Micellar-mediated general acid catalysed acetal hydrolysis. Reactions in comicelles

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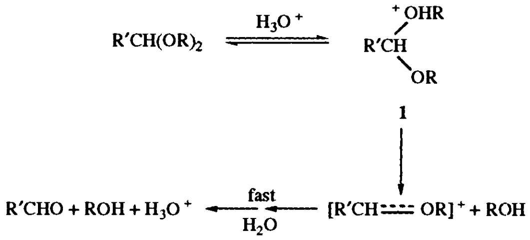
Anionic micelles of sodium dodecyl sulfate (SDS) increase the rates of acid hydrolyses of dibutyl and di-*tert*-butyl benzaldehyde acetal (BBA and BTBA, respectively). The rate surfactant profiles are fitted by a pseudophase, ion-exchange, model and second-order rate constants in the micellar pseudophase are slightly lower than in water. In both media BTBA is considerably more reactive than BBA. The reaction of BTBA is general acid catalysed and with micellar-bound BTBA the first-order rate constant of hydrolysis in comicelles of SDS and sodium decyl hydrogenphosphate increases linearly with increasing mole fraction of the phosphate surfactant, which is a general acid catalyst in the micellar pseudophase. However, the rate constant of the specific hydrogen ion catalysed hydrolysis of BBA is independent of the mole fraction of the phosphate surfactant.

Introduction

Most acetals are hydrolysed in aqueous solution with A-1 mechanisms in which the hydronium ion is fully transferred in the transition state and reactions are specific hydrogen ion catalysed.[1] In the simplest description (Scheme 1) the first step



Scheme 1

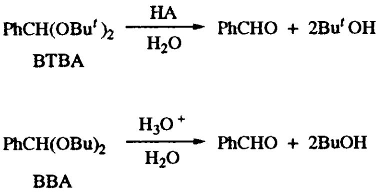
is an equilibrium and the rate-limiting step is decomposition of protonated substrate **1** to an alcohol and a resonance-stabilized carbocation.

It is possible to observe general acid-catalysis of these hydrolyses by disrupting equilibrium formation of **1** by, for example, speeding its decomposition to products relative to loss of H^+.[2-4] This approach has been used by Anderson and Fife who used *tert*-butyloxy leaving groups, in which the steric strain in the ground state is relieved in the transition state, so that protonated substrate **1** is no longer an intermediate and proton transfer and C–O bond breaking are concerted.[2]

We are interested in the ability of aqueous micelles to control reaction rates and equilibria.[5-10] Anionic micelles increase rates of specific hydrogen ion catalysed reactions and the rate enhancements are treated quantitatively in terms of concentration of reactants (substrate and H_3O^+) in the interfacial region at the micellar surface.[5-10]

General acid (or base) catalysis is usually demonstrated by observation of catalysis by an undissociated acid (or base) as well as by H_3O^+ (or OH^-). Buffer solutions are used in this work and ionic micelles can affect buffer equilibria by preferentially binding one species of the buffer. We planned to avoid this problem by using a long-chain monoalkyl phosphate, which is a surfactant and exists largely in the micellar pseudophase. These surfactants are well-studied and their micellization is understood.[11-13]

We used mixed micelles of sodium dodecyl sulfate (SDS, $C_{12}H_{25}OSO_3Na$) and sodium decyl hydrogen phosphate (NaDeP, $C_{10}H_{21}PO_3HNa$). As substrates we used di-*tert*-butyl benzaldehyde acetal (BTBA) and dibutyl benzaldehyde acetal (BBA), which should react with general and specific acid catalysis, respectively (Scheme 2).[2-4]



$$\underset{\text{BTBA}}{\text{PhCH(OBu}^t)_2} \xrightarrow[H_2O]{HA} \text{PhCHO} + 2\text{Bu}^t\text{OH}$$

$$\underset{\text{BBA}}{\text{PhCH(OBu)}_2} \xrightarrow[H_2O]{H_3O^+} \text{PhCHO} + 2\text{BuOH}$$

Scheme 2

The reactions can be followed spectrophotometrically with dilute substrate and the substrates are sufficiently hydrophobic as to be extensively micellar-bound.

