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SPECIFIC MICELLAR RATE EFFECTS ON UNIMOLECULAR DECARBOXYLATION AND CYCLIZATION

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Decarboxylation of 6-nitrobenzisoxazole-3-carboxylate ion and cyclization of *o*-3-halopropyloxyphenoxide ion (PhY7; Y = Br, I) are accelerated by aqueous cationic and zwitterionic micelles. For cationic micelles the rate enhancements (k_M'/k_W') increase with increasing bulk of the surfactant head groups but are largest for decarboxylation. There are good linear free energy relationships between micellar effects on these reactions and the plots of log k_M' for cyclization against log k_M' for decarboxylation have slopes of 0·46 and 0·64 for Y = Br and I, respectively. Surfactants that have twin tail or tri-*N*-alkylbenzyloxy head groups do not fit the relationship. Despite mechanistic differences between decarboxylation and cyclization (an intramolecular S_N2 reaction), similar factors control micellar effects on these reactions. In the absence of surfactant there is only a qualitative relationship between free energies of activation of cyclization and decarboxylation in different solvents.

INTRODUCTION

Rate enhancements by colloidal assemblies such as aqueous micelles, vesicles and microemulsion droplets are readily understandable in terms of pseudo-phase models.[1–3] The overall reaction rate is the sum of rates in water and in the colloidal assembly, which are treated as distinct reaction media. For spontaneous unimolecular or bimolecular, water-catalysed, reactions, the observed first order-rate constants, k_{obs}, depends on the first-order rate constants in the aqueous and micellar pseudo-phases (k_W' and k_M', respectively) and the extent of substrate transfer between the pseudo-phases. At high surfactant concentrations, with fully bound substrate, $k_{obs} = k_M'$. For spontaneous hydrolysis k_M' is usually smaller than k_W' and generally in cationic and zwitterionic micelles the difference is much smaller for bimolecular than for unimolecular spontaneous hydrolyses, but the opposite situation holds for anionic micelles.[3] Hence there seems to be a relationship between the charge effect of the micelle and the molecularity of the reaction.

Spontaneous decarboxylations of anionic substrates[4] are faster in cationic and zwitterionic micelles than in water and values of k_M'/k_W' range up to *ca* 10^3. These rate enhancements are understandable because these reactions are accelerated by aprotic solvents and by a decrease in the water content of mixed solvents.[5] Surfaces of micelles and other surfactant assemblies are less polar than water, based on spectral probes,[1–3,6] water activity is lower[7] and there is less hydration of bromide ion.[8]

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The situation is more complicated for bimolecular, non-solvolytic reactions, but micellar rate effects can be treated in terms of models that estimate the partitioning of the two reagents between water and micelles and second-order constants in each pseudo-phase. There is limited evidence that this model can also be applied to reactions in vesicles[1,9] and microemulsions.[10] For many bimolecular reactions, second-order rate constants at micellar surfaces are similar to those in water and the rate enhancements are due to a concentration of the two reactants at the surface of the micelle or other colloid.[2,3]

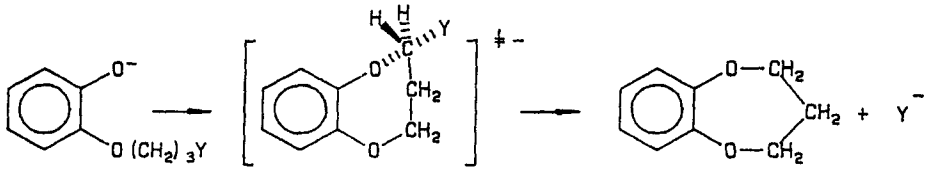
Despite the success of this model, it has severe weaknesses, both conceptual and experimental. Second-order rate constants of reactions in bulk solvents include the dimensions of reciprocal concentration, generally written as molarity. Therefore, if we wish to compare second-order rate constants in aqueous and micellar pseudo-phases, in terms of the units of $M^{-1}\ s^{-1}$, we have to define molarity in the micellar pseudo-phase, even though its molar volume is uncertain and the reagent concentration in that pseudo-phase may not be uniform.[2,3] It is sometimes possible to measure reagent partitioning directly, but often, especially with hydrophilic ions, it is calculated by using equations that contain parameters whose values are uncertain.[2,3,11-13] In addition, most ionic reactions have been examined in solutions of surfactants that have trimethylammonium head groups and hexadecyl (cetyl) apolar groups, and there is some evidence that second-order rate constants at micellar surfaces depend on the nature of the head group.[14] Such a dependence is understandable because values of k_M' for spontaneous reactions are sensitive to changes in size and structure of head groups.[4c,d,15]

