Micellar Catalysis of the Deamination of *O*-Alkylhydroxylamines

By **M. Hutchinson** and **G. Stedman**,* University College of Swansea, Singleton Park, Swansea SA2 8PP

The bromide and thiocyanate ion-catalysed deamination of long-chain *O*-alkylhydroxylamines show normal reactivities at low substrate concentrations. There is a rapid increase in reactivity at the critical micelle concentration, the bromide-catalysed reaction showing a rather greater increase than the thiocyanate-catalysed reaction. The reactivity of the micelle increased with increased chain length. The origin of the micellar catalysis is discussed, and is ascribed to the association of catalytic anions at or close to the surface of the cationic micelle, in the immediate vicinity of the substrate amine groups.

THERE is interest in the mechanism of reactions occurring in micellar systems.[1,2] Some reactions show very large catalytic effects, and many factors may be involved. In some cases catalysis is associated with the presence of micelles of a particular charge type. Thus reactions involving anionic species may be catalysed by cationic micelles, but may be unaffected or inhibited by anionic micelles. The interpretation is complicated by the fact that the substrate will generally be distributed between the micellar phase and the bulk of the solution, and also by uncertainty about the location of the substrate within the micelle. We report an investigation where the latter factors do not complicate the interpretation.

The deamination of the *O*-alkylhydroxylamines by nitrous acid has been studied in some detail.[3,4] The mechanism can be summarised by reactions (1)—(4).

$$\begin{array}{llll}
H^+ + HNO_2 + X^- \rightleftharpoons ONX + H_2O & \text{Fast} & K_{NOX} & (1)\\
RONH_3^+ \rightleftharpoons RONH_2 + H^+ & \text{Fast} & K_a & (2)\\
ONX + RONH_2 \longrightarrow RNHNO + H^+ + X^- & \text{Slow} & k & (3)\\
RNHNO \longrightarrow ROH + N_2 & \text{Fast} & & (4)
\end{array}$$

Under the conditions of our work (pH 1) the alkylhydroxylamines exist almost 100% in the protonated form and the nitrite exists almost entirely as molecular nitrous acid. The rate law observed is $-d[HNO_2]/dt = k_3^X[RONH_3^+][HNO_2][X^-]$ where $k_3^X = kK_{NOX}K_a$. Values of K_a and K_{NOX} are known, and substitution shows that k has values in the range 10^6—10^7 l mol^{-1} s^{-1} at 0 °C for X = Cl, Br, and SCN, well below the encounter limit. In the absence of nucleophilic anions reaction can occur by attack of the nitrous-acidium ion on the neutral *O*-alkylhydroxylamines, with a rate law $-d[HNO_2]/dt = k_4[RONH_3^+][HNO_2]$. Because the deamination is catalysed by nucleophilic anions, and since such anions are associated with cationic micelles, it was decided to investigate the deamination of long-chain alkylhydroxylamines that form cationic micelles, and compare the result with those for non-micellar systems.

EXPERIMENTAL

The *O*-alkylhydroxylamines were a gift from Vitamins Ltd. (now Beecham Research Laboratories) supplied through the courtesy of Dr. P. Mamalis. The other materials used were as described in previous papers.[3]

The kinetics were followed by standard methods. An ice–water mixture was used as a thermostat. Aliquot portions were removed from the reaction solution at known times and quenched in a solution of sulphanilic acid, sodium bromide, and perchloric acid. Unchanged nitrous acid rapidly diazotised the sulphanilic acid, and the change in light absorption due to the diazonium ion formed was measured on a Unicam SP 500 spectrophotometer. The main experimental problem was the limited solubility of the *O*-alkylhydroxylamines under our conditions, and it was not possible to extend our measurements to concentrations much in excess of the critical micelle concentration. Surface tensions were measured by the drop-size method and the bubble method.[5]

RESULTS

The kinetics were investigated by following the disappearance of nitrous acid. In runs where there was a large excess of alkylhydroxylamine good first-order kinetics were observed during several half-lives: $-d[HNO_2]/dt = k_1[HNO_2]$. Reaction was catalysed by chloride, bromide, and thiocyanate ions, the results fitting the equation $k_1 = k_2[X^-]$. Changes in acidity over the range 0·01—0·1M-perchloric acid had no effect on the rate. The effect of changes in the concentration of the alkylhydroxylamines was more complex. At high and at low concentration k_2 obeyed the relationship $k_2 = k_3^X[RONH_3^+]$, but the values of k_3^X were different in the two concentration ranges. A plot of k_3^X against $[RONH_3^+]$ for R = n-$C_{10}H_{21}$ is shown in the Figure. It has the typical sigmoid shape observed for many reactions involving micellar catalysis, the limiting low-concentration value presumably being characteristic of the monomeric alkylhydroxylamine, while the limiting high-concentration value is characteristic of the micelle. We have made an estimate of the critical micelle concentration from our kinetic data by taking the intersection of a tangent passing through the point of inflexion on the steeply rising part of the curve and a tangent to the low-concentration end of the curve. This is shown in the Figure by the broken lines. We note that the same value of the critical micelle concentration was obtained for bromide- and thiocyanate-catalysed reactions. The critical micelle concentrations for two of the alkylhydroxylamines were also obtained from conventional surface-tension measurements made under the same conditions used for the kinetic runs. The critical micelle concentrations obtained by the two methods were in satisfactory agreement, although those obtained by the

---

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

[2] E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.