Results and discussion

Hydrolyses in water

Hydrolysis of BTBA is catalysed by succinate buffer and from the intercepts and slopes of plots of first-order rate constants, k_{obs}, against [succinate] at various pH values (Fig. 1, part *a*) we estimate second-order rate constants k_H and k_{HA} for the hydrogen ion and succinic acid, respectively. The ionic strength was 0.5 (NaCl).

For reaction of BTBA $k_H = 2000 \pm 110\ dm^3\ mol^{-1}\ s^{-1}$, in reasonable agreement with $k_H = 2950\ dm^3\ mol^{-1}\ s^{-1}$ determined by Anderson and Fife.[2] The difference is probably due to the higher ionic strength ($I = 1$) used in the latter work.[2] Our value of $k_{HA} = 0.20\ dm^3\ mol^{-1}\ s^{-1}$ was calculated from the slopes (insert in Fig. 1) by using 6.21×10^{-5} and 2.31×10^{-6} as the first and second dissociation constants, respectively, of succinic acid,[14] and it agrees reasonably well with the value of $k_{HA} = 0.234\ dm^3\ mol^{-1}\ s^{-1}$ by Anderson and Fife who used higher ionic strength.[2]

The first-order rate constant of acid hydrolysis of BBA [Fig. 1(*b*) and Table 1] is, as expected, buffer independent and

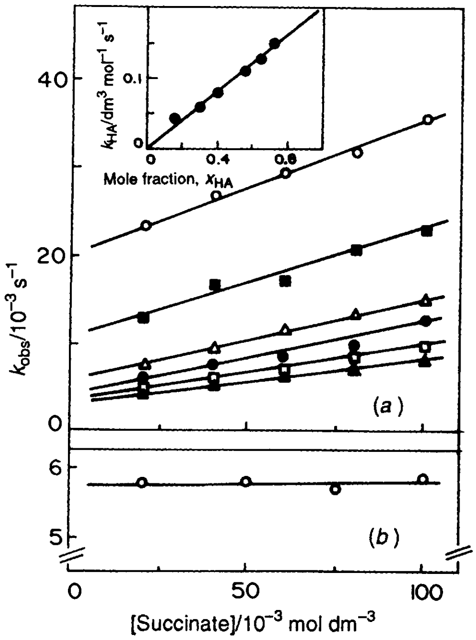


Fig. 1 Effect of succinate buffer concentration on rate constants for the hydrolyses of (*a*) BTBA, at 25.0 °C, (○) pH = 5.00, (■) pH = 5.30, (△) pH = 5.50, (●) pH = 5.80, (□) pH = 6.00, (▲) pH = 6.30 and (*b*) BBA at pH = 5.00. The insert shows the dependence of the second-order rate constant for the succinate buffer catalysed hydrolysis of BTBA on the mole fraction of hydrogen succinate ion.

Table 1 Dependence of k_{obs} on [H$^+$] for the hydrolysis of BBA[a]

$k_{obs}/10^{-3}$ s^{-1}	[H$^+$]/10^{-5} mol dm^{-3}
0.66	1.0
1.20	1.6
1.88	2.5
3.80	5.0
7.30	10

[a] At 25.0 °C in 0.02 mol dm^{-3} succinate buffer.

k_H = 73 dm^3 mol^{-1} s^{-1}, consistent with the value of k_H = 12 dm^3 mol^{-1} s^{-1} reported for benzaldehyde diethyl acetal in 50% dioxane–water at 30 °C.[3]