We attempted to answer some of these questions by examining the intramolecular S_N2 reactions of *o*-3-halopropyloxyphenoxide ions (Phy7; Y = Br, I) which give seven membered cyclic ethers[16] (Scheme 1).

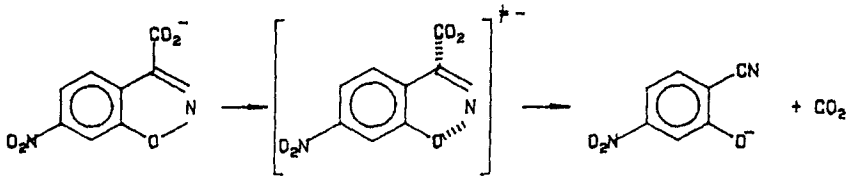
These cyclizations should have transition states that are similar to those of an intermolecular S_N2 reaction of an aryloxide ion and an alkyl halide, and the two sets of reactions have similar solvent effects.[5a,16] Therefore, values of k_M' for reaction of PhY7 should be a good model for second-order rate constants of bimolecular nucleophilic reactions at a micellar surface. Values of k_M'/k_W' are 1·8 and 3·9 for Y = Br and I, respectively, i.e. close to unity, for cyclizations in micelles that have trimethylammonium head groups.[15] This result is in reassuring agreement with the pseudo-phase treatments of bimolecular reactions in aqueous cationic micelles.[2,3] However, values of k_M'/k_W' for cyclizations increase with increasing head group bulk,[15] and for S_N2 reactions of Cl^- and Br^- the second-order rate constants at micellar surfaces also increase with increasing bulk of the cationic head groups.[14] Therefore, the widely observed similarity of second-order rate constants in micellar and aqueous pseudo-phases may be less general than had been assumed.

We have attempted to understand the factors that control rate constants at micellar surfaces by comparing values of k_M' for the S_N2 model reactions of PhY7 and for the spontaneous decarboxylation of 6-nitrobenzisoxazole-3-carboxylate ion (NBIC). Reaction of NBIC (Scheme 2) involves only bond breaking and its rate is very sensitive to solvent composition[5a] and the nature of colloidal surfaces.[4]

Charge in decarboxylation is dispersed in the transition state, as in S_N2-like reactions of cyclizations, but in the latter it is located on electronegative residues rather than being delocalized in a π-system. Despite these differences, $k_M'/k_W' > 1$ for both sets of reactions,[4,15] and both are favoured by cationic surfactants that have bulky head groups. We have obtained



Scheme 1



Scheme 2

Table 1. Rate constants of cyclization[a]

Surfactant	10^3[surfactant] (M)							
	0·7	1·0	6·0	8·0	10·0	100	250	580
9					4·76(7·16)			
10			(8·74)		4·81(8·94)			
11				(9·58)	5·96(9·83)			
12						3·00(3·75)	3·02	3·00(3·9)
13						2·64(2·12)		
14					10·4(20·7)			
15					5·16(9·02)			
16			3·61(6·83)	3·64(6·62)	3·71(6·63)			
17	(15·1)	10·1	10·4(15·8)					

[a]Values of $10^4 k_{obs}$ (s^{-1}) at 25·0 °C for reaction of PhBr7. Values in parentheses are for the iodide (PhI7).

additional data for cyclizations, so that we can compare free energies of activation, as log k'_M, for the cyclization of PhY7 (Y = Br, I) and for the decarboxylation of NBIC.