[3] M. N. Hughes, T. D. B. Morgan, and G. Stedman, *J. Chem. Soc.* (*B*), 1968, 344.

[4] J. E. Leffler and A. A. Bothner-By, *J. Amer. Chem. Soc.*, 1951, **73**, 5473.

[5] A. Findlay and J. A. Kitchener, 'Practical Physical Chemistry,' Longmans, London, 1965, pp. 97—101.

kinetic method were certainly subject to greater error. The results are summarised in the Table. In addition we have one result for chloride catalysis with n-$C_{12}H_{25}ONH_3^+$ micelles and $k_3^{Cl} = 1{\cdot}2$ l^2 mol^{-2} s^{-1}. This compares with a value for 0·14 obtained for $MeONH_3^+$, representing an acceleration of a factor of *ca.* 9.

DISCUSSION

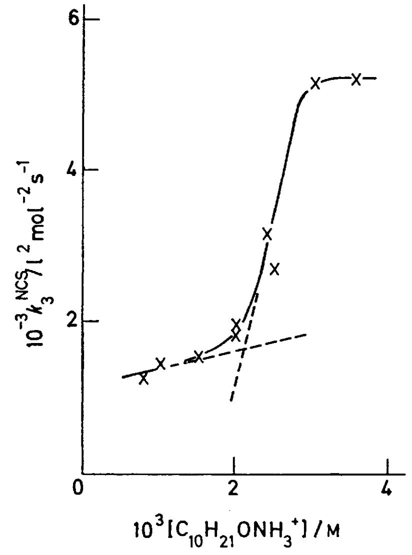
The limiting low-concentration values of k_3^X are all very similar for a given nucleophilic anion, and are close to the values observed for compounds with short-chain alkyl groups. Thus the reactivities of the monomeric species seem to be quite normal, and essentially independent of chain length.

Rate constants and critical micelle concentrations for the deamination of *O*-alkylhydroxylamines at 0 °C and 0·3M ionic strength

R	Low concn. k_3^{Br}/l^2 mol^{-2} s^{-1}	Low concn. k_3^{NCS}/l^2 mol^{-2} s^{-1}	Critical micelle concn./M Kinetic method	Critical micelle concn./M Surface tension	High concn. k_3^{Br}/l^2 mol^{-2} s^{-1}	High concn. k_3^{NCS}/l^2 mol^{-2} s^{-1}
Me	7·4 [a]	1190 [a]				
$Bu^t{\cdot}CH_2{\cdot}$		1640 [a]				
n-C_7H_{15}	6·5		5×10^{-2}			
n-$C_{10}H_{21}$	7	1150	$2{\cdot}1 \times 10^{-3}$		>42 [b]	5140
$Bu^t{\cdot}[CH_2]_6{\cdot}CH_2{\cdot}$	8·9	1200	$7{\cdot}1 \times 10^{-4}$	$8{\cdot}0 \times 10^{-4}$	>137 [b]	>24,000 [b]
n-$C_{12}H_{25}$	9	1650	$1{\cdot}6 \times 10^{-4}$	$2{\cdot}25 \times 10^{-4}$	180	22,000
n-$C_{14}H_{29}$					390	40,000 [c]

[a] Values from ref. 3. Limiting high-concentration value not observed. [c] Preliminary value.

The general form of the plots of k_3^X against $[RONH_3^+]$ and the rapid increase at a concentration close to the critical micelle concentration is a clear indication that the increased reactivity is due to micelle formation. The agreement between the critical micelle concentration obtained by the kinetic and surface tension methods is within the uncertainty of the former. The critical micelle concentrations (c.m.c.) decrease as the chain length increases, and fit the equation log(c.m.c.) = **2·41** — **0·51***n* where *n* is the number of carbon atoms in the chain. Equations of this form commonly describe the variation of critical micelle concentration with chain length.[6, 7]



The dependence of k_3^{NCS} upon concentration of n-$C_{10}H_{21}ONH_3^+$

The high concentration values of k_3^X increase markedly with chain length (and hence micelle size), and there appears to be a greater acceleration for the bromide-catalysed reaction than the thiocyanate-catalysed reaction. There seems no reason to doubt that in the micellar system we are observing the same basic mechanism as is found with monomeric alkylhydroxylamines, a rate-determining nitrosation of the free alkylhydroxylamine by an equilibrium concentration of a nitrosyl compound. However in this case the reactive centre, the amino-group, will be located at the surface of the micelle. Reaction will thus occur at the micelle surface, and it will be the conditions in the Gouy and Stern layers that will determine the rate of reaction. In general the acidity, ionic strength, dielectric constant, concentrations of anions, *etc.* will be different in these regions from the values for the bulk of the solution.