Reactions in anionic micelles of SDS

Hydrolyses were followed in 0.2 mol dm^{-3} succinate buffer, pH 6.0, over a range of [SDS]. Values of k_{obs} pass through maxima with increasing [surfactant], as is typical of ion–molecule reactions, and the rate–surfactant profiles for BTBA and BBA (Fig. 2) can be fitted by the widely-used pseudophase, ion-exchange, model. We assume that SDS does not perturb the overall acid dissociation of succinic acid because the species are hydrophilic and/or anionic and should be largely in the aqueous pseudophase. The first-order rate constant is given by eqn. (1),[5]

$$k_{obs} = \frac{[\mathrm{H_w}^+]\{(k_{2m}/V_M)K_S K_{H/Na}([\mathrm{Na_m}^+]/[\mathrm{Na_w}^+]) + k_{2w}\}}{1 + K_S[\mathrm{SDS_m}]} \quad (1)$$

where [H$_w^+$] is given by the pH of the bulk solution; k_{2m} and k_{2w} are second-order rate constants (dm^3 mol^{-1} s^{-1}) in the micellar and aqueous pseudophases, respectively; V_M is the molar volume of the interfacial reaction region; $K_{H/Na}$ is an ion exchange constant which describes competition between H$^+$ and Na$^+$ for the micelle and K_S is the binding constant of the substrate to the micelle in terms of micellized surfactant whose concentration is the total less that of monomer which is assumed to be given by the critical micelle concentration (cmc). The terms in square brackets are concentrations in terms of total solution volume. The transfer of H$^+$ and Na$^+$ between water and micelles depends upon the ion exchange constant, $K_{H/Na}$ = 1, and the fractional micellar ionization, α, as discussed in detail elsewhere.[5-10] We took α = 0.25 and V_M = 0.25 dm^3 mol^{-1} in agreement with earlier work[11] and other parameters were estimated by fitting the rate data to eqn. (1). The concentration of monomer given by the cmc was allowed to vary modestly with the hydrophobicity of the substrate, which is higher for BBA than for BTBA.

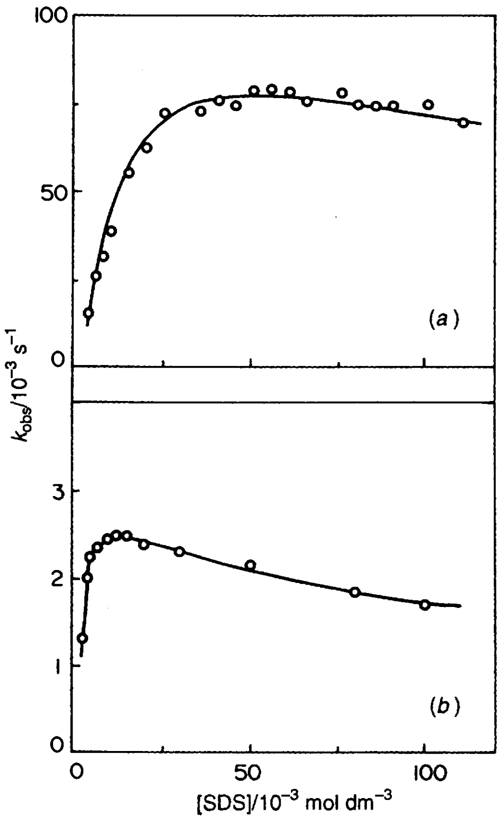


Fig. 2 Effect of increasing concentration of SDS on rate constants of hydrolyses of (*a*) BTBA and (*b*) BBA in 0.02 mol dm^{-3} succinate buffer, pH = 6.00, at 25.0 °C. The curves are predicted.

Table 2 Fitting parameters for reactions in SDS[a]

	BTBA	BBA
K_S/mol dm^{-3}	70	1650
k_{2m}/dm^3 mol^{-1} s^{-1}	1754	34
k_{2w}/dm^3 mol^{-1} s^{-1}	2000	73
cmc/mol dm^{-3}	0.003	0.0025

[a] At 25.0 °C, pH 6.0, succinate buffer 0.02 mol dm^{-3}, values of α = 0.25, V_M = 0.25 dm^3 mol^{-1}.