The surfactants studied were as follows:

cetyltrimethylammonium X, $C_{16}H_{33}NMe_3X$; CTAX X = Br (**1**); Cl (**2**); NO_3(**3**); $(SO_4)_{0·5}$, (**4**); OH, (**5**);

cetyltrialkylammonium bromide, $C_{16}H_{33}NR_3Br$, R = Et, CTEABr, (**6**); n-Pr, CTAPABr (**7**); n-Bu, CTBABr (**8**);

N-cetyl-*N*-methylmorpholinium bromide, CMMBr (**9**); cetylcyclohexyldimethylammonium bromide, CCDABr (**10**);

Tetradecylquinuclidinium bromide, TdQBr (**11**);

dodecyltrimethylammonium bromide, DoTABr (**12**);

p-octyloxybenzyltrialkylammonium bromide, n-$C_8H_{17}O(C_6H_4)CH_2NR_3Br$, R = Me, pOOTABr (**13**); n-Bu, pOOTBABr, (**14**);

cetylbetaine, $C_{16}H_{33}N^+Me_2CH_2CO_2^-$, Bet16 (**15**);

didodecyldimethylammonium chloride, DDDACl (**16**);

1,3-bis(*N*-cetyl-*N*,*N*-dimethylammonio) propane dibromide, $C_{16}H_{33}NMe_2(CH_2)_3NMe_2C_{16}H_{33}2Br$, $(CDA)_2C_32Br$ (**17**).

RESULTS

The new data for cyclizations are given in Table 1 for reactions at high surfactant concentrations with fully bound substrate. All the values of k'_M for cyclizations and decarboxylation are given in Table 2.

The plot of log k_M^{Br} against log k_M^{I} for cyclization (Figure 1) has a slope of 0·72 and micelles favour cyclization of the iodide relative to the bromide. For cyclizations in the absence of surfactant there is a linear relationship with a slope of approximately unity for log k_{obs} in alcohols (Table 3), with deviations

Table 2. Values of k'_M for cyclization and decarboxylation[a]

Surfactant	PhBr7[b]	PhI7[b]	NBIC[c]
1	4·10	5·50	3·30
2	4·40	5·70	3·20
3	3·50	4·70	
4	4·80	6·47	3·90
5	3·50		1·80
6	6·10	10·0	10·0
7	13·0	26·0	41·0
8	16·8	41·0	85·0
9	4·76	7·16	4·80
11	5·96	9·83	6·60
12	3·00	3·90	2·10
13	2·64	2·12	2·20
14	10·4	20·7	37·0
15	5·16	9·02	11·0
16	3·71	6·69	15·0
17	10·4	15·8	77·0

[a]Values of $10^4 k'_M$(s^{-1}) at 25·0 °C.
[b]From Ref. 15, except for surfactants **9**–**17** (Table 1).
[c]Ref. 4a–c.

Table 3. Solve effects on cyclization and decarboxylation[a]

Solvent	Cyclization[b]		Decarboxylation
	PhBr7	PhI7	
Acetonitrile	−1·97	−1·49	−0·6[c]
Isopropanol	−2·82	−2·66	
Ethanol	−3·33	−3·05	−3·0[c]
Methanol	−3·99	−3·80	−3·6[c]
Water	−3·66	−3·85	−5·5[d]

[a]Values of log k_{obs} at 25·0 °C unless specified otherwise.
[b]Ref. 15; the organic solvents contained 3 vol.-% water.
[c]Ref. 5a at 30·0 °C.
[d]Ref. 4a.

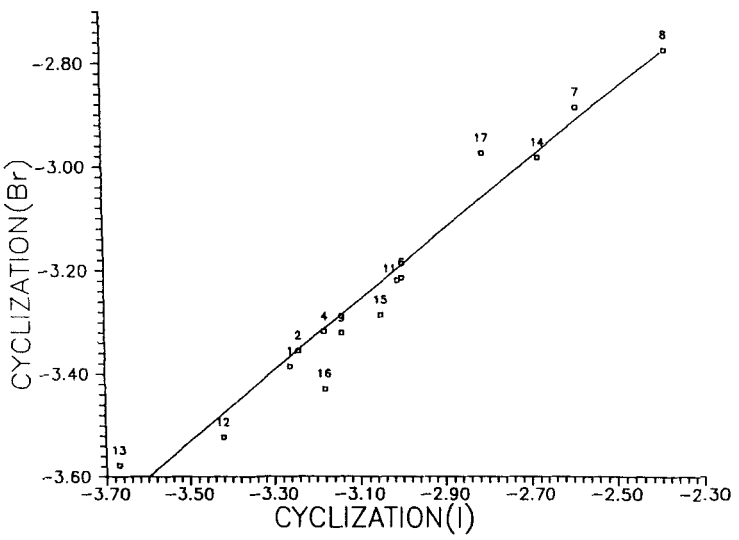


Figure 1. Plot of log k_M^{Br} against log k_M^{I} for cyclization in various surfactants

for water and acetronitrile. There are some data for decarboxylation, mostly at 30 °C.[5a]