There are a number of factors that may influence the rate. The ionisation constant of the alkylhydroxylammonium ion may be greater in a micelle than for monomeric species, thus leading to an increased concentration of the reactive free base. However this factor should affect the bromide- and thiocyanate-catalysed reactions equally. As the rate-determining step involves reaction between two neutral molecules there seems unlikely to be much effect on the value of *k*. The results summarised by Fendler and Fendler [2] support this view. There could also be an effect of the micellar environment in the value of K_{NOX}. The effect of cationic and anionic micelles on a number of acid-base indicator equilibria have been investigated and rationalised in terms of the charge type by the Hartley ' sign rule '. Fendler and Fendler have summarised these results. They quote only one example of an equilibrium of the same charge type as (1), and for this case there was no effect of cationic or anionic micelles on the position of equilibrium.[2] Turning now to the effective concentrations of the reactants, we find no obvious reason why the concentration of molecular

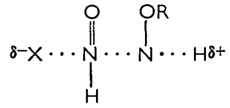
---

[6] P. Molyneux, C. T. Rhodes, and J. Swarbrick, *Trans. Faraday Soc.*, 1965, **61**, 1043.

[7] H. L. Rosano, A. P. Christodoulou, and M. E. Feinstein, *J. Colloid Interface Sci.*, 1962, **29**, 335.

nitrous acid in the vicinity of the micelle should be markedly different from the bulk concentration. If there were such an effect it should produce the same change in rate for both bromide- and thiocyanate-catalysed reactions. However there is likely to be a high local concentration of anions in the Stern and Gouy layers of the micelle. Measurements have been made by a number of techniques, and in many cases 70—90% of the charge on a micelle is neutralised by associated counterions. In the presence of excess of perchloric acid and sodium perchlorate this percentage is likely to be even higher. This association is likely to bring the catalytic anion into very close proximity to the reactive amino-group, and we suggest that this is the main cause of the enhanced rates. The increase in reactivity with chain length is consistent with this picture as there is evidence that the binding of counterions is stronger with larger micelles.[8] There are, however, other factors to be considered. Our experiments were performed at 0·3M ionic strength, made up of the sodium salt of the catalytic ion, sodium perchlorate, and perchloric acid. In general one may expect the more weakly hydrated ions to be bound most strongly at the micelle surface, and thus the likely sequence is $ClO_4^- > SCN^- > Br^- > Cl^-$. In the thiocyanate experiments usually $[SCN^-] < 10^{-3}$M and in the bromide experiments $[Br^-] < 10^{-1}$M. Thus it is likely that most of the anions associated with the micelles were perchlorate. If the perchlorate ion were very much more strongly bound to the micelle than either bromide or thiocyanate ion, these catalysts could be excluded from the vicinity of the micelle, and their reactivity reduced. We are investigating this aspect of the problem.

Another possible explanation, for which we are indebted to a Referee, is in terms of the difference in free energy between the reactants and the transition state. If the $RONH_3^+$ were destabilised in the micelle (relative to the monomeric species) while the less polar transition state were less affected then this might account for the acceleration in rate in the micelle. Differing degrees of bond breaking in the system (I)



$${}^{\delta-}X\cdots\underset{\underset{H}{|}}{\overset{\overset{O}{\|}}{N}}\cdots\overset{\overset{OR}{|}}{N}\cdots H^{\delta+}$$

(I)

would result in different accelerations for different anions X^-.

Our results are consistent with those of Moss and Talkowski [8] who examined the deamination of 2-amino-octane in nitrite buffers at pH 4 and 1·6M ionic strength. Under their conditions dinitrogen trioxide is the nitrosating agent ($X^- = NO_2^-$ in our mechanism). Here again reaction was considerably faster at amine concentrations above the critical micelle concentration, rate accelerations by factors of 6—16 being reported. Moss and Reger have also observed unusual stereochemical results [9] in the deamination of optically active 2-amino-octane at concentrations above the critical micelle concentration (retention of configuration rather than the normal inversion) and claims that the presence of perchlorate counterion is essential to the micellar stereochemical effects. Our results represent an initial survey and particular aspects are being further studied.

We thank Mr. B. James for preliminary work.

[2/1136 *Received*, 19*th May*, 1972]

---

[8] R. A. Moss and C. J. Talkowski, *Tetrahedron Letters*, 1971, 703.

[9] R. A. Moss and D. W. Reger, *J. Amer. Chem. Soc.*, 1969, **91**, 7539.