Reactivity in Reverse Micelles: Acid-catalysed Hydrolysis of *para*-Substituted Benzaldehyde Diethyl Acetals

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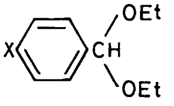
Acid-catalysed hydrolysis for a series of *para*-substituted benzaldehyde diethyl acetals in the presence of reverse micelles prepared from water, heptane, and bis-(2-ethylhexyl) sodium sulphosuccinate (AOT) have been studied. The measured rate constants, k_{obs}, are not proportional to the catalyst concentration $[H_3O^+]$; each substituted benzaldehyde diethyl acetal yields a plot of k_{obs} *versus* $[H_3O^+]$ which exhibits a sharp break. Above and below this break, the variation is roughly linear; this seems to indicate two domains of proton activity. In the two proton concentration ranges, we have determined the Hammett ρ constant of the reaction ($\rho = -2.46$ at weak proton concentrations; $\rho = -2.59$ at high proton concentrations). Comparison of our results with ρ-values determined in homogenous media leads to the conclusion that the reaction occurs in the very polar environment of the interface where the positively charged transition state of the reaction is stabilized by the sulphonate head-groups of the surfactant.

Several surfactants form micelles in organic solvents in the presence of water; reverse micelles are formed with an inner core of water surrounded by the surfactant monolayer. Among such compounds, bis-(2-ethylhexyl) sodium sulphosuccinate (AOT) is the only one that allows the formation of 'water pools', the size of which is sufficient to allow hydrophilic compounds to dissolve. The physicochemical properties of reverse micelles have been investigated extensively during recent years.[1–6] Reverse micelles can be viewed as the best models of the active sites of enzymes,[7] as chemical micro-reactors, which may lead to new methods in organic synthesis,[8] as new devices for photochemical solar energy conversion,[6] and finally as carriers of drugs.[9] We are interested in the use of reverse micelles as a reaction medium. The surface of the interface separating the two phases can reach values as high as 5×10^4 m^2 per litre of micellar solution;[10] thus these mediums offer a possible alternative to the phase-transfer catalysis procedure for reactions where the reagent and the substrate are hydrophilic and lipophilic, respectively.

Knowledge of the properties of these mediums provides insights into the mechanisms of chemical processes in reverse micelles. It is particularly important to know where the reaction actually takes place—whether in the inner water core, the continuous organic phase, or at the interface? In an attempt to answer this question, we have undertaken the study of acid-catalysed hydrolysis of a series of *para*-substituted benzaldehyde diethyl acetals in reverse micellar medium prepared from AOT in heptane; the aqueous phase containing the catalyst (HCl) at different concentrations.

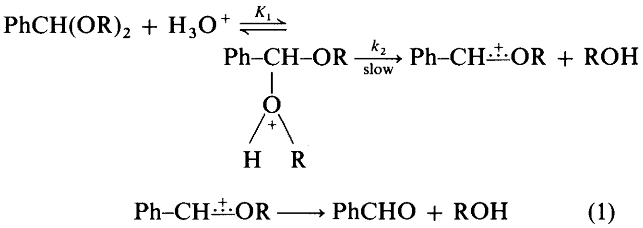


X = H, Cl, CN, Me, OMe

Determination of the Hammett ρ constant permits us to evaluate more precisely the nature of the reaction site. Indeed, the Hammett ρ constant can be considered as a measure of the variation in electronic density at the reaction site of the substrate between the ground state and the transition state; it is known that the ρ-value is sensitive to the polarity of the medium.[11]

Results and Discussion

For the hydrolysis of acetals in homogeneous medium the mechanism commonly proposed is an A_1 mechanism corresponding to a specific acid catalysis[12,13] represented by equation (1).



$$PhCH(OR)_2 + H_3O^+ \overset{K_1}{\rightleftharpoons} Ph\text{-}\underset{\substack{|\\ \overset{+}{O}\\ H\quad R}}{CH}\text{-}OR \xrightarrow[slow]{k_2} Ph\text{-}CH\overset{+}{\cdots}OR + ROH$$

$$Ph\text{-}CH\overset{+}{\cdots}OR \longrightarrow PhCHO + ROH \qquad (1)$$

In this mechanism, the proton is completely transferred before the limiting step; under these conditions the rate can be represented by equation (2) where H_3O^+ is the catalyst; its

$$v = k_2K_1[\text{Acetal}][H_3O^+] \qquad (2)$$

concentrations remains constant so that the rate constant can be expressed by the relationship (3).

$$v = k_{obs}[\text{Acetal}] \text{ with } k_{obs} = k_2K_1[H_3O^+] \qquad (3)$$

The reaction is first-order and the plot of k_{obs} *versus* $[H_3O^+]$ is a straight line with zero intercept. The hydrolysis reaction of the substituted benzaldehyde diethyl acetals in micellar medium was followed by monitoring the formation of the corresponding benzaldehyde with respect to time by u.v. spectrophotometry. The hydrolysis rate was determined within a proton concentration range from 10^{-3}—50×10^{-3}M in the aqueous phase; the k_{obs} values are given in Table 1.

