, such as hydroxide, relative to their stabilities in water, and therefore increase the reaction rate. The results in Table III, which show that a bulky anion, such as tosylate, interacts with the cationic micelle much more strongly than does the small chloride ion, illustrate how charge density affects the interaction between an ion and a micelle, and a cationic micelle should therefore interact more strongly with the transition state of an ion–molecule reaction than with the initial state.

We can use either of these alternative descriptions of micelle catalysis, but the second one is useful if we attempt to compare the kinetic effects of ionic micelles with those of simple salts.[3] For example, we have already noted that a cation of low charge density such as a tetramethylammonium ion assists reaction between hydroxide ion and 2,4-dinitrochlorobenzene, because it increases the activity coefficient term $f_{\mathrm{O\bar{H}}}/f_{\mathrm{X}}{}^*$ more than it decreases f_{s}, and similarly a low charge density anion such as perchlorate hinders reaction because it decreases both f_{s} and $f_{\mathrm{O\bar{H}}}/f_{\mathrm{X}}{}^*$. We can therefore draw simple analogies between the rate-enhancing effects of a tetramethylammonium ion and the cationic cetyltrimethylammonium micelle and the rate-reducing effects of a perchlorate ion and the anionic lauryl sulfate micelle, although as might be expected the ionic micelles have much larger effects than the simple salts.[23]

In this context it is useful to compare the kinetic effects of CTA and NaLS in water and ethanol–water 44:56 w/w. In water the detergents form micelles with large aggregation numbers and have very marked effects upon the reaction rates, but in the aqueous ethanolic solvent they form micelles with very low aggregation numbers,[19] if at all, and their effects are much smaller, but in the same directions. For reactions of thiosulfate ion with *n*-pentyl bromide in this solvent of relatively low water content CTA and NaLS have similar but larger kinetic effects than the other salts which generate ions of higher charge densities.

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