

Micellar Effects on the Hydrolysis of Benzylidene-*t*-butylamine *N*-Oxide and 3-Phenyl-2-*t*-butyloxaziridine

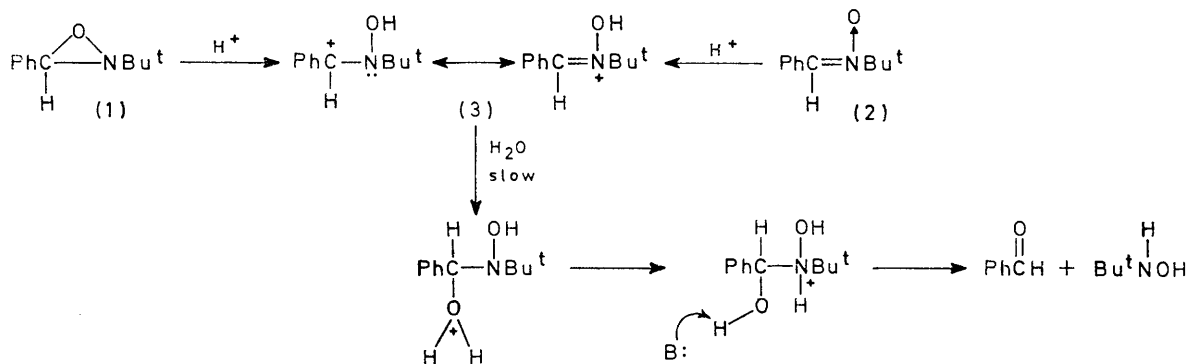
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Micellar sodium dodecyl sulphate (NaLS) enhances the rate constants for the hydrolysis of benzylidene-*t*-butylamine *N*-oxide and 3-phenyl-2-*t*-butyloxaziridine by factors of 40 and 68, respectively. Hexadecyltrimethylammonium bromide and 3-(dodecylmethylammonio)propane-1-sulphonate have no effects on the rates while polyoxyethylene(15)nonylphenol (Igepal CO-730) and 3-(dodecyldimethylammonio)propane-1-sulphonate enhance them slightly. Catalysis by NaLS of these two compounds is quite similar and originates from binding to the negatively charged micelle where the common intermediate, the positively charged protonated nitron, and the transition state for the rate-limiting steps are stabilized.

RATES of hydrolysis of 3-phenyl-2-*t*-butyloxaziridine (1) and benzylidene-*t*-butylamine *N*-oxide (*N*-*t*-butylbenzaloxime) (2) have been determined recently at pH 2–4 and in up to 10M-HCl, -HClO₄, and -H₂SO₄.¹ The mechanism has been discussed in terms of a bimolecular specific acid catalysed reaction involving the protonated nitron (3) as the common intermediate.

We have examined the effects of cationic micellar hexadecyltrimethylammonium bromide (CTAB), anionic sodium dodecyl sulphate (NaLS), zwitterionic 3-(dodecyldimethylammonio)propane-1-sulphonate (DDAPS) and

Rates of hydrolysis were followed spectrophotometrically on a Beckman Kintrac VII recording spectrophotometer by measuring the disappearance of the substrates at 287 nm. The temperature of the thermostatted bath and the cell compartment was maintained within $\pm 0.05^\circ$ as monitored by NBS thermometers. Reactions in NaLS were allowed to run for 8–10 half-lives and good first-order plots were obtained up to 90% reaction. The pseudo-first-order rate constants, k_{ψ} , for the hydrolysis in CTAB, Igepal CO-730, DDAPS, DAPS, and sodium acetate buffer have been calculated by the Guggenheim method.³ Reactions were initiated by injecting small



3-(dodecylmethylammonio)propane-1-sulphonate (DAPS), and uncharged polyoxyethylene(15)nonylphenol (Igepal CO-730), on the rates of hydrolysis of (1) and (2) at pH 4.55.