As expected, the hydrolysis reaction is first-order but, in contrast with the homogeneous medium, the rate constants measured in the presence of reverse micelles are not proportional to the catalyst concentration (H_3O^+) in the aqueous phase. A sharp break at low proton concentration is observed for all substituted benzaldehydes as exemplified by *p*-methoxybenzaldehyde diethyl acetal (Figure 1). On either side of the break the variation appears to be linear. It seems that above a given concentration, the catalyst exhibits greater activity. We have determined the value of the Hammett ρ constant at two concentrations of catalyst ($[H_3O^+] = 10^{-2}$M, and 2.5×10^{-2}M

Table 1. Rate constants (k_{obs}) for the hydrolysis of p-$XC_6H_4CH(OEt)_2$ in the presence of AOT reversed micelles at 25 °C[a]

	$10^4k_{obs}/s^{-1}$				
$10^3[H_3O^+]$/M	X = OMe	X = Me	X = H	X = Cl	X = CN
1.00	3.88	0.160	—	—	—
5.00	6.96	0.350	—	—	—
10.00	20.3	0.890	0.21	0.040	0.0058
15.00	38.1	3.04	0.30	0.126	0.0078
20.00	53.5	11.5	1.18	0.703	0.016
22.5	110.0	—	—	—	—
24.0	232.0	—	—	—	—
25.0	801.0	27.6	7.51	1.40	0.058
32.5	—	70.8	15.5	3.80	0.24
40.0	—	137.0	24.0	6.10	0.53
50.0	—	187.0	36.0	9.60	0.96

[a] [AOT] = 0.1M; ω = $[H_2O]/[AOT]$ = 40.

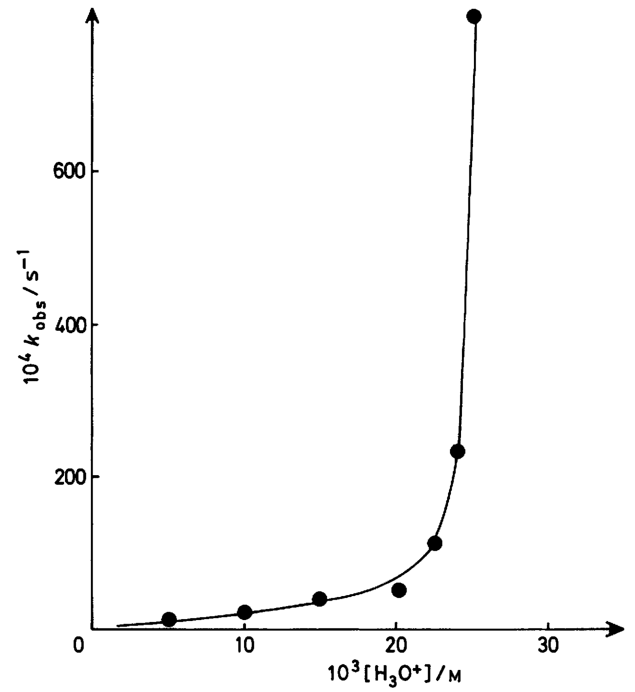


Figure 1. Observed rate constants as a function of $[H_3O^+]$ for hydrolysis of p-$MeOC_6H_4CH(OEt)_2$ in the presence of AOT reverse micelles in heptane at 25 °C

respectively). The corresponding graphs are shown in Figure 2. We have used σ^+ values for the plots since these are appropriate when conjugation exists between a substituent and a positive charge at the reaction site,[14] here exemplified by the proximity of the carboxonium ion in the transition state. The two ρ-values (−2.46 and −2.59) are close to each other, and this result seems to indicate that for both proton concentrations, the reaction mechanism remains the same and consequently, the break observed in the plot k_{obs} *versus* $[H_3O^+]$ cannot be explained by a change in mechanism. It is interesting to compare these ρ-values with those already determined by Jensen[13] for the hydrolysis of benzaldehyde diethyl acetals in homogeneous medium in different solvents (Table 2).

As we can see, the value of the Hammett ρ constant is dependent upon the solvent polarity; the more polar the solvent, the less the absolute value of the ρ constant. The absolute ρ-value may be used as a criterion to appreciate the importance in charge variation at the substrate reaction site.[15] Theoretical proof of the use of Hammett ρ constants has been provided by Henri-Rousseau.[16] From Table 2 it is clear that in all reaction mediums the ρ-value is negative. A negative ρ-value is consistent with a decrease in electronic density at the reaction site and our results confirm the carboxonium ion as intermediate. A decrease in the absolute ρ-value when the polarity of the medium increases is, furthermore, in agreement with an enhanced stabilization of the transition state by the more polar solvents. For the reverse micelles, the absolute ρ-value observed is weaker than that found in water.

