

# Reactions within association complexes: acid catalysed hydrolysis of substituted benzaldehyde acetals in the presence of detergents

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First order rate constants for decomposition of substituted benzaldehyde dimethyl acetals at constant pH in solutions of sodium dodecyl sulfate (SDS) and Aerosol AOT (AOT) maintained at constant  $[\text{Na}^+]$  are linear in surfactant concentration. When the only  $\text{Na}^+$  is that derived from the added SDS the kinetics exhibit a saturating rate law in SDS concentration. The present study shows that the curvature is not due to complexation of substrate but to ion exchange whereby increasing  $[\text{Na}^+]$  expels  $\text{H}^+$  from the Stern region where reaction of the substrate occurs. Increasing  $[\text{Na}^+]$  at constant [SDS] inhibits the SDS-catalysed acid hydrolysis of 4-isopropylbenzaldehyde dimethyl acetal and the dissociation constant of the  $\text{Na}^+$ -SDS micelle complex is 0.0281 M which agrees with values calculated from previous data using different reactions. The complex to SDS of a neutral analogue of the acetals exhibits a dissociation constant ( $K_i$ ) which is not significantly dependent on the overall concentration of  $\text{Na}^+$  ions in the range 0.07 to 0.42 M. Increasing concentrations of cetyltrimethylammonium bromide (CTAB; cetyl = hexadecyl) inhibit the acid catalysed hydrolysis; equilibrium constants ( $K_i$ ) for the dissociation of the CTAB-complexed acetals fit a Hansch plot and possess *no* contribution from Hammett's sigma.

## Introduction

Reactions which are catalysed by micelles are of interest in the study of artificial enzyme systems because the micelle has a size commensurate with that of many enzymes and complexation with the substrate is necessary for the catalytic function. The analogy with enzymes is only loose as the micelle has a fluxional structure and can complex more than one substrate molecule at large substrate concentrations altering the micellar structure substantially. Even though a catalytic micelle may possess the groups necessary for catalysis observed in an enzyme system it has no analogous structural integrity to enable the groups to perform at their optimum efficiency. Although micellar and enzymic catalysis have similar characteristics no micellar system has the specificity and catalytic advantage of an enzyme.<sup>1</sup> Artificial enzyme systems are composed of relatively large complex molecules, usually based on macrocycles, possessing their own characteristic kinetic properties which are different from those of enzymes.<sup>2</sup> Polar groups need to be attached to the artificial enzyme to solubilise it and these are often charged species. Aggregation phenomena and ion exchange are thus very likely complications in the development of an artificial enzyme; experience gained from the study of micellar catalysis is therefore apposite if an appraisal of the catalytic advantage of an artificial enzyme is to be made.

The catalysis of the hydrolysis of acetals under conditions of mild acid pH in the presence of sodium dodecyl sulfate (SDS) has been studied under conditions of varying  $\text{Na}^+$  concentration,<sup>3,4,6</sup> the influence of increasing SDS concentrations on the hydrolysis of acetals involves an initial increase up to about 3.6 mM [SDS] followed by a decrease at higher SDS concentrations. This was attributed to association of the acetal with the micellar particle and expulsion of  $\text{H}^+$  at higher  $\text{Na}^+$  concentrations. Substituent effect studies assumed the catalytic rate constant to be that of the optimal rate constant and that the data represented the hydrolysis of the fully complexed acetal.<sup>3-6</sup> We reinvestigated this system because of the possibility it appeared to offer for experimentally determining the dissociation constant of the acetal-micelle complex ( $K_s$ )

and the explicit determination of the catalytic component ( $k_{\text{cat}}$ ).

The specific acid catalysed hydrolysis of benzaldehyde dimethyl acetals at constant  $[\text{Na}^+]$  (by adding compensating quantities of NaCl) was measured in varying SDS concentrations to attempt to measure the dissociation constant of SDS-acetal complex ( $K_s$ ) but the kinetics exhibited only linear plots up to 0.2 M in [SDS]. The linear data indicate that substantial complexation of acetal to SDS is not occurring at the concentrations employed. The Hammett  $\rho$  values of the previous work are called into question because of the use of arbitrary concentrations of SDS to determine  $k_{\text{cat}}$ . The saturation phenomenon needs reinvestigation under conditions of constant ionic atmosphere in the Stern layer so that the substituent effects could be appraised satisfactorily. Knowledge of the substituent dependence of  $K_s$  and  $k_{\text{cat}}$  would enable us to determine the source of the kinetic advantage of the micellar catalysis.

## Experimental

### Materials

Sodium dodecyl sulfate (SDS) was obtained from BDH, cetyltrimethylammonium bromide (CTAB) from Sigma and Aerosol AOT (AOT) from Lancaster Synthesis.

The substituted benzaldehyde dimethyl acetals were prepared by mixing trimethyl orthoformate (10 mL), methanol and substituted benzaldehyde in equimolar proportions. A single drop of concentrated HCl was added whereupon the mixture became warm. The product solution was allowed to stand overnight at room temperature and neutralised with solid  $\text{K}_2\text{CO}_3$ . The mixture was then diluted with petroleum ether (bp 40–60°), filtered and evaporated *in vacuo*. The resultant oil was taken up in more petroleum ether (bp 40–60°), filtered to remove any remaining solid and evaporated *in vacuo*. The oil was distilled *in vacuo* and then stored over solid  $\text{K}_2\text{CO}_3$ . Boiling point ranges are recorded in Table 1 and those for the known acetals agree with the literature values. 2-Chlorophenyl acetate was donated by Dr A. B. Maude.

