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MICELLAR CATALYSIS OF THE REACTION OF 2,4-DINITROFLUOROBENZENE WITH PHENOXIDE AND THIOPHENOXIDE IONS

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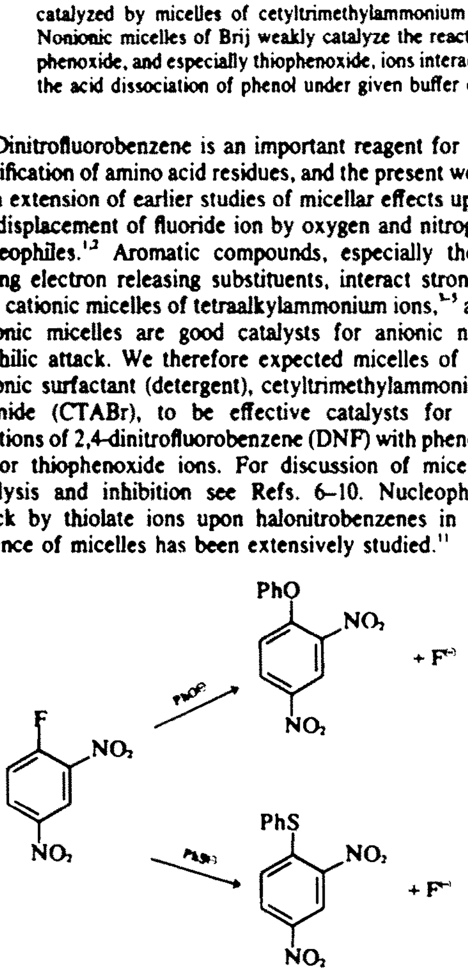
Abstract—The reactions of 2,4-dinitrofluorobenzene with phenoxide and thiophenoxide ion in water are strongly catalyzed by micelles of cetyltrimethylammonium bromide (CTABr) by factors of 230 and 1100 respectively. Nonionic micelles of Brij weakly catalyze the reaction with thiophenoxide ion. Spectral measurements show that phenoxide, and especially thiophenoxide, ions interact strongly with micelles of CTABr which also markedly change the acid dissociation of phenol under given buffer conditions.

2,4-Dinitrofluorobenzene is an important reagent for the modification of amino acid residues, and the present work is an extension of earlier studies of micellar effects upon the displacement of fluoride ion by oxygen and nitrogen nucleophiles.[1,2] Aromatic compounds, especially those having electron releasing substituents, interact strongly with cationic micelles of tetraalkylammonium ions,[3-5] and cationic micelles are good catalysts for anionic nucleophilic attack. We therefore expected micelles of the cationic surfactant (detergent), cetyltrimethylammonium bromide (CTABr), to be effective catalysts for the reactions of 2,4-dinitrofluorobenzene (DNF) with phenoxide or thiophenoxide ions. For discussion of micellar catalysis and inhibition see Refs. 6–10. Nucleophilic attack by thiolate ions upon halonitrobenzenes in the absence of micelles has been extensively studied.[11]



Reactions of n-alkyl thiols with p-nitrophenyl acetate are strongly catalyzed by cationic micelles, and the catalysis increases sharply with increasing length of the n-alkyl group, but in this system it is difficult to separate the micellar effects upon the thiol ionization and attack of the thiolate ion upon the ester.[12] In another very interesting study Heitman has shown that functional micelles derived from cysteine are effective deacylating agents.[13]

EXPERIMENTAL

Materials. Thiophenol (Eastman) was vacuum distilled before use and was stored under N_2. Brij 58 (polyoxyethylene 20 cetyl ether, Lot 8·0-1150, Sigma) was used without further purification. The purification of the other surfactants has been described.[2] Deoxygenated redistilled water was used in all the experiments.