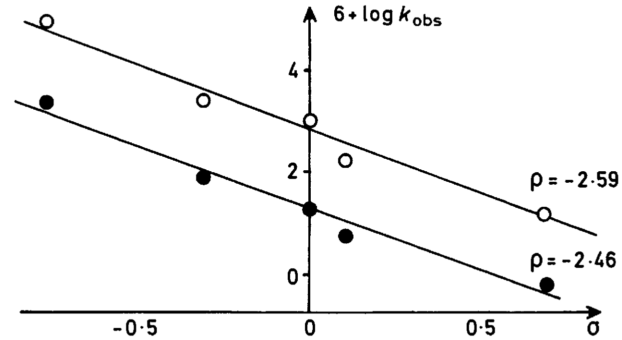


Figure 2. Hammett relationship. Variation of k_{obs} as a function of σ^+ for hydrolysis of p-$XC_6H_4CH(OEt)_2$; ○, $[H_3O^+]$ = 0.025M; ●, $[H_3O^+]$ = 0.01M

This result indicates that the hydrolysis reaction occurs in a micro-environment more polar than water. We believe this constitutes a good argument in favour of the reaction taking place near the surfactant head-groups; the surfactant sulphonate groups are able to stabilize the positively charged transition state (Figure 3). Furthermore, we have shown[17] that the hydrolysis of enantiomeric pairs of activated amino acid esters takes place in the mesophase structure, formed by the surfactant monolayer surrounding the aqueous core. In fact, using a chiral AOT analogue, we have prepared chiral reverse micelles and observed that the membrane is enantioselective with respect to the enantiomeric pair of amino acid esters. This led us to believe that the reaction occurred in a chiral micro-environment in the immediate vicinity of the micellar membrane.

We have reported that the rate constant is not proportional to the acid concentration and a sharp break is observed. This unexpected behaviour has been reported by El Seoud[18] in the hydration reaction of 1,3-dichloroacetone catalysed either by imidazole or H_3O^+ in the presence of AOT reverse micelles. In each case, this author has observed a break in the graph k_{obs} *versus* catalyst concentration. It seems that, above a given catalyst concentration, there is a sudden increase in the catalytic activity of the hydronium ion or imidazole.

On the basis of ^1H n.m.r. spectroscopy El Seoud[18] assigned these breaks to interactions between hydronium ions or imidazole and surfactant sulphonate groups close to the interface. However, Menger *et al.*[19] failed to detect any breaks in the hydrolysis of p-nitrophenyl ecetate catalysed by imidazole in presence of AOT reverse micelles.

Further studies are necessary in order to explain these contradictory results; work is currently under way in our laboratory.

Experimental

Acetal Synthesis.—Acetals were obtained from the corresponding benzaldehydes by using the procedure described by Fife.[20]

Table 2. Hammett ρ constants for hydrolysis of *para*-substituted benzaldehyde diethyl acetals in homogeneous medium in different solvents

Solvent	ρ
H_2O–dioxane (50:50)	−3.58
H_2O–dioxane (80:20)	−3.35
H_2O	−3.16
AOT–H_2O–heptane	−2.50

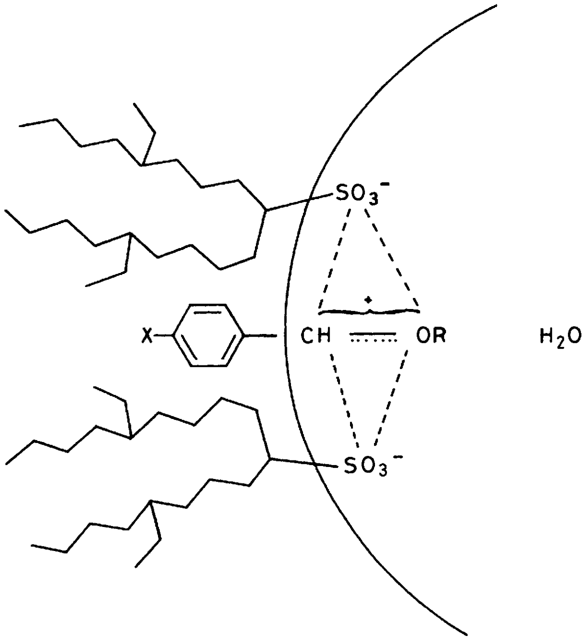


Figure 3. Stabilization of the transition state by sulphonate head groups

Kinetic Studies.—AOT in n-heptane (0.2M; 5 ml) was mixed with aqueous catalyst (HCl) in a 10 ml volumetric flask such that the ω ratio was 40 (ω = $[H_2O]/[AOT]$). The solution was diluted to the mark with n-heptane. A stoppered 10mm cuvette was filled with AOT–H_2O–n-heptane (2 ml) and acetal (2 μl) in n-heptane. The solution was stirred and the cuvette placed in the thermostatted cell holder (25 ± 0.1 °C) of a Gilford 250 spectrophotometer. Hydrolysis of the acetals was followed by monitoring the appearance of corresponding benzaldehydes at a suitable wavelength (X = H, 277.5 nm; X = Cl, 245.7 nm; X = CN, 287.5 nm; X = Me, 247.5 nm; X = OMe, 265 nm). First-order plots were linear to greater than 80% of the reaction. The observed rate constants (k_{obs}) were evaluated from the absorbance–time data using a least-squares computing method. For slow kinetics, we have used the method of initial rates, *i.e.* increasing the initial acetal concentration by a factor of ten. Each rate is the mean of at least three independent determinations differing by 3%.

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