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DECARBOXYLATION OF 6-NITROBENZISOXAZOLE-3-CARBOXYLATE ION IN CATIONIC MICELLES: EFFECT OF HEAD GROUP SIZE

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ABSTRACT

The rate of decarboxylation of 6-nitrobenzisoxazole-3-carboxylate ion increases sharply with increasing head group size in a series of cetyltrialkylammonium bromides ($C_{16}H_{33}NR_3Br$: R = Me, CTABr; R = Et, CTEABr; R = n – Pr, CTPABr; R = n – Bu, CTBABr) with rate enhancements of 10^2 (CTABr) and $2{\cdot}8 \times 10^3$ (CTBABr). Micellized tetradecylquinuclidinium bromide and hexadecyl-*N*-methylmorpholinium bromide are slightly better catalysts than CTABr, as is 1,3-bis(*N*-cetyl-*N*,*N*-dimethylamino)propane dibromide, but *p*-octyloxybenzyltrialkylammonium bromides (alkyl = Me, n – Bu) are less effective than the corresponding CTA^+ surfactants. These differences in catalytic efficiency depend on the head group structure and the extent to which the cationic head groups become less accessible to water rather than the overall micellar structure.

The rates of spontaneous anionic decarboxylations increase sharply with decreasing polarity of the medium.[1] The decarboxylation of 6-nitrobenzisoxazole-3-carboxylate ion (6NBIC) is accelerated by a variety of aqueous colloidal assemblies that provide submicroscopic reaction media.[2–5] These rate enhancements are ascribed to changes in hydrogen bonding and a decrease in the polarity of the submicroscopic reaction medium which lead to stabilization of the transition state, relative to the initial state (**1**), due to coulombic and dispersive interactions with the assemblies, and a decrease in hydrogen bonding.

Micelles of aqueous cationic and zwitterionic surfactants accelerate decarboxylation, generally by factors of 10^2 or more,[2] and reaction is faster in zwitterionic than in similar cationic micelles. Much of the work has involved cationic surfactants with the trimethylammonium head group and we now describe a study of the effects of changes in the

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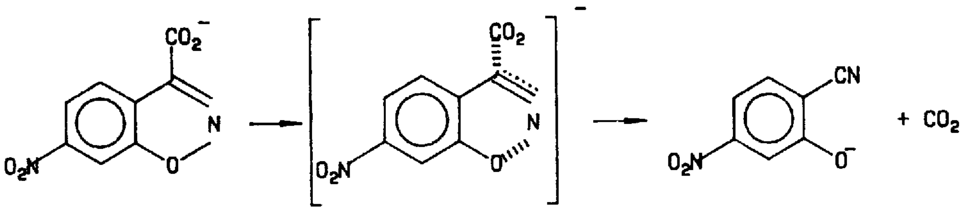

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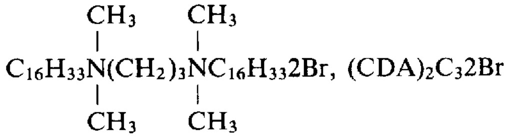
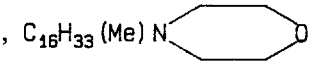
size of the head group and shape of the micelle. Reviews of micellar rate effects are given in ref. 3. Most of the surfactants had the cetyl(hexadecyl) group as the hydrophobic residue (Scheme 1), but we also examined a dicationic surfactant, 1,3-bis(*N*-cetyl-*N*,*N*-dimethylamino)propane dibromide [$(CDA)_2C_32Br$], and the *p*-octyloxybenzyltrialkylammonium surfactants pOOTABr and pOOTBABr and the quinuclidinium surfactant TDQBr.