Kinetics. All the reactions were followed at 25·0° using a Cary 14 spectrophotometer for reactions with phenoxide ion and a Durrum stopped flow spectrophotometer for reactions with thiophenoxide ion. The reaction with thiophenoxide ion was followed at 350 nm, in 10^{-2} M borate buffer, pH 9·27. Thiophenol is fully ionized at this pH.[14] The concentration of DNF was $1{\cdot}25$–5×10^{-5} M and that of thiophenol was $2{\cdot}5$–5×10^{-4} M. The quoted rate constants are the mean of between 2 and 6 values, and these values were usually within 4% of the mean and always within 10%. For the reactions with phenoxide ion the concentration of phenol was $1{\cdot}67$–$6{\cdot}67 \times 10^{-4}$ M, and that of DNF was *ca.* 10^{-4} M. These reactions were followed in 10^{-2} M borate buffer, pH 10. Most experiments were carried out using cationic micelles of CTABr. In the absence of phenoxide or thiophenoxide ion the reaction of DNF was relatively slow at pH 10. The possibility that thiophenoxide ion might reduce the nitro groups of DNF in CTABr was excluded by showing that no nitroaniline was formed, because the spectra of the reaction products did not change when the solutions were made strongly acidic.

Ionization of phenol in CTABr. Phenol was not fully ionized under the reaction conditions employed.* The surfactant could change the acid dissociations of both boric acid and phenol, and in estimating the micellar catalysis it was necessary to take these changes into account. This was done by measuring the equilibrium between phenol and phenoxide ion spectrophotometrically in the presence and absence of CTABr using borate buffer, pH 10 before addition of CTABr. (CTABr has little effect upon the pH of 10^{-2} M borate buffer, which was only slightly decreased by the addition of $1{\cdot}5 \times 10^{-2}$ M CTABr, cf Ref. 5.) In order to calculate the relative amounts of phenol and phenoxide ion in solutions of CTABr and borate buffer we first measured the absorbances of phenol and phenoxide ion in aqueous CTABr, and used the extinction coefficients of each species in aqueous CTABr. Because of the rapid reaction of DNF with hydroxide ion in aqueous CTABr it was impracticable to use a pH high enough to ensure complete ionization of phenol.[2]

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*The pK_a of phenol in water at 25° is approx. 10.[15]

Spectra of thiophenoxide ion in CTABr. The UV spectra of thiophenoxide in the presence of CTABr were measured in a Cary 14 spectrophotometer at pH 9·27.

Difference spectra. Because the kinetic data suggested that there was an interaction between $PhS^{\ominus}$ and DNF in the presence of micelles of CTABr we examined the difference spectrum of $PhS^{\ominus}$ and m-dinitrobenzene in the presence of CTABr in the region 270–295 nm using a Cary 14 spectrophotometer. (At lower wavelengths the absorbances were too high for difference spectra to be obtained.) Spectra 1-3 were measured in independent experiments with the matched cells being emptied, cleaned and refilled for each experiment. Spectra 3 were recorded in duplicate and the differences showed the errors in the actual spectral determination. These difference spectra (Fig. 1) suggest that there was an interaction between thiophenoxide and m-dinitrobenzene in micelles of CTABr.

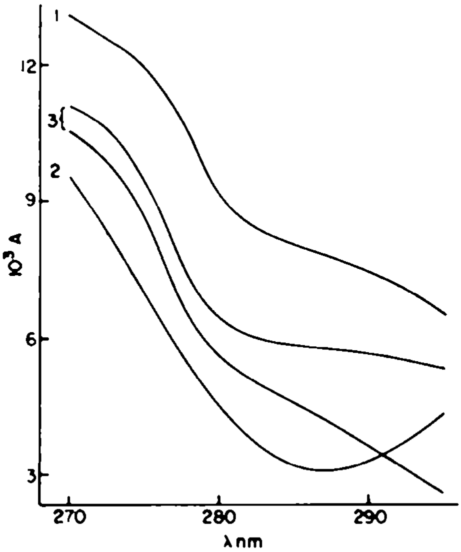

Fig. 1. Difference spectra of $6{\cdot}7\times10^{-5}$ M m-dinitrobenzene and $6{\cdot}7\times10^{-5}$ M thiophenoxide ion in the presence of 0·33 M CTABr and 0·017 M borate buffer.