EXPERIMENTAL

The preparation and purification of (1), (2), and the surfactants have been described.^{1,2} Doubly distilled water was used for the preparation of the buffer and surfactant solutions. The pH of the buffer solutions was adjusted by the addition of hydrochloric acid at 25.0° using a Radiometer PHM-26 expanded scale pH meter. No change in the pH of the solutions was found before and after the reactions.

¹ C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J.C.S. Perkin II*, 1973, 1744.

² E. J. Fendler, C. L. Day, and J. H. Fendler, *J. Phys. Chem.*, 1972, **76**, 1460.

³ E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

⁴ E. H. Cordes and R. B. Dunlap, *Accounts Chem. Res.*, 1969, **2**, 329.

volumes (ca. 5 μ l) of an aqueous solution of the substrate to thermostatted, buffered surfactant solutions.

RESULTS AND DISCUSSION

Rate constants for the hydrolysis of oxaziridine (1) and *N*-oxide (2) in aqueous surfactant solutions at pH 4.55 and 38.5° are given in the Table. CTAB and DAPS have virtually no effect on the rate, Igepal CO-730 and DDAPS increase the rate only slightly, but NaLS causes marked rate enhancements. The surfactant concentration–rate profiles for the catalyses are analogous to those observed for numerous other micellar catalysed reactions;^{4–7} there is a rapid increase in the rate with increasing NaLS concentration up to

⁵ E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.

⁶ T. C. Bruice, in 'The Enzymes,' Academic Press, New York, 1970, 3rd. edn., vol. 2, p. 217.

⁷ E. H. Cordes and C. Gitler, *Progr. Bioorganic Chem.*, 1973, **2**, 1.

a maximum, followed by a very short plateau after which the catalytic effectiveness decreases relatively slowly. However, the majority of cases in which rate maxima have been observed previously involve catalysis by cationic rather than anionic micelles.⁵ Just as rate constants for the acid catalysed reactions of (1) parallel that of (2),¹ the catalytic behaviour of NaLS toward (1) and (2) is identical (Table). The implication of this result is, of course, that the micellar catalysed hydrolysis of the oxaziridine (1) and the *N*-oxide (2) have a common intermediate, most probably the protonated nitrene (3). At the 'plateau' region in micellar NaLS rate constants for the hydrolysis of (1) and (2) are factors of 68 and 40 greater than those in pure water. The difference in the magnitude of the rate enhancements is a consequence of the different hydrolysis rates of (1) and (2) in aqueous buffers (Table).

Making the usual assumptions and simplifications⁵ the kinetics of micellar catalysis have been successfully

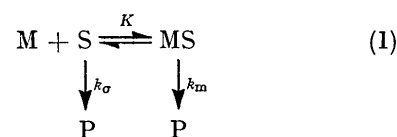
Rate constants of hydrolysis of oxaziridine (1) and *N*-oxide (2) in aqueous micellar solutions at 38.5° and pH 4.55^a

$10^3[\text{NaLS}]/\text{M}$	$10^6 k_{\psi}/\text{s}^{-1}$	
	(1) ^b	(2) ^c
0	2.00	3.51
1.00	5.75	8.72
2.00	15.2	11.5
5.00	39.4	32.2
7.50	60.9	51.4
10.0	74.0	73.5
12.5	76.5	90.6
15.0	92.5	98.3
20.0	113	110
25.0	126	122
35.0	133	133
35.0 ^d		102
50.0	137	141
75.0	132	131
100.0	122	120
175	87.6	95.0
250	69.5	70.6
375	49.8	45.6
500		32.9
$10^4[\text{CTAB}]/\text{M}$		
10.0	2.07	3.62
25.0	2.23	3.50
100.0	3.62	3.92
$10^4[\text{Igepal CO-730}]/\text{M}$		
1.00	3.93	4.47
2.50	3.79	4.35
10.0	4.07	4.47
25.0		4.35
$10^2[\text{DDAPS}]/\text{M}$		
1.0		6.15
$10^2[\text{DAPS}]/\text{M}$		
4.0		3.66