**Table 1** Acid-catalysed hydrolysis of substituted benzaldehyde dimethyl acetals in the presence of increasing concentrations of SDS and constant  $[\text{Na}^+]$

Substituent	$k_{\text{H}}/\text{M}^{-1}\text{s}^{-1}$	$k_{\text{SDS}}/\text{M}^{-2}\text{s}^{-1}$	$\Delta k_{\text{obs}} \times 10^3/\text{s}^{-1}$	$\Delta\text{pH}^m$	$\lambda/\text{nm}^n$	$N^k$	bp/°C ( $\tau/\text{mmHg}$ )	Lit. bp/°C ( $\tau/\text{mmHg}$ )
3-CH <sub>3</sub> O	22.4 ± 0.2	726 ± 54	4.15–27.6	3.80–3.54	254	6	74–78(0.70) <sup>g,i</sup>	96.5–114.0(1.0) <sup>a</sup>
4-CH <sub>3</sub> O	900 ± 9	8.71 ± 0.54, 10 <sup>4</sup>	26–97.9	5.25–5.06	283	6	78–80(0.35)	194–196(760) <sup>b</sup>
H	61.1 ± 0.6	797 ± 52	1.41–6.46	4.36–4.68	246	6	84–86(23)	106(15) <sup>c</sup>
2-Cl	2.79 ± 0.06	9.36 ± 0.27	3.83–5.6	2.77–2.96	252	12	113–115(23)	125.5–126.0(35) <sup>a</sup>
4-Cl	15.8 ± 0.1	316 ± 22	0.547–2.01	4.61–4.39	246	10	110–112(23)	121.0–121.5(1.0) <sup>a</sup>
3-NO <sub>2</sub>	0.181 ± 0.003	1.40 ± 0.09	0.16–0.37	3.01–2.68	250	7	100–103(0.35)	124.0–124.5(35) <sup>a</sup>
3-Cl	3.42 ± 0.08	23.0 ± 1.3	4.71–13.6	2.9–2.72	250	6	111–113(23)	294.0–296.0(774) <sup>c</sup>
4-NO <sub>2</sub>	0.118 ± 0.01	0.797 ± 0.04	0.0804–0.223	3.04–2.68	265	7	90–92(0.35)	210(760) <sup>d</sup>
4-CN	0.315 ± 0.02	1.23 ± 0.10	0.43–0.696	2.9–2.74	260	6	95–99(0.75) <sup>h,i</sup>	113.5–114.0(35) <sup>a</sup>
4-Isopropyl	149 ± 2	9910 ± 165	12.9–118	5.27–5.04	270	6	100–102(23)	
4-CH <sub>3</sub>	178 ± 7	11000 ± 802	1.53–12.9	5.27–5.05	270	6	105–108(23)	

<sup>a</sup> R. L. Huang and H. K. Lee, *J. Chem. Soc.*, 1963, 5963. <sup>b</sup> R. L. Huang and H. K. Lee, *J. Chem. Soc.*, 1963, 5957. <sup>c</sup> Beilstein's *Handbuch der Organische Chemie*, Hauptband, Springer Verlag, Berlin, 1925, Vol. 7, p. 258. <sup>d</sup> C. Morel, *Soap. Perfum. Cosmet.*, 1954, 27, 279. <sup>e</sup> W. Kanteleiner, H.-D. Gutbrod and P. Gross, *Liebigs Ann. Chem.*, 1979, 522. <sup>f</sup> [SDS] 0–0.2 M, total  $[\text{Na}^+] = 0.21\text{ M}$  (made up with NaCl) (the lowest concentration of SDS was 0.01 M), 25 °C. Buffers are chloroacetate up to pH 3.54 and acetate up to 5.06. Dimethyl acetal concentrations range from  $5 \times 10^{-3}$  to  $10^{-3}\text{ M}$ . <sup>g</sup> Found: C, 65.4; H, 7.7%;  $\text{C}_{10}\text{H}_{14}\text{O}_3$  requires: C, 65.9; H, 7.7%. <sup>h</sup> <sup>1</sup>H-NMR  $\delta$  3.33 (s, 6H), 5.44 (s, 1H), 7.62 (dd, 4H). <sup>i</sup> Found: C, 68.1; H, 6.3; N, 7.8%.  $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2$  requires: C, 67.8; H, 6.3; N, 7.9%. <sup>1</sup>H-NMR  $\delta$  3.31 (s, 6H), 3.78 (s, 3H), 5.34 (s, 1H), 6.82–7.29 (m, 4H). <sup>j</sup> The relatively poor carbon analyses of these acetals is due to the difficulty inherent in the protocol for elemental analysis of liquids. The <sup>1</sup>H-NMR spectra exhibited no extraneous peaks. <sup>k</sup> In order to avoid assumptions about aggregation numbers of the micelles the concentration units of the rate and equilibrium constants ( $k_{\text{surface}}, K_{\text{f}}$  and  $K_{\text{s}}$ ) are expressed in terms of monomer surfactant rather than in terms of the molarity of the micelle species. <sup>l</sup> Number of data points not including duplicates. <sup>m</sup> Range of observed rate constants. <sup>n</sup> Wavelengths for kinetics. <sup>o</sup> Wavelengths for kinetic studies.

All solutions for kinetics were prepared with water double distilled from glass and degassed. Buffer materials and salts to maintain cation or anion concentrations were either of A.R. grade or purified before use.

## Methods

A series of buffered solutions for studies of rates at different SDS concentrations (0–0.2 M) were prepared by dilution of a stock solution containing the SDS (0.2 M) and buffer (0.01 M) with a diluent solution of NaCl (0.2 M, identical in respect of pH, ionic strength and buffer identity and concentration) but without SDS. Dilution of the stock SDS with the diluent altered the pH slightly due to differential absorption of buffer species into the micelles. Experiments with CTAB at varying concentrations were carried out using stock CTAB and diluent so that the total Br<sup>-</sup> (and buffer anion) concentrations were invariant.