RESULTS

Reaction with thiophenoxide ion. Micellar effects upon the reaction of thiophenoxide ion with DNF are relatively simple, except that the rate enhancement by micelles of CTABr is unusually large for an organic bimolecular reaction in water, and the second order rate constant, k_2, increases to a plateau value and there is no rate maximum (Fig. 2), whereas most micellar catalyzed bimolecular reactions show well defined rate maxima.[7,9,10,14] In water the second order rate constant, $k_2 = 260$ l. mol^{-1} sec^{-1},[*] and in the plateau region with CTABr it is $2{\cdot}8\times10^5$ l. mol^{-1} sec^{-1} for 5×10^{-5} M DNF, so that the rate is increased by a factor of 1100.

Nonionic micelles of Brij 58 speed the reaction but the effect is relatively small (Table 1). The simple electrostatic explanation of micellar catalysis predicts no kinetic effect upon this reaction by nonionic micelles, as is generally observed. However there are other cases where the simple explanation fails and reaction rate changes,[2,7,9,10,17] probably because the relatively hydrophobic reagents, DNF and thiophenoxide ion are brought together in nonionic micelles of Brij. However the relation between rate constant and the concentration does not show the sigmoidal form which is characteristic of micellar catalysis, and the surfactant itself could cause a kinetic solvent effect.

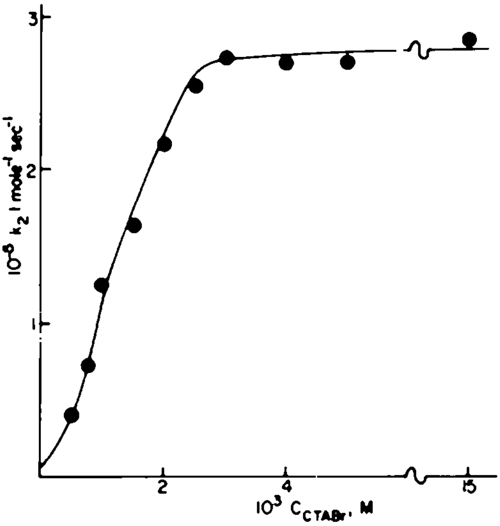

Fig. 2. Reaction of thiophenoxide ion with 2,4-dinitrofluorobenzene in the presence of CTABr at 25·0°.

Effect of CTABr on the ionization of phenol. In order to allow the calculation of the extent of ionization of phenol in the presence of CTABr under our kinetic conditions we examined the UV spectra of phenol and phenoxide ion in aqueous CTABr, and aqueous CTABr and nominal pH 10 buffer. The ionization of phenol is increased with the addition of up to 5×10^{-3} M CTABr (Table 2), in agreement with other observations of micellar effects upon the ionization of uncharged acids.[5,18]

Reaction with phenoxide ion. The reaction between DNF and phenol in borate buffer, pH 10, is effectively catalyzed by micelles of CTABr (Fig. 3). The open symbols represent the apparent second order rate constants calculated by dividing the first order rate constants, k_ψ, by the stoichiometric concentration of phenol, and the closed represent the rate constants calculated in terms of the concentration of phenoxide ion in the solution determined spectrophotometrically. Table 2 shows the effect of CTABr upon the equilibrium between phenol and phenoxide ion, although it should be noted that this experiment does not differentiate between solutes in the aqueous and micellar phases. The maximum second order rate constant is at 4×10^{-3} M CTABr, and is

Table 1. Effect of Brij 58 upon the reaction of DNF and thiophenoxide ion[a]

10^3 C_D, M	k_2, l. mol^{-1} sec^{-1}
	260
0·06	386
0·80	1320
3·34	3940[b]
15·0	9340

[a] At 25·0°, pH 9·27, 10^{-2} M borate buffer and 5×10^{-4} M PhS^{-}; $2{\cdot}5\times10^{-5}$ M DNF unless specified.

[b] 5×10^{-3} M DNF

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[*] The rate constant for reaction in the absence of micelles is the mean of 6 runs with concentrations varying from 0·25–0·5 mM $PhS^{\ominus}$ and 0·0125–0·05 mM DNF.

Table 2. Effect of CTABr on the ionization of phenol*

$10^3 C_{CTABr}$, M	$C_{PhO^-}/(C_{PhO^-} + C_{PhOH})$
	0·48
1·0	0·49
2·0	0·55
2·0	0·57
3·0	0·63
4·0	0·66
5·0	0·70
6·0	0·71
7·0	0·71
7·0	0·74^b
8·0	0·70^b
9·0	0·74
9·0	0·72^b
50·0	0·74

*At 25·0° under kinetic conditions with $6{\cdot}67 \times 10^{-4}$ M phenol unless specified.
^{b}$3{\cdot}33 \times 10^{-4}$ M phenol.