The fitting parameters for specific hydrogen ion catalysed reactions in SDS are given in Table 2 based on the plots in Fig. 2. The dependence of the forms of the plots on substrate hydrophobicity is general, and the rate maximum is more pronounced and appears at lower [SDS] for hydrolysis of BBA as compared with hydrolysis of the less hydrophobic substrate, BTBA.[5] Second-order rate constants in the micellar pseudophase, k_{2m} (Table 2) are slightly lower than values of k_{2w} in water. The binding constant, K_S, is, as expected, lower for BTBA than for BBA, consistent with results for other branched-chain compounds which are more water-soluble than their straight chain analogues. This difference in the hydrophobicity of branched and straight-chain compounds is often observed in micellar systems.[15] As described by Lissi *et al.*, the number of carbon atoms does not relate linearly with hydrophobicity and, in general, the hydrophobicity decreases as the degree of branching increases. As an example, the octanol/water partition coefficient of 2,2,3-trimethlylpentan-3-ol corresponds to that of an alkan-1-ol of *ca.* six carbon atoms.[15]

Mixed micelles of SDS and NaDeP

The two surfactants have different cmc values, largely because of differences in chain lengths (experimental) and it is necessary to consider the behaviour of the mixed system.[16,17] Eqn. (2),

$$\mathrm{cmc} = \frac{\mathrm{cmc_{SDS}cmc_{NaDeP}}}{x_{\mathrm{NaDeP}}\mathrm{cmc_{SDS}} + x_{\mathrm{SDS}}\mathrm{cmc_{NaDeP}}} \qquad (2)$$

where x_{SDS} and x_{NaDeP} are mole fractions, has been proposed for surfactants that follow ideal mixing, and fits the data very well, as shown in Fig. 3. This result is understandable because both surfactants have hydrophilic, monoanionic, head groups.

First-order rate constants, k_{obs}, were monitored as a function of x_{NaDeP} for 0.1 mol dm^{-3} total surfactant, SDS + NaDeP, in 0.02 mol dm^{-3} succinate buffer, pH 6.0 (Fig. 4). The results for hydrolysis of BBA are very simple because this reaction is specific hydrogen ion catalysed and the hydrogen ion concentration at the micelle–water interface is governed by the concentration in bulk solvent, water, the ion exchange constant $K_{\mathrm{H/Na}} = 1$ and $\alpha = 0.25$ for SDS and we expect these parameters to be very similar for the mixed micelles.[11,16]

Results are very different for hydrolysis of BTBA (Fig. 4), where k_{obs} increases linearly with x_{NaDeP} which is a general acid catalyst, and the extent of this catalysis depends on the concentration of general acid at the micelle–water interface, *i.e.* on x_{NaDeP}. This increase of k_{obs} is not due to an extensive transfer of BTBA from water into micelles. The binding constant $K_{\mathrm{S}} = 73$ dm^3 mol^{-1} in SDS (Table 2) so the substrate is *ca.* 85% micellar bound in 0.1 mol dm^{-3} surfactant, and the pH is such that there will be little hydrogen ion catalysed hydrolysis in the aqueous pseudophase. Inspection of Figs. 1 and 4 confirms that under these conditions there is very little reaction in the bulk solvent so the increase of k_{obs} with increasing x_{NaDeP} is due to the introduction of a new reaction path in the micellar pseudophase.

The independence of k_{obs} on x_{NaDeP} (Fig. 4) where BBA is very strongly micellar bound shows that the concentration of H_3O^+ in the micelle is independent of x_{NaDeP}.

The reaction of BTBA fits eqn. (3), where k_{m} is a second-order rate constant written with concentration as a mole fraction and $\mathrm{H_m^+}$ is the local molarity in the micellar pseudophase.

$$k_{\mathrm{obs}} = k_{\mathrm{m}}x_{\mathrm{NaDeP}} + k_{2\mathrm{m}}\mathrm{H_m^+} \qquad (3)$$