Linear free energy plots for cyclizations and decarboxylation in micelles are shown in Figures 2 and 3. Data points for reactions in methanol and ethanol, with no surfactant, would be close to the lines, but there are large deviations for water and acetonitrile. Decarboxylation is more sensitive than cyclization to micellar effects and plots of log k_M' (cyclization) against log k_M' (decarboxylation) have slopes of 0·46 and 0·64 for reactions of bromide (PhBr7) and iodide (PhI7), respectively (Figures 2 and 3).

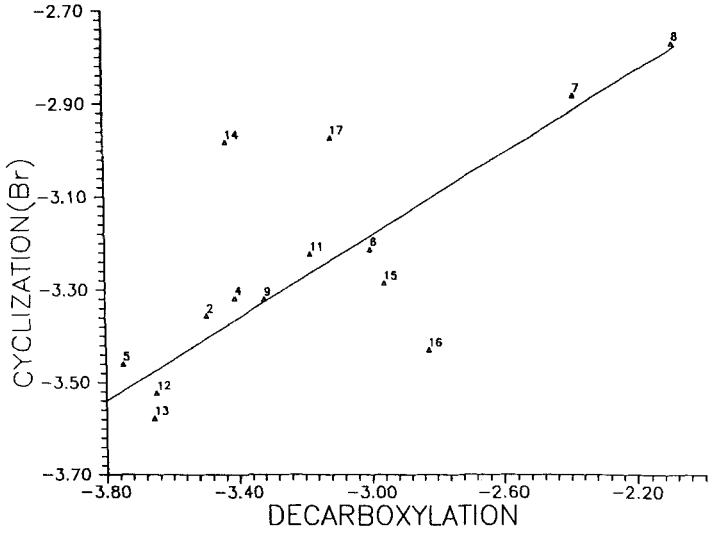


Figure 2. Relationship between log k_M' for cyclization of PhBr7 and decarboxylation in various surfactants

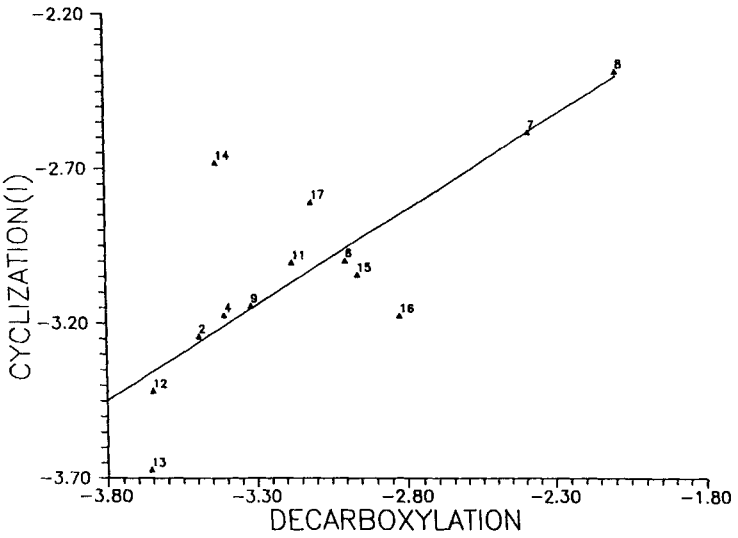


Figure 3. Relationship between log k_M' for cyclization of PhI7 and decarboxylation in various surfactants

DISCUSSION

Cyclization and decarboxylation have qualitatively similar solvent effects (Table 3), although water favours cyclization of the bromide (PhBr7) relative to the iodide (PhI7), probably by hydrating the leaving bromide ion, whereas acetonitrile has the opposite effect.[15] Reaction of the iodide is more sensitive to micellar effects (Figure 1) probably because of interactions of the leaving iodide with bulky, weakly hydrophilic, head groups.