Buffered solutions of AOT required the addition of acetonitrile in order to prepare solutions with a reasonably high AOT concentration. The protocol for mixing was as for the SDS solutions except that 30% acetonitrile–water (v/v) was required as solvent and a maximum [AOT] of only 0.1 M was attainable before the onset of cloudiness.

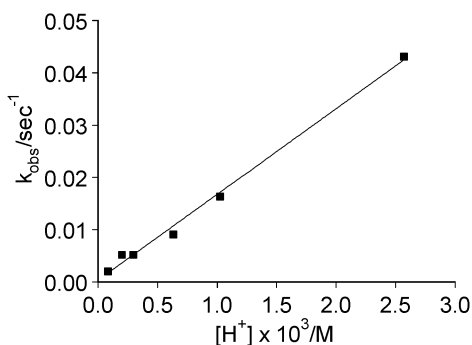
Reactions were initiated by the addition of an aliquot (0.01 to 0.05 mL) of a solution of the benzaldehyde acetal (in acetonitrile) to 2.5 mL of buffered solution, contained in a 1 cm path-length silica cuvette in the thermostatted cell compartment of a Pye Unicam SP 8-200 Uv/visible spectrophotometer. The pH of the solution was measured before and after each kinetic run using a Radiometer PHM62 pH-meter with a Russell CMAWL combined electrode, calibrated with BDH buffers. Wavelengths for studying the kinetics of the reactions were determined initially by repetitively scanning the spectrum during a reaction and are recorded in Table 1. The reactions were followed kinetically by measuring the absorbance ( $A_t$ ) at the optimal wavelength as a function of time. Kinetics of the reaction between 2-chlorophenyl acetate and imidazole were determined as previously described.<sup>7</sup>

Pseudo-first order rate constants were obtained by fitting the value of  $A_t$  (which increases with time in these cases) to the equation  $A_t = A_{\infty} - (A_{\infty} - A_0)\exp(-kt)$ . Data were fit to theoretical equations by use of standard software. In the case of the more weakly reactive 4-nitrobenzaldehyde dimethyl acetal the rate constants were obtained from initial rates ( $-dA_t/dt$ ) by division by the final absorption change measured at lower pH where the reaction is fast. <sup>1</sup>H-NMR spectra were determined using CDCl<sub>3</sub> solvent and a 270 MHz spectrometer.

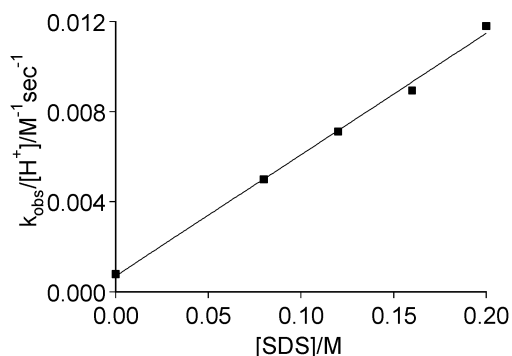
## Results

Repetitive scanning of the ultra-violet absorption spectrum of the reacting solutions and comparison of the final spectra with those of the corresponding aldehydes show that all the acetals hydrolysed in aqueous solutions of micelles to yield aldehyde as product in stoichiometric yield. The scanning spectra exhibit sharp isosbestic wavelengths consistent with a 1 : 1 reaction with any intermediate present in very low concentration compared with that of reactants and products. The reactions, followed at constant wavelength (Table 1), exhibit excellent pseudo first order kinetics up to at least 90% of the total progress of the reaction. The pseudo first order rate constants were measured as a function of pH at constant [SDS] and constant  $[\text{Na}^+]$  and shown to be proportional to the hydrogen ion concentration (Fig. 1) in the case of the parent acetal. It is assumed that this proportionality holds for all the substrates.

The rate constants increase with increasing [SDS]. Depending on the buffer in use the pH varied showing a slight increase from [SDS] = 0 M to [SDS] = 0.2 M. The effect of the increase is



**Fig. 1** Plot of  $k_{\text{obs}}$  versus  $[\text{H}^+]$  at constant  $[\text{SDS}]$  (0.04 M) for benzaldehyde dimethyl acetal at 25 °C (total  $[\text{Na}^+] = 0.06$  M); line is theoretical from eqn. (1) and parameters in Table 1.



**Fig. 2** Plot of  $k_{\text{obs}}/[\text{H}^+]$  versus  $[\text{SDS}]$  for 4-isopropylbenzaldehyde dimethyl acetal at 25 °C; line is theoretical from eqn. (1) and parameters in Table 1.

corrected by division of  $k_{\text{obs}}$  by  $[\text{H}^+]$  and the resulting second order rate constants are linearly dependent on  $[\text{SDS}]$  in the concentration range employed (Fig. 2 and eqn. (1)).

$$k_{\text{obs}}/[\text{H}^+] = k_{\text{H}} + k_{\text{surfactant}}[\text{surfactant}] \quad (1)$$

The intercept at  $[\text{SDS}] = 0$  M is the second order rate constant for acid-catalysed hydrolysis in the absence of micelle ( $k_{\text{H}}$ ). The parameter  $k_{\text{surfactant}}$  for SDS ( $k_{\text{SDS}}$ ) is a third order rate constant which measures the micelle-catalysed acid reaction. The parameters are recorded in Table 1.