We can calculate a second-order rate constant for hydrolysis with general acid catalysis by NaDeP in terms of V_{M} [eqn. (4)],

$$k_{2\mathrm{m}} = k_{\mathrm{m}}V_{\mathrm{M}} \qquad (4)$$

and if $V_{\mathrm{M}} = 0.25$ dm^3 mol^{-1}, as assumed for SDS, $k_{2\mathrm{m}} = 0.19$ dm^3 mol^{-1} s^{-1}. This value is larger (but not markedly so) than the second-order rate constant of 0.029 dm^3 mol^{-1} s^{-1} for hydrolysis of BTBA catalysed by hydrogen phosphate ion in water,[16] especially given that the differences in strengths of these acids are difficult to evaluate since the acidity of decyl phosphate monoanion in micelles is not known. Indeed, it has been proposed that the pK_{a} of the phosphate head group must be higher for the surfactant molecule in the micelle than for the surfactant monomer because head group interactions disfavour dissociation of the head group of the surfactant.[12]

These comparisons of second-order rate constants in water and at micellar interfaces depend on the selected values of parameters such as V_{M} which are uncertain but not grossly wrong so it appears that second-order rate constants are not very different in water and at micellar interfaces for micellar-mediated specific and general acid catalysed hydrolyses. We do not expect rate constants to have exactly the same values except fortuitously, because bulk water and micellar interfaces have different properties as kinetic media.[5]

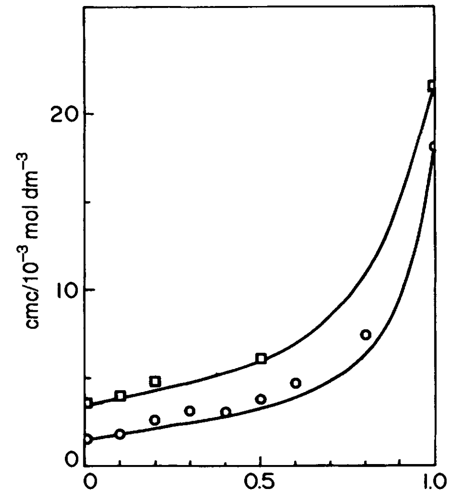


Fig. 3 Effect of increasing mole fraction of NaDeP on the critical micelle concentration of NaDeP/SDS mixtures, pH 6.00, at 25 °C, (□) 0.02 mol dm^{-3} and (○) 0.05 mol dm^{-3} succinate buffer. The curves are predicted.

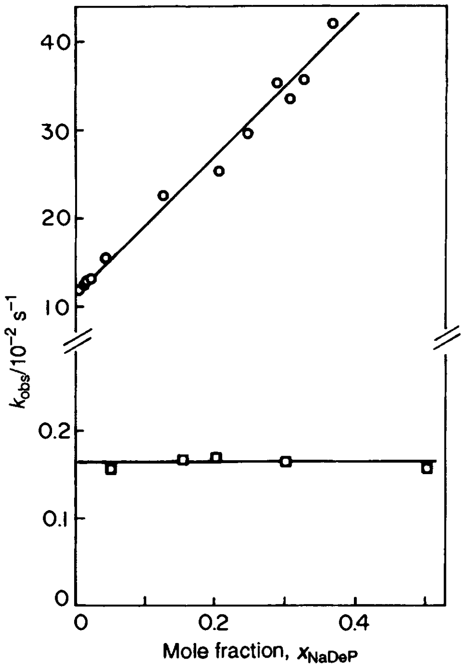


Fig. 4 Effect of increasing mole fraction of NaDeP at 0.1 mol dm^{-3} of [NaDeP] + [SDS] on rate constants in the micellar pseudophase of hydrolyses of (○) BTBA and (□) BBA in 0.02 mol dm^{-3} succinate buffer, pH = 6.00, at 25.0 °C

Reactivities in micellar pseudophases and general acid catalysis

The higher reactivity of BTBA over BBA in hydrogen ion catalysed hydrolyses is readily understandable because steric acceleration assists bond-breaking so that it is concerted with protonation rather than following it.[2,3]

The use of the functional surfactant NaDeP as the general acid in micelle-mediated hydrolyses avoids micellar perturbation of buffer equilibria and ensures that general acid catalysed hydrolysis makes a significant contribution to the overall reaction. The concentration of the general acid is high at the micellar surface and the molarity in the interfacial region is $x_{\mathrm{NaDeP}}/V_{\mathrm{M}}$, *i.e.* with $x_{\mathrm{NaDeP}} = 0.4$ and $V_{\mathrm{M}} = 0.25$ dm^3 mol^{-1} as used in the kinetic fitting, the local concentration of decyl hydrogen phosphate monoanion is *ca.* 1.6 mol dm^{-3}. The solvating power of water is probably lower in the micellar interfacial region than in bulk solvent,[18] which would also increase catalysis by the general acid.