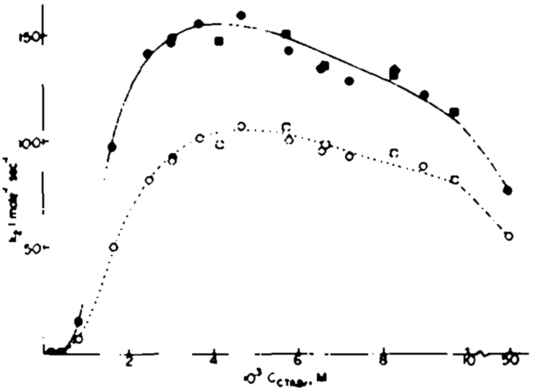

Fig. 3. Reaction of phenoxide ion with 2,4-dinitrofluorobenzene in the presence of CTABr. Solid symbols represent values of k_2 corrected for the ionization of phenol. ◇◆, $1{\cdot}67 \times 10^{-4}$; □■, $3{\cdot}33 \times 10^{-4}$; ○●, $6{\cdot}7 \times 10^{-4}$ M total phenol.

158 l. mol^{-1} sec^{-1} based on the phenoxide concentration, whereas it is 107 l. mol^{-1} sec^{-1} based on the total concentration. The difference between these two sets of data shows the importance of allowing for the effect of micelles upon acid–base, or other, equilibria involving reactants.

The second order rate constant for reaction in water in the absence of micelles is 0·68 l. mol^{-1} sec^{-1} calculated in terms of actual phenoxide ion concentration,[c] so that the reaction rate is increased by a factor of 230-fold by CTABr, allowing for the effect of CTABr on the dissociations of phenol. (The maximum rate enhancement based on stoichiometric phenol concentration is 315.) The rate profile shows the maximum which is so typical of bimolecular micellar catalyzed reactions.

Only qualitative experiments were done using anionic micelles of sodium lauryl sulfate and nonionic micelles of Brij. As expected anionic micelles retarded the reaction and nonionic micelles slightly catalyzed it, however no account was taken of any effects upon the phenol-phenoxide ion equilibrium, and these surfactants were not studied further.

Micellar effects upon the UV spectra of thiophenoxide and phenoxide ions. Addition of a small amount of CTABr does not markedly change the spectrum of thiophenoxide ion, but there is a marked change when the surfactant concentration is large enough for thiophenoxide ion to be taken up wholly by the micelle. The complete spectra are shown in Fig. 4, for $1{\cdot}25 \times 10^{-4}$ M thiophenoxide ion in water and with up to 3×10^{-3} M CTABr, and the extinction coefficients at λ_{max} for free and micellar bound CTABr are shown in Table 3. The results in Table 3 show that only relatively small amounts of CTABr are needed to take up the thiophenoxide ion, and this is confirmed by measurements of the areas under the peaks for mixtures of CTABr and thiophenoxide ion (Fig. 5). These areas were estimated in two ways using plots of absorbance against frequency. In the first, we measured the area from ν_{max} to the lowest frequency, 31,300 cm^{-1} (320 nm) and in the second from 43,500 cm^{-1} (230 nm) to the peak. These two areas, and their sum (in arbitrary units) are plotted against the concentrations of CTABr in Fig. 5. Despite the arbitrary estimation of peak areas the results qualitatively