Cetyltrialkylammonium bromide, $C_{16}H_{33}NR_3Br$: R = Me, CTABr;
R = Et, CTEABr; R = n − Pr, CTPABr; R = n − Bu, CTBABr
1,3-Bis(*N*-cetyl-*N*,*N*-dimethylamino)propane dibromide,



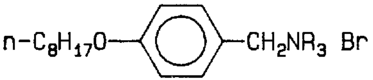
$$\underset{CH_3}{\overset{CH_3}{C_{16}H_{33}N}}(CH_2)_3\underset{CH_3}{\overset{CH_3}{N}}C_{16}H_{33}2Br,\ (CDA)_2C_32Br$$

N-Cetyl-*N*-methylmorpholinium bromide, 

Br, CMMABr;

N-Tetradecylquinuclidinium bromide, 

Br, TDQBr;

p-Octyloxybenzyltrialkylammonium bromide, 

R = Me, pOOTABr; R = n − Bu, pOOTBABr

Scheme 1

The tetradecyl surfactant TDQBr was used because the hexadecyl analog is sparingly soluble in water. Reaction of **1** in CTABr and the tetra- and hexa-methylene dicationic surfactants $(CDA)_2C_42Br$ and $(CDA)_2C_62Br$ had already been examined.[2a] These various micelles have different structures, for example CTABr grows and becomes rod-like on addition of NaBr and the solutions become viscous, whereas CTBABr appears to remain spherical, based on the low viscosity of its solutions even with added NaBr.[4]

Spontaneous reactions are useful probes of micellar structure because with fully bound substrate rate effects are due wholly to changes in the relative free energies of the initial and transition states involving only one molecule or ion.[2,3] The situation is more complicated for non-spontaneous bimolecular reactions where the distribution of two species has to be considered. The large effects of the medium on the rates of anionic decarboxylations[1] make these reactions excellent probes of colloidal surface structure.[2,3,5,6]

RESULTS AND DISCUSSION

The first-order rate constants of decarboxylation (k_{obs}) increase monotonically with increasing surfactant concentration as substrate is incorporated into the micelles and become constant when the substrate is fully bound (Tables 1 and 2). Under these conditions $k_{obs} = k'_M$, where k'_M is the first-order rate constant in the micellar pseudophase (Table 3). Table 3 also gives values of k'_M/k'_W, where k'_W is the first-order rate constant of reaction in water.

The most striking observation is the rate increase as R (Scheme 1) is changed from Me ($k'_M/k'_W \approx 10^2$) to Bu ($k'_M/k'_W = 2800$). This rate increase is not due solely to a change in the bulk of the *N*-alkyl group because the morpholine and quinuclidine derivatives (CMMABr and TDQBr) are little more effective than CTABr in accelerating the reaction (Tables 1 and 2). The decrease in length of the hydrophobic alkyl group from hexadecyl to tetradecyl in TDQBr may

Table 1. Rate constants of decarboxylation in hexadecyl surfactants[a]

10^3[Surfactant], M	CTEABr	CTPABr	CTBABr	CMMABr	(CDA)$_2$C$_3$2Br[b]
0·4	4·43	14·6	39·7		
0·6	5·99	20·1	46·6	1·90	
0·9			52·3	3·59	
1·0	7·00	23·0	53·2		5·01
2·0	7·55	23·7	60·6	4·32	7·67[b]
3·0		26·0	61·2		7·66[b]
4·0	8·08		65·4	4·64	
6·0	8·67	27·8	68·3	4·82	
10		31·0	72·1	4·98	
15				4·57	
20	9·42	34·0	80·5		
30		36·0			
40	10·1	41·3	85·3		
50	10·1				
80		41·4			

[a] Values of 10^4 k_{obs} (s^{-1}) at 25·0 °C.
[b] in 10^{-3} M NaOH.

Table 2. Effects of chain length and head group on rate constants of decarboxylation[a]

10^3[Surfactant], M	pOOTABr	pOOTBABr	TDQBr
2·0			3·23
4·0		1·36	5·84
8·0		1·82	6·63
9·0	1·23		
10			6·60
15	1·55	2·30	
30	1·66		
40		2·94	
50	1·79	3·10	
80		3·65	
100	2·20	3·72	

[a] Values of 10^4 k_{obs} (s^{-1}) at 25·0 °C.