^a In the presence of $1.0 \times 10^{-2}\text{M}$ -NaOAc buffer. ^b [Substrate] = $1.8 \times 10^{-4}\text{M}$. ^c [Substrate] = $2.5 \times 10^{-5}\text{M}$. ^d In the presence of $1.0 \times 10^{-3}\text{M}$ -Igepal CO-730.

treated in terms of micelle-substrate binding and reaction in the aqueous bulk and micellar phases [equation (1) where k_{σ} and k_m are the rate constants for product

formation in the bulk solvent and micellar phase, respectively, and K is the micelle-substrate binding or



association constant]. The observed rate constant, k_{ψ} , for the hydrolysis of (1) and (2) is given by equation (2)

$$k = \frac{k_{\sigma} + k_m K[\text{M}]}{1 + K[\text{M}]} \quad (2)$$

which using the relationship (3) (where C_D and $[\text{M}]$ are

$$[\text{M}] = (C_D - \text{CMC})/N \quad (3)$$

the stoichiometric surfactant and micellar concentrations, respectively, N is the aggregation number, and CMC is the critical micelle concentration) and upon rearrangement leads to equations (4) and (5). Equations (4) and (5) have often been used previously for the

$$\frac{1}{k_{\sigma} - k_{\psi}} = \frac{1}{k_{\sigma} - k_m} + \left(\frac{1}{k_{\sigma} - k_m} \right) \left(\frac{1}{C_D - \text{CMC}} \right) \frac{N}{K} \quad (4)$$

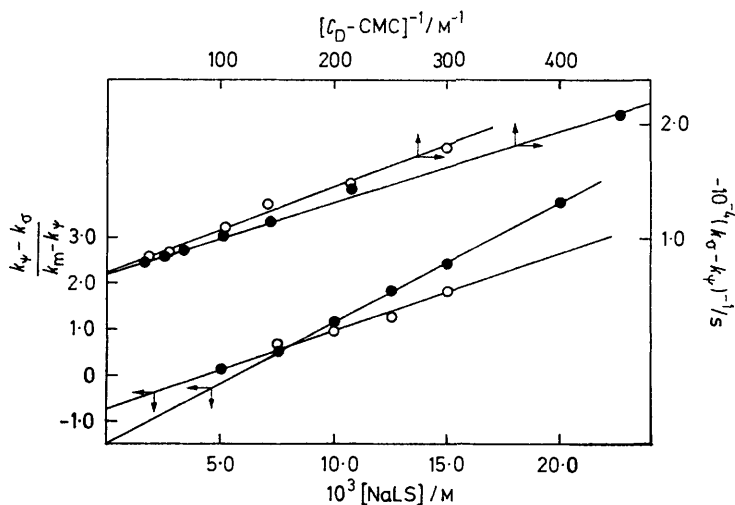
$$\frac{k_{\psi} - k_{\sigma}}{k_m - k_{\psi}} = \frac{K}{N}(C_D - \text{CMC}) \quad (5)$$

calculation of K .⁵ Applying equations (4) and (5) to the present data is somewhat hampered by the uncertainties in the values of k_m and CMC, since the plateau for the rate maxima is rather short and since substrates are known to alter the CMC values.⁸ Using both equations binding constants have been obtained, however, between NaLS and (1) and (2). Making the assumption that the critical micelle concentration of NaLS is not changed appreciably and is $8 \times 10^{-3}\text{M}$,⁸ good linearity has been obtained on plotting the data according to equation (4) (Figure). From the intercepts of these plots k_m values of 1.56×10^{-4} and $1.45 \times 10^{-4}\text{s}^{-1}$ have been calculated for (1) and (2), respectively. These calculated values agree well with those obtained for the maximum observed rate constants (Table) and therefore these rate constants define true plateau regions. From the slopes of the lines values for K/N of 178 and 221 l mol^{-1} have been obtained. Using the k_m values obtained from equation (4), the kinetic data have been treated according to equation (5) by plotting the left hand side against C_D . Once again good straight lines are obtained (Figure). From the slopes of these lines values for K/N of 175 and 265 l mol^{-1} are obtained. Agreement between these sets of K/N values using equations (4) and (5) is considered to be very good considering the assumptions involved in their derivation.⁵ From the intercepts of the plots according to equation (5) critical micelle concentrations of 4.0×10^{-3} and $5.5 \times 10^{-3}\text{M}$ have been obtained for NaLS in the presence