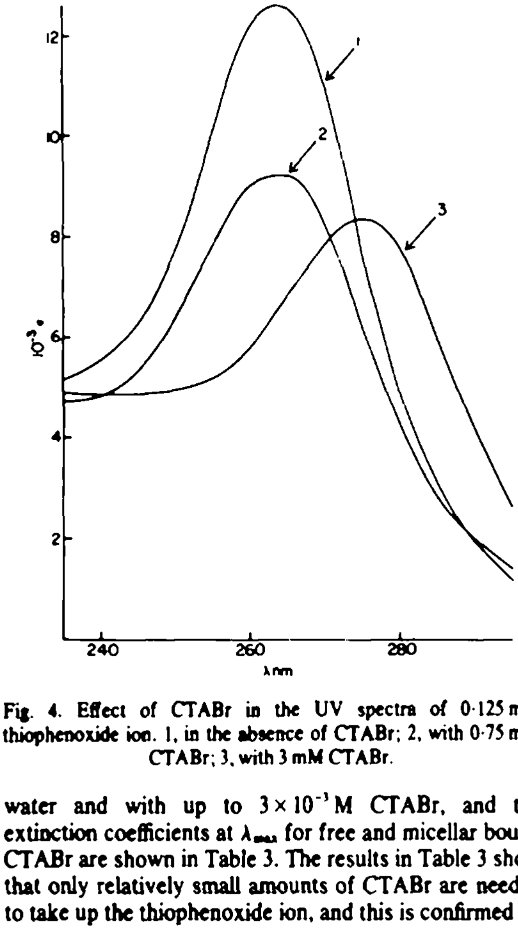

Fig. 4. Effect of CTABr in the UV spectra of 0·125 mM thiophenoxide ion. 1, in the absence of CTABr; 2, with 0·75 mM CTABr; 3, with 3 mM CTABr.

Table 3. UV spectra of thiophenoxide ion in the presence of CTABr*

$10^3 C_{CTABr}$, M	λ_{max}	ε_{max}	ε_{263}	ε_{274}
	263	12,600	12,600	8,750
0·75	264	9,250	9,230	6,450
1·50	271	7,570	7,000	7,500
2·00	272	7,670	6,740	7,600
3·00	274	8,320	6,420	8,320

*With $1{\cdot}25 \times 10^{-4}$ M PhS$^-$, λ in nm.

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[c] The second order rate constant calculated from the stoichiometric concentration of phenol is 0·33 l. mol^{-1} sec^{-1}, based on experiments with $6{\cdot}67 \times 10^{-4}$ DNF and $13{\cdot}3 \times 10^{-4}$ M phenol.

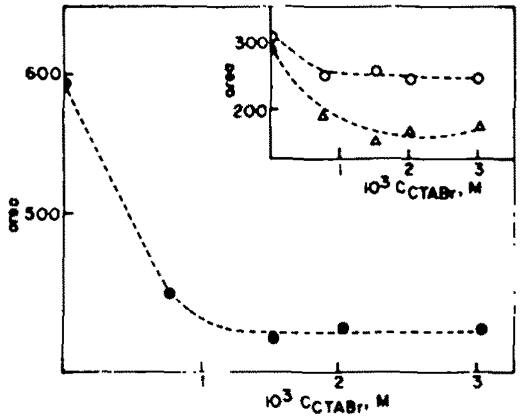

Fig. 5. Effect of CTABr upon the peak areas (in arbitrary units) of the UV spectra of thiophenoxide ions; ○ from ν_{max} to 43,500 cm^{-1}; △ ν_{max} to 31,300 cm^{-1}; ● total area.

show the marked effect of CTABr upon the spectra of the thiophenoxide ion, and the approximate constancy of these areas for CTABr concentrations greater than $1{\cdot}5 \times 10^{-3}$ M confirms that at higher concentrations thiophenoxide is incorporated wholly into the micelles, and that it interacts strongly with the ionic head groups.

Additional evidence on the strong interaction between thiophenoxide ion and CTABr comes from the decrease of the critical micelle concentration (cmc) of CTABr in addition of thiophenoxide ion. The cmc of CTABr is 9×10^{-4} M,[19] but addition of 4×10^{-3} M thiophenoxide ion at pH 10 (10^{-2} M borate buffer) decreases it to $0{\cdot}8 \times 10^{-4}$ M at 25°, and at pH 9·1 at 30° the cmc is decreased to 1×10^{-4} M. (Micellization was followed spectrophotometrically by the change in the absorbance of thiophenoxide ion at 275 nm.)