It is necessary to determine the effect of change in  $\text{Na}^+$  ion concentration on the dissociation constant of the complex between acetal and SDS micelle. Because  $K_{\text{S}}$  cannot be determined explicitly for the acetals (the rate law is linear in  $[\text{SDS}]$  over the range studied) it was decided to employ 2-chlorophenyl acetate as an analogue and the dissociation constant for this ester is available from studies on its reaction with imidazole in the presence of increasing concentrations of SDS.<sup>7</sup> The binding of a neutral substrate, 2-chlorophenyl acetate, to SDS micelles was studied by measuring the rate constants for reaction of the ester with imidazole in the presence of increasing amounts of SDS for a range of total  $[\text{Na}^+]$  values as described previously.<sup>7</sup> The data are analysed according to eqn. (2) where  $k_{\text{imidazole}}$  is the second order rate constant for reaction of neutral imidazole with ester in the absence of surfactant; the values of  $K_{\text{I}}$  are  $8.79 \pm 1.50$  mM (0.07 M  $[\text{Na}^+]$ ),  $6.90 \pm 0.29$  mM (0.22 M  $[\text{Na}^+]$ ) and  $6.67 \pm 0.34$  mM (0.42 M  $[\text{Na}^+]$ ).

$$k_{\text{obs}}/[\text{imidazole}] = k_{\text{imidazole}}K_{\text{I}}/(K_{\text{I}} + [\text{SDS}]) \quad (2)$$

The rate constants for acetal hydrolysis ( $k_{\text{obs}}/[\text{H}^+]$ ) are lower than those previously determined for SDS<sup>4</sup> because the relatively large  $\text{Na}^+$  counterion concentration exchanges for the  $\text{H}^+$  in the micellar Stern layer thus reducing its overall catalytic

advantage. The hydrolysis of 4-isopropylbenzaldehyde dimethyl acetal was carried out in buffer at constant  $[\text{SDS}]$  and increasing total  $[\text{Na}^+]$ . The hydrolysis was inhibited by the addition of  $\text{Na}^+$  and a dissociation constant of  $0.0281 \pm 0.003$  M was estimated for the complex of  $\text{Na}^+$  with SDS by fitting the data to eqn. (3).

$$k_{\text{obs}}/[\text{H}^+] = k_{\text{o}}K_{\text{exch.}}/(K_{\text{exch.}} + [\text{Na}^+]) \quad (3)$$

Similar values may be calculated from previous data for the effect of added  $\text{Na}^+$  on the SDS catalysed hydrolysis of methyl orthobenzoate.<sup>6</sup> The rate constants for acid catalysed hydrolysis of acetals follow a rate law derived from Romsted's pseudo phase theory when there is no cation compensation.<sup>4,8</sup>

Acid-catalysed acetal hydrolysis is inhibited in the presence of increasing concentrations of CTAB because the micelle does not exchange  $\text{H}^+$  into its Stern layer. The second order rate constants obtained from  $k_{\text{obs}}/[\text{H}^+]$  decrease with increasing  $[\text{CTAB}]$  according to eqn. (4).

$$k_{\text{obs}}/[\text{H}^+] = k_{\text{H}}K_{\text{I}}/(K_{\text{I}} + [\text{CTAB}]) \quad (4)$$

The kinetic parameters are recorded in Table 2.

We attempted to find a catalytic system where the complexation constant ( $K_{\text{S}}$ ) as well as the catalytic constant ( $k_{\text{cat}}$ ) could be measured independently unlike that of the SDS system. This proved not to be possible with the materials available.<sup>9</sup> The low solubility of Aerosol AOT in aqueous solution required the use of 30% acetonitrile–water compositions to obtain kinetically useful concentrations. Plots of  $k_{\text{obs}}/[\text{H}^+]$  versus  $[\text{AOT}]$  exhibit a catalytic advantage and obey eqn. (1) in the concentration range between 0 M and 0.1 M (Table 3). Other micelle-forming anionic surfactants such as those with phosphate head groups could exhibit complexation within the concentration range available before aggregation but these systems were not investigated. The main problem is that aggregation of the micelles is likely to occur unless the head group is very polar; the sulfate group studied here is probably the best candidate to keep the micelle in solution up to tenth molar concentrations of the surfactant molecules. We chose to employ CTAB as an analogue of SDS and investigate its dissociation constant ( $K_{\text{I}}$ ) from inhibition studies.

Studies of acid-catalysed aromatic ketal hydrolysis and addition reactions at benzaldehyde derivatives in the absence of detergents have indicated that a Yukawa–Tsunno-type equation correlates the data better than the Hammett equation; this is due to the development of resonance between aromatic substituent and the reaction centre.<sup>10,11</sup> The parameters of Table 1 fit Young's modified Yukawa–Tsunno equation<sup>11</sup> ( $\log k = \rho\sigma + \rho^+(\sigma^+ - \sigma) + \log k^\circ$ , eqns. (5) and (6)) and the  $K_{\text{I}}$  parameters of Table 2 fit the Hansch equation as follows (eqn. (7)); values of  $\sigma$  and  $\sigma^+$  employed in the correlations are from Hansch and Leo<sup>12</sup> and Leffler and Grunwald.<sup>13</sup> ( $k_{\text{SDS}}^\circ$  and  $k_{\text{H}}^\circ$  are rate constants for the unsubstituted benzaldehyde acetal.) The deviations in the Hansch plot are due to the relatively large discrepancy between the micelle-binding equilibrium and the reference system for  $\pi$ ,<sup>14</sup> the transport of a substituted phenyl species between water and *n*-octanol. The fit to the Hansch equation is not particularly good in common with other Hansch relationships.<sup>15</sup>

$$\log k_{\text{H}} = -3.30 \pm 0.03\sigma - 0.69 \pm 0.32(\sigma^+ - \sigma) + \log k_{\text{H}}^\circ \quad (r = 0.9971) \quad (5)$$

$$\log k_{\text{SDS}} = -4.21 \pm 0.17\sigma - 1.62 \pm 0.41(\sigma^+ - \sigma) + \log k_{\text{SDS}}^\circ \quad (r = 0.9972) \quad (6)$$