Except for a few surfactants there are good linear free energy relationships (LFER) between cyclizations and decarboxylation (Figures 2 and 3), despite marked differences in surfactant structure. It will be useful to consider micellar effects on the initial and transition states of these reactions. Cyclization involves bond breaking and making, and decarboxylation, which involves only bond breaking, is therefore more sensitive to solvent and micellar effects[5a,15] (Figures 2 and 3). The charged centres in the initial states should strongly hydrogen bond to protic solvents. Aryloxide ions, e.g. PhBr7 and PhI7, should interact strongly with cationic micelles,[2,3] which inhibits cyclization, but this inhibition is offset by interaction with the leaving halide ion and decreased hydration of the oxide residue. Micellar-bound Cl^- and Br^+ are hydrated less than in water, based on NMR line widths,[8,17] so partial dehydration of the oxide or carboxylate resides is also to be expected. There is also evidence from ketone hydration that micelles decrease water activity at their surfaces.[7] It is important to note that, based on interionic competition, Br^- and especially I^- interact more strongly with cationic micelles than oxyanions such as OH^- or RCO_2^-.[2]

Transition states for cyclization and decarboxylation differ in some key respects. In cyclization, as in S_N2 reactions, charge is localized on oxide and halide residues, but it is delocalized into a π-system in decarboxylation and thus delocalization should be favoured by cationic micelles. Transition state formation in decarboxylation does not involve major conformational changes, but the S_N2 transition state has strict conformational requirements,[18] so its formation in cyclization involves extensive changes in geometry because the substrates probably have extended conformations.

Neither cyclization nor decarboxylation involves a change in net charge in transition-state formation, so coulombic micellar interactions with the micelles should not be very important kinetically and rate effects are due largely to specific interactions at the micellar surfaces. Consistently the data points for the betaine surfactant (**15**) do not deviate markedly (Figures 1 and 3), even though it forms a zwitterionic rather than a cationic micelle.

Insofar as micellar effects on cyclization involve a plethora of interactions, deviations from the LFER (Figures 1 and 3) are not unexpected. The deviations are large for surfactants that form relatively rigid assemblies, e.g. DDDACl (**6**) or $(CDA)_2C_32Br$ (**7**), based on NMR line widths,[4d] or the benzyloxy surfactants [pOOTABr (**13**) and pOOTBABr (**14**)]. The ethereal function in **13** interacts strongly with water, based on solubilization of it in dichloromethane,[19] and the bulk of the n-Bu_3N group in **14** makes it difficult to predict initial and transition-state interactions with

micelles. Micelles for which rate data fit an LFER have readily deformable structures that can readily accommodate conformational changes in bound solutes.[1,3] Consistently, non-functional, chiral micelles are not sufficiently rigid to control the stereochemistry of nucleophilic attack on chiral substrates.[20]

We can make some generalizations about micellar medium effects on rates of unimolecular reactions, e.g. *decarboxylation*, and of bimolecular nucleophilic reactions provided that they are based on rate constants *at the micellar surface*. Effects will be larger on the unimolecular reactions, but the generalization that second-order rate constants are similar in water and at cationic micellar surfaces is probably satisfactory only with small head groups, e.g. Me_3N^+. As head groups become larger, second-order rate constants may increase at micellar surfaces, as is found for S_N2 reactions of halide ions.[14] It is important to note that this prediction does not necessarily apply to micellar effects on the overall reaction rate, because they depend on the distribution of reactant(s) between water and micelles and also on rate constants in water and at the micellar surfaces.[2,3]

EXPERIMENTAL

Materials. The preparation and purification of the 3-halopropyloxyphenoxide ions and the surfactants have been described.[4,15] Reactions were followed in redistilled carbon dioxide-free water.

Kinetics. Cyclizations were followed spectrophotometrically at 230 nm as described,[15,16] with 10^{-4} M substrate at 25·0 °C. Surfactant concentrations were high enough to ensure complete binding of the substrates.[15]

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