The effects of CTABr upon the UV spectra of both phenol and phenoxide ion are much less marked than those found for thiophenoxide ion. There are bathochromic shifts (Fig. 6), which are as expected much larger for phenoxide ion than for phenol because of its stronger interactions with the cationic micelle, but the effects on the absorbances are much less marked than for thiophenoxide ion. However both λ_{max} and ϵ_{max} of phenol and phenoxide are changed by incorporation into micelles of CTABr. The difference between phenoxide and thiophenoxide is understandable because hydrogen bonds to sulfur are much weaker than to oxygen so that thiophenoxide ion should interact much more strongly than phenoxide ion with a cationic micelle.

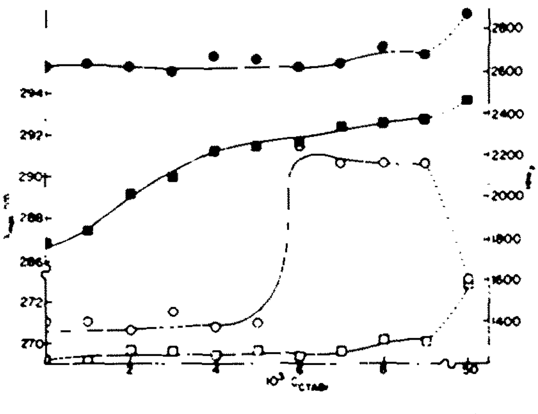

Fig. 6. Effect of CTABr upon λ_{max} (□■) and ϵ_{max} (○●) of phenol (open points) and phenoxide ion (solid points).

DISCUSSION

Relative rate enhancements by CTABr. In general it is difficult to measure the second order rate constant for that part of a bimolecular reaction which occurs on the micellar surface, because although it is usually easy to ensure that all of a nonionic organic substrate is taken up by the micelles it is much more difficult to estimate the extent of partitioning of hydrophilic ionic reagents between water and the micellar pseudophase.[16] The relative rate enhancements by micellized CTABr which are given in Table 4 for the reactions of DNF with various ionic nucleophiles are calculated from the rate maxima at the optimum surfactant concentration. As is generally found the micellar catalysis increases markedly and the concentration, C_D^{max}, of surfactant for maximum rate enhancement decreases with increasing hydrophobicity of the ionic nucleophile.[9,20] These differences could arise in two ways. Micellar incorporation will be greater for the more hydrophobic nucleophiles, thiophenoxide and phenoxide ion, and at the same time these hydrophobic ions should be drawn more deeply into the Stern layer at the micelle-water interface which is the site of reaction. Aromatic compounds, especially those having electron releasing substituents interact very strongly with cationic micelles.

Table 4. Catalysis by CTABr of nucleophilic attack upon 2,4-dinitrofluorobenzene[a]

Nucleophile	k_{rel}
OH	58[b]
$H_2NCH_2CO_2$	30[b]
$PhNH_2$	8[b]
PhO	230
PhS	1100

[a] At 25·0° and relative to reaction in water.
[b] ref. 2.

Reaction with thiophenoxide ion. Micellar catalyzed bimolecular reactions generally exhibit rate maxima with increasing surfactant concentration. These maxima have been ascribed to negative salt effects by the counterion of the ionic surfactant,[9] or to a partitioning of ionic reagents between water and micelle,[21] and this second "dilution" explanation has been applied quantitatively to acetal hydrolysis catalyzed by sodium lauryl sulfate.[16]

The reaction of DNF and thiophenoxide in aqueous CTABr is an exception to the norm. In applying the "dilution" treatment to the rate maxima it was assumed that one reagent did not affect the incorporation of the other into the micelle. The observation of a plateau in the reaction of thiophenoxide (Fig. 2) suggests that here one reagent does affect the interaction of the other with micelle, although this is apparently not the case with phenoxide ion (Fig. 3). If thiophenoxide ion and DNF form a complex in the micelle the rate constant-surfactant profile could be a plateau, as is found for unimolecular reactions catalyzed by micelles.[22] Alternatively we could assume that one reagent changes the micellar structure so that the restructured micelle more readily incorporates the other reagent. The very strong interactions between micelles of CTABr and thiophenoxide ion make this second hypothesis an attractive one, and it is supported by observation of a difference spectrum involving m-dinitrobenzene and thiophenoxide ion in the presence of CTABr (Fig. 1).

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