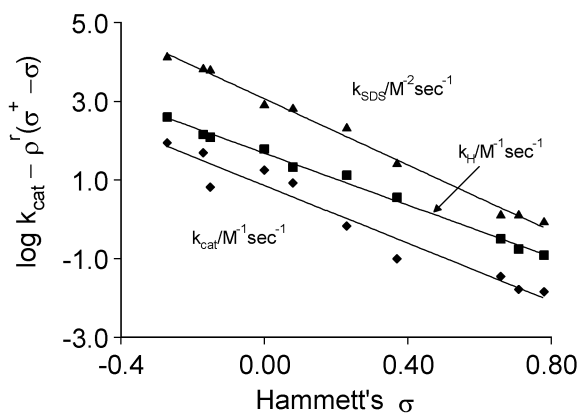
$$\log K_{\text{I}} = -0.702 \pm 0.072\pi - 1.742 \pm 0.048 \quad (r = 0.9553) \quad (7)$$

**Table 2** Acid-catalysed hydrolysis of substituted benzaldehyde dimethyl acetals in the presence of increasing concentrations of CTAB and constant  $[\text{Br}^-]^a$

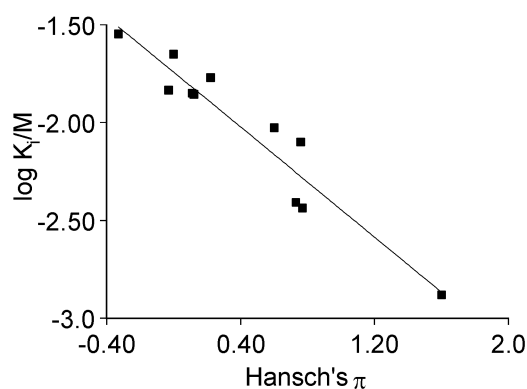
Substituent	$K_i/\text{mM}^c$	$\Delta k_{\text{obs}} \times 10^3/\text{s}^{-1d}$	$\Delta\text{pH}^e$	$N^f$	$k_{\text{SDS}}K_i/\text{M}^{-1}\text{s}^{-1b} \equiv k_{\text{cat}}$
3-CH <sub>3</sub> O	13.9 ± 0.27	30.3–8.52	2.87–2.77	5	10.1
4-CH <sub>3</sub> O	14.6 ± 0.413	5.05–1.63	5.25–5.09	5	1270
H	22.4 ± 0.8	1.58–0.61	4.43–4.51	4	17.9
2-Cl	7.95 ± 0.54	3.58–0.81	2.89–2.65	5	0.0744
4-Cl	3.91 ± 0.11	19.4–2.23	2.91–2.74	5	1.24
3-NO <sub>2</sub>	14.1 ± 0.81	0.357–0.104	2.89–2.73	6	0.0197
3-Cl	3.66 ± 0.35	4.31–0.584	2.9–2.72	5	0.0842
4-NO <sub>2</sub>	17 ± 4.5	0.0598–0.0172	2.89–2.73	6	0.0135
4-CN	28.4 ± 6	0.407–0.201	2.89–2.70	4	0.0349
4-Isopropyl	1.32 ± 0.16	5.82–0.42	4.41–4.28	5	13.1
4-CH <sub>3</sub>	9.41 ± 1.1	6.03–1.23	4.47–4.18	5	104

<sup>a</sup> [CTAB] = 0.01–0.05 M, total  $[\text{Br}^-]$  = 0.05 M (made up with KBr), 25 °C. Buffers are chloroacetate up to pH 2.73 and acetate up to 5.09. Acetal concentrations as in Table 1 footnote *f*. <sup>b</sup> This value is proportional to  $k_{\text{cat}}$  (see eqn. 13). <sup>c</sup> See footnote *j* of Table 1. <sup>d</sup> Range of observed rate constants. <sup>e</sup> Range of pH values for kinetics. <sup>f</sup> Number of data points not including duplicates.

Figs. 3 and 4 illustrate the free energy relationships of the parameters. The corresponding Yukawa–Tsuno–Young coefficients for  $k_{\text{H}}$  in the AOT system are:  $\rho^r = -1.18 \pm 0.54$ ,  $\rho = -2.71 \pm 0.54$ ,  $\log k_{\text{H}}^\circ = 0.926 \pm 0.097$  ( $r = 0.9804$ ) and for  $k_{\text{AOT}}$ :  $\rho^r = -0.86 \pm 0.46$ ,  $\rho = -3.14 \pm 0.47$ ,  $\log k_{\text{AOT}}^\circ = 1.93 \pm 0.08$  ( $r = 0.9866$ ).



**Fig. 3** Yukawa–Tsuno–Young dependence of  $k_{\text{SDS}}$ ,  $k_{\text{H}}$  and  $k_{\text{cat}}$ . Data are from Table 1 and lines are theoretical from eqns. (5), (6) and (14).



**Fig. 4** Hansch dependence of  $K_i$ . Line is theoretical from eqn. (7); data are from Table 2.

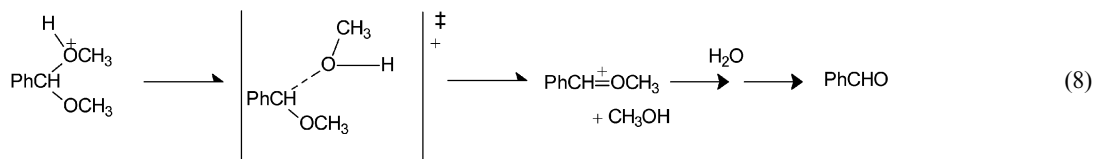
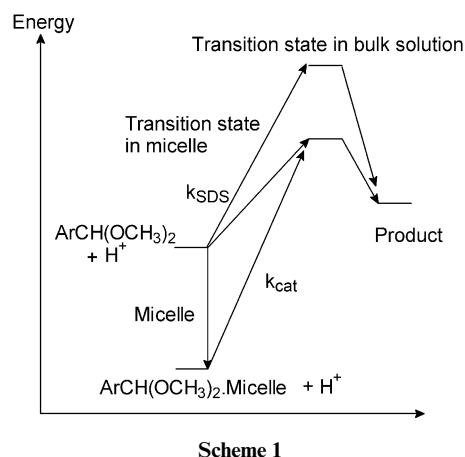
Fits of the parameters  $k_{\text{H}}$ ,  $k_{\text{SDS}}$  and  $k_{\text{AOT}}$  to regular Hammett equations have poorer correlation coefficients than those from the Yukawa–Tsuno–Young equation.

