Micellar Catalysis of the Reaction of Hydroxide Ion with Tetranitromethane

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Micellar hexadecyltrimethylammonium bromide and polyoxyethylene (15) nonylphenol (Igepal CO-730) enhance the rate constant for the reaction of hydroxide ion with tetranitromethane by factors of 400 and 5, respectively, while micellar sodium dodecyl sulphate has no effect on it. The binding constant between the substrate and hexadecyltrimethylammonium bromide has been calculated to be $4{\cdot}5 \times 10^4$ l mol^{-1} from the kinetic data.

TETRANITROMETHANE has been increasingly used as a nitrating agent in aqueous neutral solutions to modify tyrosyl residues in proteins.[1] The suggested mechanism for tetranitromethane nitrations of phenolic model compounds involves the initial formation of a charge-transfer complex followed by a rate-determining electron-transfer forming nitroform anion and phenoxide and nitrite radicals, which in a final step give the nitrated product.[2] The extent of protein modification is followed by measuring the release of nitroform anion. However, in a number of cases the amount of nitroform anion produced has been reported to be in excess of that which could be accounted for by tyrosine modification.[1] At higher pH values hydroxide ions are known to react with tetranitromethane to form nitroform anion.[3] Under the experimental conditions for the nitration of the phenolic model compounds, however, this reaction is negligible compared with that of nitration.[2] It therefore appears likely that the hydroxide ion reaction of tetranitromethane, the nitration or, indeed, both steps are different in biological environments from those in pure water. In order to assess the effects of macromolecular environments on the rate of hydroxide ion attack on tetranitromethane, we have investigated this reaction in aqueous charged and uncharged micellar solutions.[4]

EXPERIMENTAL

Tetranitromethane (Aldrich) was washed 3—5 times with $0{\cdot}8\text{N-}H_2SO_4$, then 5 times with double-distilled water. After each washing the solution was cooled to 10 °C to freeze the tetranitromethane (m.p. 13 °C) and the supernatant liquid was discarded. After this treatment no absorbance was observed at 350 nm in alcoholic 10^{-2}M solutions of tetranitromethane. The purifications of hexadecyltrimethylammonium bromide (CTAB) and sodium dodecyl sulphate (NaLS) have been described.[5] Nonionic polyoxyethylene (15) nonylphenol (DNPE) (Igepal CO-730), a gift from the General Aniline and Film Corporation, was used without further purification. Surface tensions of each of the surfactants were measured with a du Noüy tensiometer. No minimums in the plots of surface tension against surfactant concentration were observed, indicating the absence of impurities. Since electrolytes affect micellar parameters,[4] only low concentrations of buffers were used without any added salt to maintain ionic strength. Under these conditions values for the critical micelle concentrations were found to differ appreciably from those in pure water. Deionized distilled water was used for the preparation of the buffer and surfactant solutions. The pH of the buffer solutions was adjusted by addition of hydrochloric acid or sodium hydroxide.

Rates of nitroform anion appearance were determined spectrophotometrically at 350 nm $\{\varepsilon[(NO_2)_3C^-] = 13{,}400$ l mol^{-1} cm$^{-1}\}$ in the thermostatted cell compartment of a Beckman DU-2 spectrophotometer. An energy-recording adaptor (ERA) was used in conjunction with a Hewlett–Packard recorder. The temperature was measured inside the cells and was maintained within $\pm 0{\cdot}02$ °C. Runs were started by injecting aqueous solutions of tetranitromethane into a cell containing the thermostatted surfactant solution. The concentration of tetranitromethane in the individual runs was *ca.* 5×10^{-5}M. The pH of each solution was determined inside the spectrophotometric cell before and after the kinetic runs. Runs with greater than 0·03 pH change were discarded. Good pseudo-first-order plots, up to 98% reaction, were obtained for each run.