⁸ P. Mukerjee and K. J. Mysels, 'Critical Micelle Concentrations of Aqueous Surfactant Systems,' NSRDS-NBS, Washington, 1971.

of (1) and (2), respectively. These kinetically determined CMC values are smaller than that determined for pure NaLS in water, presumably because solubilization of the substrate and the buffer lowers the CMC. Using an aggregation number of 61,⁹ the binding constants for the interaction of (1) and (2) with NaLS are calculated to be 1.0×10^4 and 1.5×10^4 l mol⁻¹, respectively. The magnitude of this binding constant is of the order generally found for micelle-substrate interactions,⁴⁻⁷ and binding, or solubilization, is undoubtedly the consequence of electrostatic interactions between the positively charged protonated nitrene (3) and the

equilibrium to the left. Additionally, whereas an anionic micelle would stabilize the transition state for the rate-limiting attack of water on (3) which necessarily has positive character, cationic, zwitterionic, and nonionic micelles would predictably destabilize or have little effect on it. Slight inhibition (by factors of *ca.* 2) have been found for the hydrolysis of methyl orthobenzoate in the presence of zwitterionic and nonionic surfactants, a reaction which is catalysed 41-fold by NaLS,¹¹ and these results and those for other orthoesters⁷ are explicable in a generally similar manner. Since (1) and (2) bind equally effectively to NaLS and



Micelle-substrate association constant plots for binding of (1) (O) and (2) (●) to NaLS micelles according to equations (4) and (5)

negatively charged surface of the NaLS micelle.¹⁰ However, unlike enhancement of CTAB catalysis by a nonionic surfactant which may result from a partial decrease in the charge on the micellar surface, the addition of 1.0×10^{-3} M-Igepal CO-730 to 3.5×10^{-2} M-NaLS inhibits the catalysis by the small factor of 1.3 (Table). The absence of catalysis by micellar cationic CTAB and zwitterionic DAPS and the slight catalysis by zwitterionic DDAPS and nonionic Igepal CO-730 (factors of 1.8 and 1.3, respectively) are consistent with this electrostatic interpretation.

It is probable that each charge type micelle may well solubilize or bind, the neutral substrates (1) and (2) in the Stern layer to approximately the same extent.⁴⁻⁷ However, unlike the anionic micellar surface of NaLS which acts as a 'sink' for cations including the hydronium ion thereby promoting the formation of the intermediate (3), the hydronium ion concentration at anionic, zwitterionic, and nonionic micellar surfaces would reasonably be less than that in the bulk aqueous phase due to electrostatic repulsion. Hence the micelle solubilized substrates (1) and (2) would be shielded from hydronium ions thereby shifting the rapid pre-

$k_{\psi_{\max}}$ and k_m are essentially identical for the two substrates, it is apparent that the magnitude of the catalysis is solely the consequence of the difference in the rate in the bulk aqueous phase (*vide supra*).

The origin of the NaLS catalysis is explicable in terms of the formation and stabilization of the common intermediate (3). The negatively charged Stern layer of the NaLS micelle, not improbably, stabilizes the transition state for the rate-limiting addition of water to the protonated nitrene to a greater extent that it stabilizes the initial states [(3) and H₂O] thereby decreasing the overall free energy of the reaction.

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¹⁰ C. A. Bunton and M. J. Minch, *Tetrahedron Letters*, 1970, 3881.

¹¹ R. B. Dunlap and E. H. Cordes, *J. Phys. Chem.*, 1969, **73**, 361.

⁹ K. J. Mysels and L. H. Princen, *J. Phys. Chem.*, 1959, **63**, 1969.