Table 3. Rate constants of decarboxylation in aqueous micelles[a]

Surfactant	$10^4 k'_m$, s^{-1}	Surfactant	$10^4 k'_m$, s^{-1}
CTABr	~3·3 (10^2)[2a]	pOOTABr	>2·2 (>73)
CTEABr	10 (330)	pOOTBABr	3·7 (124)
CTPABr	41 (1400)	$(CDA)_2C_32Br$	7·7 (290)
CTBABr	85 (2800)	$(CDA)_2C_42Br$	10 (330)[2a]
CMMABr	4·8 (160)	$(CDA)_2C_62Br$	12 (400)[2a]
TDQBr	6·6 (220)		

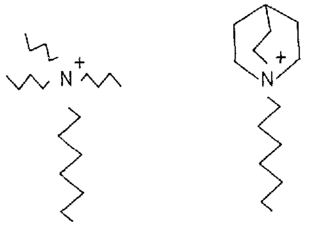
[a] At 25·0 °C; values in parentheses are relative to $k_{obs} = 3{\cdot}0 \times 10^{-6}\ s^{-1}$ in water.

decrease the rate enhancement, but the effect should not be large because the rates of decarboxylation are similar in micellized C_{14} and C_{16} betaine surfactants.[2c]

This effect of head group size is also shown to a limited extent by the *p*-octyloxy surfactants pOOTBABr and pOOTABr, although here the rates increase slightly with increasing surfactant concentration even at concentrations of 0·1 M (Table 2). Reaction in pOOTABr is slower than in CTABr and in pOOTBABr is much slower than in CTBABr. It appears that the benzyloxy group is less hydrophobic than the alkyl group in the CTA^+ surfactants so that water can penetrate more deeply into the micelles, which should slow decarboxylation.

A decrease in the hydrogen-bonding ability of the medium should destabilize the initial state relative to the charge-delocalized transition state.[1] Based on NMR line widths, hydration of Br^- decreases with increasing bulk of the alkyl groups of $C_{16}H_{33}NR_3Br$ in the sequence R = Me < Et < Pr < Bu,[4] so that hydration of **1** should also decrease as R is changed from Me to Bu. Reactions that involve charge delocalization in forming the transition state are generally accelerated by a decrease in solvent polarity.[7] This general effect of the medium should be important for reactions at micellar surfaces, because they are less polar than water,[8,9] and bulky alkyl groups should further decrease the polarity at the micellar surface. The butyl groups of CTBABr do not extend into the water but are oriented along the micellar surface[4] to reduce water–alkyl group contact (Scheme 2) so that decarboxylation of bound substrates then takes place in a region of relatively low polarity. The quinuclidine moiety in TDQBr probably extends away from the micellar surface (Scheme 2) so that reaction takes place in a region that is exposed to water, with a consequent rate enhancement similar to that given by CTEABr (Table 3). We know of no evidence concerning the conformation of the morpholine moiety in CMMABr, but we assume that it too will extend away from the micellar surface, so that rate enhancements by micellized CMMABr should not be large (Table 3).

The methylene-bridged dicationic surfactants $(CDA)_2C_n2Br$ give larger rate enhancements than CTABr (Table 3) because the bridging methylene groups should force water molecules away from the micellar surface. However, these dicationic surfactants give smaller rate



Scheme 2

enhancements than CTPABr and CTBABr and we only have a minimum value of k'_M/k'_W for $(CDA)_2C_3Br$ (Table 3).

Although micellizing surfactants such as CTBABr accelerate decarboxylation they are less effective catalytically than such non-micellizing amphiphiles as $(C_8H_{17})_3N^+EtMeSO_3^-$ [5] because micelles with their high surface charge density interact coulombically with small ions of high charge density. This interaction stabilizes the anionic substrate, whereas small clusters of tri-n-octylalkylammonium ions do not interact strongly with the substrate, although they interact with, and stabilize, the transistion state.[2] The rate effects do not correlate closely with the overall structure or aggregation number of the surfactant assembly because, based on NMR evidence (see Experimental), the tetramethylene surfactant $(CDA)_2C_42Br$ forms very large assemblies, but is a much less effective catalyst than large synthetic cationic vesicles,[5a] spherical micelles of CTBABr or small assemblies of non-micellizing amphiphiles of tri-n-octylalkylammonium ions.[5] The rate enhancements by cationic micelles are controlled by the nature of the surface, rather than the size of the micelles. The effectiveness of zwitterionic surfactants and non-micellizing hydrophobic tri-n-octylalkylammonium ions relative to otherwise similar cationic micelles is understandable in terms of destabilization of the initial relative to the transition state. These rate effects of colloidal assemblies are qualitatively similar to solvent effects and have a similar origin.[3]