RESULTS AND DISCUSSION

Rate constants for the formation of nitroform anion increase linearly as functions of hydroxide ion concentration. Second-order rate constants for reactions of hydroxide ion with tetranitromethane, k_{OH}, were obtained from the slopes of linear plots of the pseudo-first-order rate constants against hydroxide ion concentration. Figure 1 illustrates typical plots. Values for k_{OH} in water and in the presence of aqueous surfactants solutions at 25·00 °C were derived from similar plots, each containing at least 8 individual pseudo-first-order rate constants, and are in the Table. The obtained rate constant in water at 25·00 °C ($k_{OH} = 0{\cdot}60$ l mol^{-} s^{-1}) is in good agreement with that determined by Glover at 30 °C ($k_{OH} = 0{\cdot}77$ l mol^{-1} s^{-1}) and independently by Walters and Bruice also at 30 °C ($k_{OH} = 0{\cdot}65$ l mol^{-1} s^{-1}) although these workers adjusted the ionic strength of the solutions to 1·0M.[2]

The second-order rate constants for the reaction of

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[1] J. F. Riordan and M. Sokolovski, *Accounts. Chem. Res.*, 1971, **4**, 353, and references therein.

[2] T. C. Bruice, M. J. Gregory, and S. L. Walters, *J. Amer. Chem. Soc.*, 1968, **90**, 1612.

[3] D. J. Glover, *J. Phys. Chem.*, 1970, **74**, 21; S. L. Walters, *J. Amer. Chem. Soc.*, 1971, **93**, 2269.

[4] For reviews of micellar catalysis, see E. H. Cordes and R. B. Dunlap, *Accounts Chem. Res.*, 1969, **2**, 329; E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.

[5] L. M. Casilio, E. J. Fendler, and J. H. Fendler, *J. Chem. Soc.* (*B*), 1971, 1377.

tetranitromethane in the presence of cationic CTAB, anionic NaLS, and uncharged DNPE are collected in the Table. NaLS has no effect on the rate but DNPE and CTAB enhance it (Figure 2). The rate enhancement by CTAB is 400-fold and the dependence of k_{OH} on CTAB concentration is a sigmoidal curve followed by a plateau. Similar substrate saturation kinetics have been observed for numerous micellar-catalysed reactions.[4] Micellar catalysis arises from substrate–micelle binding and from the different reactivities of the substrate in the micellar and the bulk aqueous phases.[4]

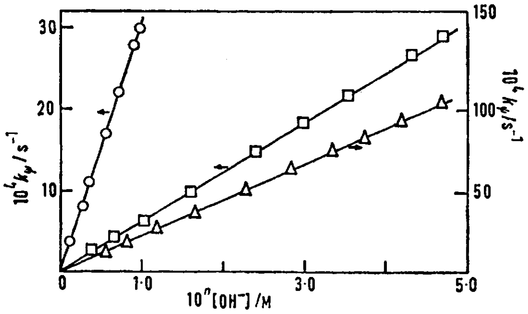

FIGURE 1 Plots of observed pseudo-first-order rate constants against hydroxide ion concentration; ○, $1{\cdot}0 \times 10^{-3}$M-Igepal CO-730, $n = 3$; □, water, $n = 3$; △, 5×10^{-3}M-CTAB, $n = 5$

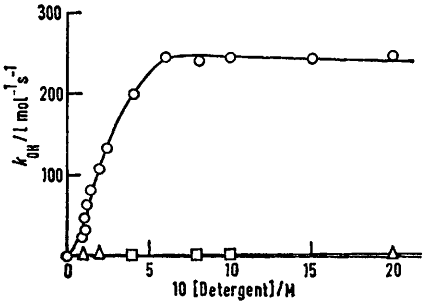

FIGURE 2 Plots of k_{OH} against detergent concentration

Reaction of tetranitromethane with hydroxide ion at 25 °C [a]

10^3[Detergent]/M	k_{OH}/l mol^{-1} s^{-1} CTAB	NaLS	DNPE
0·00		0·60	
0·95	27·8		
1·00	34·3		3·10
1·10	45·8		
1·25	63·8		
1·50	82·6		
2·00	109·3		3·05
2·50	133·8		
4·00	200·0	0·80	
5·00	222·0		
6·00	244·0		
8·00	241·0	0·70	
10·0	246·0	0·65	
15·0	243·0		
20·0	244·0		3·20

[a] In the presence of $2{\cdot}0 \times 10^{-3}$M-$Na_2B_4O_7$ or $2{\cdot}0 \times 10^{-3}$M-$NaHCO_3$ buffers. [b] $k^0_{OH} = 0{\cdot}60$ l mol^{-1} s^{-1}.