The values of  $k_{\text{H}}$  and the  $\rho$  coefficient are similar to those obtained by Fife,<sup>16</sup> Cordes,<sup>5</sup> Jensen<sup>17</sup> and Young<sup>10</sup> in aqueous and water–organic solvent mixtures.

## Discussion

It is commonly accepted that the specific acid-catalysed hydrolysis of benzaldehyde acetals in aqueous solution involves rate limiting formation of the oxocarbenium ion (eqn. (8)) and subsequent fast degradation to hemi-acetal, benzaldehyde hydrate and finally benzaldehyde (eqn. (9)). The lifetime of the oxocarbenium ion ( $\text{PhCHOCH}_3^+$ ) has been estimated to have a half life of  $3.5 \times 10^{-9}$  s in water.<sup>18</sup> In the presence of nucleophiles more reactive than water the oxocarbenium ion is diverted away from the hemi-acetal intermediate. Existence of a concerted displacement by the nucleophile depends on the lifetime of the oxocarbenium ion in the presence of the nucleophile and inverting glycosidases involve acylal intermediates formed by nucleophilic attack from a neighbouring carboxylate anion.<sup>19</sup>

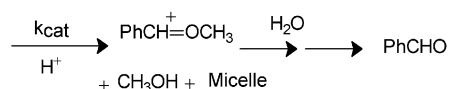
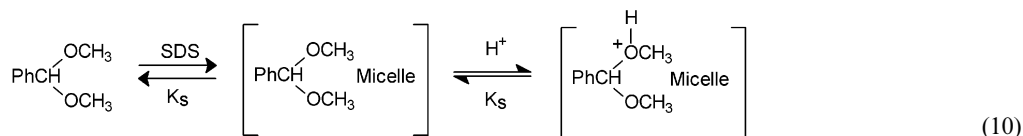
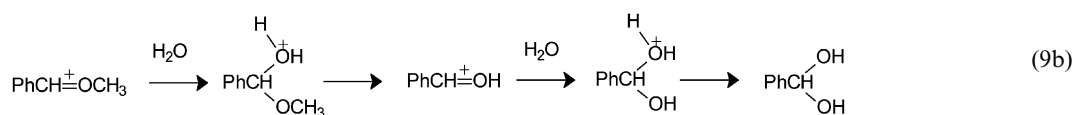
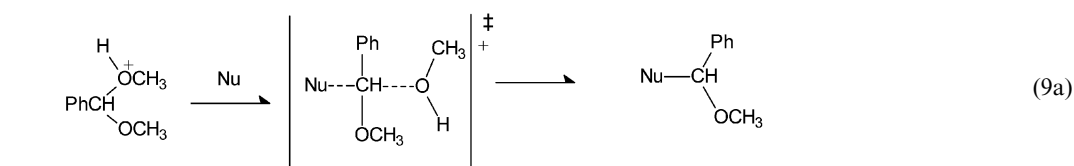
Hydrolysis may be accelerated by complexing the acetal in the Stern region of a micelle bearing anionic groups possibly by stabilisation of the protonated acetal (Scheme 1 and eqn. (10)). The substrate will be located so that only the acetal function



**Table 3** Acid-catalysed hydrolysis of substituted benzaldehyde dimethyl acetals in the presence of increasing concentrations of AOT and constant  $[\text{Na}^+]$ <sup>a</sup>

Substituent	$k_{\text{AOT}}/\text{M}^{-2} \text{s}^{-1b}$	$k_{\text{H}}/\text{M}^{-1} \text{s}^{-1}$	$10^3 \cdot \Delta k_{\text{obs}}/\text{s}^{-1c}$	$\lambda/\text{nm}^d$	$\Delta\text{pH}^e$
3-CH <sub>3</sub> O	52.8	3.29	2.9–5.7	254	2.76–3.43
4-CH <sub>3</sub> O	1510	184	73–140	283	3.12–3.65
Parent	61.5	13.5	2.3–6.6	256	3.31–3.90
4-Cl	21.8	3.02	0.67–1.7	246	3.25–3.82
4-CH <sub>3</sub>	595	29.2	10.3–15	256	3.29–3.87
4-(CH <sub>3</sub> ) <sub>2</sub> CH	271	33.1	6.1–20	270	3.21–3.93

<sup>a</sup> [AOT] 0–0.1 M, total  $[\text{Na}^+] = 0.11 \text{ M}$  (made up with NaCl) (lowest concentration of AOT was 0.02 M), 25 °C. Buffer is chloroacetate. Acetal concentrations as in footnote *f* of Table 1. <sup>b</sup> See footnote *j* of Table 1. <sup>c</sup> Range of observed rate constants. <sup>d</sup> Wavelengths for kinetic studies. <sup>e</sup> Range of pH values for kinetics.



resides in the Stern region; the fact that catalysis occurs rather than inhibition indicates that the substrate is not wholly immersed in the hydrophobic core of the micelle (although its aromatic component resides in this region).