Approximate values of the binding constants of substrate to micelles are given by the reciprocal of the surfactant concentration that gives half the maximum rate enhancement.[9] This estimate neglects the concentration of monomeric surfactant, which will be affected by NaOH and interactions between substrate and surfactant, and there are often large rate enhancements at surfactant concentrations below the critical micellar concentrations (CMC) in water (see Experimental and refs 2 and 5) owing to induced micellization or interactions of the substrate with monomeric or submicellar surfactants. For reactions in solutions of the hexadecyl monocationic surfactants, half the maximum rate enhancement is observed at $2–5 \times 10^{-4}$ M, which corresponds to binding constants of ca $2–5 \times 10^{3}$ M^{-1}, and the binding constant for the tetradecylquinuclidinium surfactant (TDQBr) is ca 500 M^{-1} (Table 2). The octyloxy surfactants pOOTABr and pOOTBABr are exceptions to this generalization and they give approximate binding constants of ca 10^2 M^{-1}, based on the rate–surfactant profiles (Table 2). This difference is consistent with other data on the CMC and solute-binding ability of pOOTABr compared with other cationic surfactants.[10]

EXPERIMENTAL

Materials

The preparation and purification of the substrate and most of the surfactants have been described.[2,3,10] The other surfactants were prepared by standard methods of quaternization or by reaction in diethyl ether at room temperature for TDQBr and pOOTBABr and in refluxing acetonitrile for CMMABr. They were purified by recrystallization from acetone, acetone–methanol and dry diethylether at −20 °C for pOOTBABr.

The CMCs are 1×10^{-3} M, for CMMABr, $2{\cdot}6 \times 10^{-3}$ M for TDQBr and $3{\cdot}1 \times 10^{-3}$ M for pOOTBABr from surface tension measurements. There were no minima in the plots of surface tension against surfactant concentration. There was a break in the conductivity of $(CDA)_2C_32Br$ at $3{\cdot}0 \times 10^{-5}$ M.

Kinetics

Reactions were followed spectrometrically at 410 nm with 10^{-4} M substrate by using a Hewlett-Packard diode-array spectrometer at 25·0 °C with 10^{-2} M NaOH, except where specified otherwise. The general procedure has been described.[2] Most of the earlier measurements were made in dilute ammonia buffers[2] and changes in electrolyte concentration slightly change the reaction rate. The dicationic surfactant $(CDA)_2C_32Br$ is sparingly soluble in water and we could not reach concentrations which gave constant values of k_{obs}. We minimized the solubility problem by using 3×10^{-3} M NaOH.

NMR

The ^1H and ^{13}C spectra of $(CDA)_2C_42Br$ (5×10^{-3} M) in D_2O and 20 vol.-% D_2O in H_2O (Varian XL 300 at ca 25 °C) have very broad signals, characteristic of the formation of large assemblies.[11] We could not detect a signal of ^{81}Br, probably because it is very broad owing to incorporation in a large, relatively immobile assembly. This behavior is completely different from those of single-chain cationic surfactants that give well resolved signals of ^1H and ^{13}C and well defined signals of ^{79}Br or ^{81}Br. It was necessary to allow these solutions to stand overnight, otherwise the NMR data were erratic. This evidence, and an increase in viscosity with increasing surfactant concentration suggest that these dicationic surfactants slowly form relatively large aggregates. We did not examine the NMR spectra of $(CDA)_2C_32Br$ because of its low solubility.

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