Conclusions

Analogies between rate enhancements, micelles and enzymes have been noted. For example, large rate enhancements have been observed with some functional micelles and molecular weights of micelles and enzymes are similar.[19–21] However, the interfacial regions of normal micelles are very different from the active sites of enzymes as regards spatial control of interacting groups and exposure to water, which is limited in the hydrophobic pockets of enzymes. Acid or base catalysed enzymic reactions involve general acid or bases, rather than hydronium or hydroxide ions, and our systems crudely model this aspect of enzyme catalysis. However, exposure to water at the interface limits general acid catalysis in a normal micelle.

Our use of decyl hydrogenphosphate monoanion as an amphiphilic general acid allows us to quantify the extent of general acid catalysis of the hydrolysis of BTBA in a normal micelle. We therefore avoid ambiguities in studies of micellar effects on buffer catalysed hydrolysis due to effects on acid–base equilibria. In these systems quantification of general acid–base catalysis requires examination of transfer equilibria of the buffer species between aqueous and micellar pseudophases. So far as we know this quantitative treatment has not been applied to any general acid–base catalysed hydrolysis in normal micelles.

In our system mixtures of SDS and NaDeP act as functional comicelles and kinetic treatments are the same as those applied to nucleophilic functional micelles and comicelles.[5,22] They show that the pseudophase treatment can be applied quantitatively to acidic functional comicelles as well as to non-functional micelles.

Experimental

Materials

The substrates dibutyl and di-*tert*-butyl benzaldehyde acetal (BBA and BTBA, respectively) were prepared from substituted α,α-dichlorotoluene and the corresponding butoxide ion by the procedure of Cawley and Westheimer.[23] Benzaldehyde di-*tert*-butyl acetal (BTBA) had n_D^{25} 1.4756 (lit.,[2] n_D^{25} 1.4752). Sodium dodecyl sulfate, SDS (Sigma, 99%), was used without further purification. The surface tension–surfactant concentration profile showed no minimum and the critical micelle concentration agrees with that reported in the literature (cmc = 8.0×10^{-3} mol dm^{-3} at 25 °C).[24] Sodium decyl hydrogen phosphate (NaDeP) was prepared as previously described.[11–13] The cmc of the mixed surfactants were measured conductimetrically in 0.020 and 0.050 mol dm^{-3} succinate buffer, pH 6.00 (Fig. 3).

Methods

All pH measurements were carried out using a Beckman pH meter (model Φ-71) which was calibrated prior to use with standard buffers of pH = 4.00 and 7.00. Conductance measurements were carried out at 25 °C, in a water jacketed flow dilution cell, with an Analion bridge-type conductivity meter model C-701. Conductivity data were stored in a microcomputer by using a Microquimica 12 bit A/D board. Values of α were determined conductometrically from the ratio of slopes of plots of specific conductance against surfactant concentration, below and above the cmc.[25,26] The slopes of the plots described above were calculated by using a standard linear regression routine. Surface tension measurements were carried out by using a Microquimica Model MQ-ST1 Surface Tensiometer based on the drop weight method.

Kinetics

Reactions were followed in aqueous 0.02 mol dm^{-3} succinate buffer at 25.0 °C in the thermostatted cell compartment of a Hewlett-Packard HP-8452-A UV–VIS diode array spectrophotometer at 252 nm for BTBA and BBA. The substrate concentration was 4.0×10^{-5} mol dm^{-3} and substrates were added in dry acetonitrile; the kinetic solutions contained 0.4% acetonitrile. The observed first-order rate constant k_{obs} s^{-1}, calculated using HP-89532-K kinetic software, for overall kinetic curves, has standard deviations $< 10^{-5}$.

Acknowledgements

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