The linearity of the dependence of  $k_{\text{obs}}/[\text{H}^+]$  on SDS concentration precludes the explicit kinetic determination of  $K_{\text{S}}$  values for the acetal/SDS and acetal/AOT systems and experiments with other anionic micelles (SHDS and STDS)<sup>9</sup> as models have encountered solubility problems when concentration dependencies have been attempted. Values of  $K_{\text{i}}$  are easily obtained for the CTAB system because they fall within the solubility range of this surfactant. CTAB partitions the acetal from aqueous solution (eqn. (11)) in this system but does not exchange protons thus inhibiting hydrolytic attack by the bulk solution of protons.



CTAB has a longer aliphatic chain than SDS and its critical micelle concentration occurs at a lower value (0.92 mM)<sup>1</sup> compared with that of SDS (8.1 mM)<sup>1</sup> indicating that CTAB should have a greater propensity to complex hydrophobic species than SDS. The effect of substituents on the value of  $K_{\text{i}}$  for binding of benzaldehyde dimethyl acetals to CTAB is therefore a reasonable measure of the effect of their complexation with SDS. Previous work indicates that the dissociation constants for complexes of aryl acetates to SDS and to CTAB both fit Hansch equations and  $K_{\text{i}}$  for SDS and CTAB are proportional to each other for these substrates. If we assume for the acetal hydrolysis system that  $K_{\text{S}}$  for SDS is proportional to  $K_{\text{i}}$  for CTAB (eqn. (12)) then we can determine  $k_{\text{cat}}$  from  $k_{\text{SDS}}$  (eqn. (13)).

$$K_{\text{S}} = aK_{\text{i}} \quad (12)$$

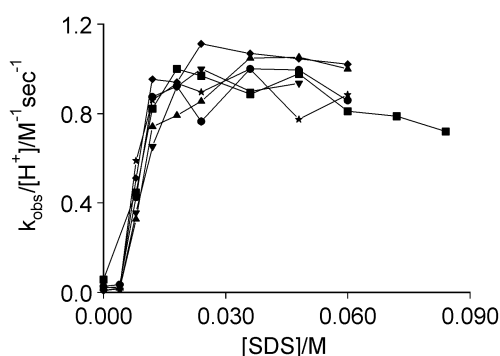
$$\log k_{\text{cat}} = \log k_{\text{SDS}} + \log K_{\text{i}} + \log a \quad (13)$$

Table 2 collects the data for  $k_{\text{cat}}$  ( $\equiv k_{\text{SDS}} \cdot K_{\text{i}}$ ) determined when  $a$  is defined arbitrarily set to unity and the resultant  $k_{\text{cat}}$  fits a Yukawa–Tsuno–Young equation (14) ( $\log k_{\text{cat}}^{\circ} = 0.861 \pm 0.21 + \log a$ ). The absolute magnitude of  $k_{\text{cat}}$  is not known but its variation as a function of  $\sigma$  is independent of the value of  $a$ .

$$\log k_{\text{cat}} = -3.68 \pm 0.42\sigma - 2.28 \pm 1.0(\sigma^+ - \sigma) + \log k_{\text{cat}}^{\circ} \quad (r = 0.9807) \quad (14)$$

The corresponding parameters for the AOT-catalysed hydrolysis for  $k_{\text{cat}}$  are:  $\rho^{\sigma} = -1.34 \pm 1.50$ ,  $\rho = -3.12 \pm 1.50$ ,  $\log k_{\text{cat}}^{\circ} = 0.0051 \pm 0.27 + \log a$  ( $r = 0.8986$ ).

Perusal of the data for the acid hydrolysis of benzaldehyde diethyl acetals in micellar solutions where the counter anion is not maintained at a constant concentration or ionic strength indicates that there is no simple relationship between reactivity ( $k_{\text{obs}}/[\text{H}^+]$ ) and surfactant concentration.<sup>5</sup> A normalised plot of  $k_{\text{obs}}/[\text{H}^+]$  (normalised on the maximal rate in each case) has approximately the same shape for each substrate and the maximal rate constant occurs at approximately the same value of [SDS] (Fig. 5). The complexation to SDS micelles of small neutral substrates analogous to the acetals (such as phenyl acetates) is markedly affected by the substituent and the dissociation constant ( $K_{\text{S}}$ ) for a range of substituents obeys a Hansch relationship.<sup>7</sup> Values of  $K_{\text{S}}$  for phenyl acetates with SDS and CTAB<sup>7</sup> vary over approximately 2 powers of 10. The rate-concentration curves for acid-catalysed hydrolysis of



**Fig. 5** Plots of  $k_{\text{obs}}/[\text{H}^+]$  (normalised on the maximal rate constant) versus  $[\text{SDS}]$  for non-compensated counterions. Data from Dunlap, Ghanim and Cordes.<sup>5</sup> ■, 4-NO<sub>2</sub> (2.25); ●, 4-Cl (5.36); ▲, 4-F (4.76); ▼, H (5.36); ★, 4-CH<sub>3</sub> (6.4); ◆, 4-OCH<sub>3</sub> (6.4). The cmc is not quoted in Cordes' paper for the experiments on SDS catalysed hydrolysis of acetals.

acetals in SDS should exhibit maxima at SDS concentrations with a wide range of values if the curvature were due to substrate complexation. It is therefore likely that the curvature previously observed in the SDS<sup>5</sup> case is due to an ion exchange effect of increasing  $[\text{Na}^+]$  and expelling proton from the Stern region rather than due to complexation although complex formation will certainly be occurring (but not to saturation). A change in cmc caused by change in ionic strength will also cause non-linearity.