Making the assumptions that the micelle–substrate interactions follow 1 : 1 stoicheiometry, and that the substrate does not alter significantly the micellization or the critical micelle concentration, one can derive equation (1), as

$$\begin{tikzcd} M + S \arrow[r, shift left, "K"] \arrow[d, "OH^-\ k^0_{OH}"] & MS \arrow[l, shift left] \arrow[d, "OH^-\ k^m_{OH}"] \\ P & P \end{tikzcd} \qquad (1)$$

shown in refs. 4 and 5, where the validity of the assumptions are also discussed. M, S, and MS represent the micelle, substrate, and micelle–substrate complex, respectively; K is the binding constant; and k^0_{OH} and k^m_{OH} are the second-order rate constants for product formation in the bulk solvent and in the micellar phase, respectively. The observed second-order rate constant for the reaction of tetranitromethane with hydroxide ions at various surfactant concentrations, k_{OH}, can be shown to be described by equation (2) where M is the

$$k_{OH} = (k^0_{OH} + k^m_{OH}K[M])/(1 + K[M]) \qquad (2)$$

concentration of micelles and is related to the stoicheiometric concentration of the surfactant, C_D, the critical micelle concentration, CMC, and the aggregation number N, by equation (3). Combination of equations (2) and

$$[M] = (C_D - CMC)/N \qquad (3)$$

(3) and rearrangement give equation (4). A plot of the

$$\frac{1}{k^0_{OH} - k_{OH}} = \frac{1}{k^0_{OH} - k^m_{OH}} + \left(\frac{1}{k^0_{OH} - k^m_{OH}}\right)\left(\frac{1}{C_D - CMC}\right)\frac{N}{K} \qquad (4)$$

left-hand side of equation (4) against $1/(C_D - CMC)$ for the CTAB catalysis is given in Figure 3.

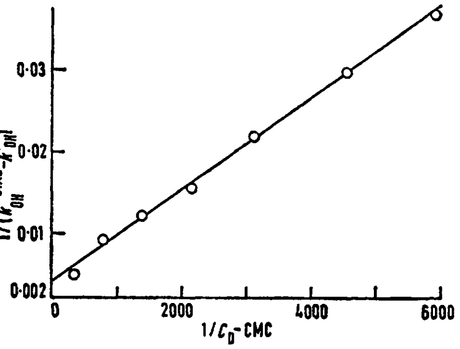

FIGURE 3 Binding constant plot according to equation (4) for CTAB catalysis; CMC = $7{\cdot}8 \times 10^{-4}$M

Assuming that the aggregation number is 61, we calculate the binding constant between CTAB and tetranitromethane to be $4{\cdot}5 \times 10^4$ l mol^{-1}. The magnitude of this binding constant is of the order generally found for interactions of nitro-substituted aromatic substrates with surfactants and is indicative of substantial solubilization of tetranitromethane.[4] From the intercept of the plot in Figure 3 the rate constant in the CTAB micellar phase,

k^{m}_{OH}, is calculated to be 238 l mol^{-1} s^{-1}, in very good agreement with the value obtained kinetically for the maximum rate enhancement (Table).

The suggested mechanism for the reaction of hydroxide ion with tetranitromethane involves the initial attack of hydroxide ion on the nitrogen atom in one of the nitro-groups of tetranitromethane.[3] The micellar catalysis is likely to arise, at least in part, from the stabilization of the transition state leading to the formation of the bulky nitroform anion. A problem inherent in determining the hydrogen or hydroxide ion concentrations in micellar solution in the pH region is the definition of the concentrations in the bulk and micellar phases. Some of the micellar effects can be due, therefore, to an increase in the effective hydroxide ion concentration in the micellar phase. Regardless of the mechanisms which may be involved in the overall micellar effects, the present work clearly implies that due care must be exercised in studies involving the use of tetranitromethane in macromolecular environments.

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