The small spread of  $K_i$  values determined for an analogous neutral substrate (2-chlorophenyl acetate) with SDS over the  $[\text{Na}^+]$  range 0.07 to 0.42 M indicates that the structure of the SDS micellar interface would not have much effect on the binding of the neutral acetals. The values of  $K_{\text{exch}}$  for the exchange of  $\text{Na}^+$  with the SDS micelle calculated from the literature and that determined from the hydrolysis of the 4-isopropylbenzaldehyde dimethyl acetal (0.0281 M) are consistent with the curvature of Fig. 5 being due to ion exchange rather than substrate complexation.

The present data indicate that when the ionic atmosphere is maintained constant the fit is to a *linear* equation up to 0.2 M SDS in all the cases shown. This fact does not mean that complexation is absent or is not important in the catalytic sequence of reactions. It merely indicates that the complex between substrate and micelle possesses a much larger dissociation constant than can be determined at the concentrations of SDS available in the experiments (without detergent precipitation). The lower limit of the value of the dissociation constant of the complexed acetal is 0.2 M, the maximum concentration of SDS employed in the experiments.

The relative reactivity of complexed and free benzaldehyde dimethyl acetals cannot be measured absolutely because the value of  $a$  in eqn. (12) is unknown. However, a lower limit can be determined for  $k_{\text{cat}}$  from the maximum concentration of SDS employed because  $K_S > [\text{SDS}]_{\text{max}}$ . Let us consider the parent acetal where  $k_{\text{SDS}} = 797 \text{ M}^{-2} \text{ s}^{-1}$ . The lower limit on  $k_{\text{cat}}$  is  $0.2 \times 797 \text{ M}^{-1} \text{ s}^{-1} = 159 \text{ M}^{-1} \text{ s}^{-1}$  which compares with the value  $61.1 \text{ M}^{-1} \text{ s}^{-1}$  for  $k_{\text{H}}$ . The reaction of  $\text{H}^+$  with complexed acetal is therefore  $>159/61$  more efficient than with uncomplexed substrate. It is possible to speculate on an *upper* limit of the

catalytic advantage of the SDS micelle in acetal hydrolysis. The  $K_S$  value is unlikely to be greater than 1 M (although this concentration would be unobtainable for SDS) so that an estimate of the *upper limit* of the catalytic advantage of the micelle is only  $(797 \times 1)/61 \sim 13$ -fold.

Comparison of the  $\rho$  parameter for  $k_{\text{cat}}$  with that of  $k_{\text{H}}$  ( $-3.68$  and  $-3.30$  respectively) indicates that the reaction of complexed acetal with  $\text{H}^+$  is slightly more sensitive to substituent than is that of the free acetal; this indicates that positive charge development in the complexed acetal is slightly greater than in the free acetal in the transition state for reaction with the proton.

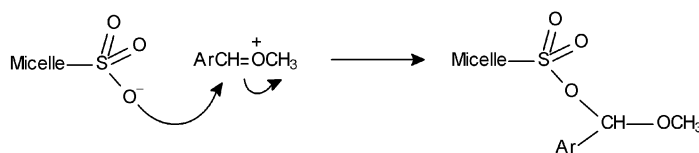
The kinetic parameter,  $k_{\text{cat}}$ , registers the free energy difference between complexed acetal and the transition state including the proton (Scheme 1). The equilibrium constant for the protonation of complexed acetal is included in  $k_{\text{cat}}$  but its measurement cannot be effected for the present results. Nevertheless, the data indicate that there is no *significant* electronic difference between complexed acetal and free acetal for the binding to CTAB because there is no Hammett dependence of  $K_i$  (eqn. (7)).

If the oxocarbenium ion were formed as an intermediate at the surface of the micelle it is possible that even the weakly nucleophilic  $-\text{SO}_3^-$  head group would react to form the sulfonylal (Scheme 2). There are no data for the reactivity of a sulfonylal ( $\text{RSO}_2-\text{O}-\text{CH}(\text{OR}')\text{Ar}$ )<sup>20</sup> but if it were formed in this system it would have to decay rapidly to aldehyde because the product UV spectrum indicates that only aldehyde is formed and gives no evidence for a stoichiometric amount of intermediate. It is not possible to distinguish the stepwise process from the one where the  $-\text{SO}_3^-$  group displaces methanol from the protonated acetal in a concerted pathway (similar to that of eqn. (9a)).

The method involved in dissection of  $k_{\text{SDS}}$  into its component  $k_{\text{cat}}$  and  $K_S$  parameters introduces uncertainty additional to that of  $k_{\text{SDS}}$  because the relationship between  $K_i$  and  $K_S$  involves non-systematic deviations caused by the different surfactant systems. These uncertainties are reflected in the magnitudes of the standard deviations for  $\rho$  and  $\rho^+$  in both SDS and AOT cases. The value of  $\rho$  for  $k_{\text{cat}}$  is more negative than that of  $k_{\text{H}}$  but the difference is within the confidence limits of both measurements and little emphasis can be placed on the differences regarding the relative charges in the transition states. The existence of only a small catalytic advantage in the surfactant-catalysed reaction is consistent with this conclusion. The relative values of  $\rho^+$  appear to indicate that there is a larger resonance contribution in the transition state for the surfactant catalysed reactions but the confidence limits on the measurements indicate that it would be unsafe to conjecture on their significance at this stage.

## Conclusions

The saturation curve obtained in studies of the acid catalysed hydrolyses of acetals in the presence of increasing concentrations of SDS without  $\text{Na}^+$  counterion compensation is due to ion exchange by  $\text{Na}^+$  depleting the proton concentration within the micelle and is not due to a complexation effect with the substrate. Values of the dissociation constants,  $K_S$ , cannot therefore be determined explicitly for this system. The difference in  $\rho$  and  $\rho^+$  between acid catalysed hydrolysis of free acetal and complexed acetal indicates that there is a marginally greater



**Scheme 2**

positive effective charge in the transition state in the micellar catalysed reaction.

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