Micellar Catalysis of Proton Transfer Reactions. 1. Hydrolysis of Covalent Arylsulfonylmethyl Perchlorates in the Presence of CTABr. Catalysis by Sulfinate, Formate, and Hydroxide Ions, and the Effect of Mechanical Agitation

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Abstract. The general-base-catalyzed hydrolysis of *p*-tosylmethyl perchlorate (**1**) is strongly accelerated by cationic micelles of CTABr (40 times at 2×10^{-3} M CTABr and 4.7×10^{-5} M **1**), slightly by nonionic micelles of Igepal CO-850 (2 times), and is retarded slightly by anionic micelles of NaLS (1.3 times). The acceleration in the presence of CTABr is mainly due to a dramatic increase in the rate contributions of *p*-toluenesulfinate and formate ions (reaction products) as well as that of hydroxide ions. The water-catalyzed reaction shows a modest acceleration by CTABr micelles (12 times in 2.0×10^{-3} M CTABr + 0.1 M HCl). Remarkably, the rates of hydrolysis of **1** and of *p*-nitrophenylsulfonylmethyl nitrate (**2**) in CTABr solutions increase upon stirring. We tentatively suggest that this effect is due to catalysis by hemimicelles.

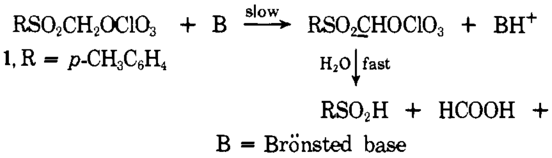
During the last decades many model systems have been designed to simulate chemical interactions relevant for enzymic catalysis. Among these studies, catalysis by micelles has significantly contributed to our insight in the importance of microenvironmental and proximity effects.[1-5]

Several similarities have been recognized between micellar catalysis and enzymic catalysis and between micellar surfaces and lipid-protein interfaces, and consequently, micellar-catalyzed reactions may serve as models for electrostatic and hydrophobic interactions in biological systems.[6]

Although various types of micellar-catalyzed reactions have been investigated, little is known about the kinetic effects of micelles on proton-transfer reactions,[7] which play such an important role in enzymic catalysis.[8]

We have initiated a program aimed at the elucidation of micellar effects on simple proton-transfer reactions involving small solutes as the substrates. In the present investigation we have studied the effect of micelles on the hydrolysis of tosylmethyl perchlorate (**1**). Previous studies have shown that this reaction is a general-base-catalyzed process.[9] The neutral hydrolysis of **1** in water involves a rate-determining deprotonation at the α-sulfonyl carbon atom by water, as indicated by the primary kinetic deuterium isotope effect $k_{\mathrm{CH_2}}/k_{\mathrm{CD_2}} = 5.6$, the solvent deuterium isotope effect $k_{\mathrm{H_2O}}/k_{\mathrm{D_2O}} = 1.6$, and the absence of H-D exchange in the substrate in D_2O solution (Scheme I).[9a,c]

Scheme I



$$\begin{array}{l} \mathrm{RSO_2CH_2OClO_3} + \mathrm{B} \xrightarrow{\text{slow}} \mathrm{RSO_2\underset{-}{C}HOClO_3} + \mathrm{BH^+} \\ \mathbf{1}, \mathrm{R} = p\text{-}\mathrm{CH_3C_6H_4} \qquad \downarrow \mathrm{H_2O}\ \text{fast} \\ \qquad \mathrm{RSO_2H} + \mathrm{HCOOH} + \mathrm{ClO_3^-} \\ \qquad \mathrm{B} = \text{Brönsted base} \end{array}$$

Recently the hydrolysis of covalent arylsulfonylmethyl perchlorates has been successfully used as a probe for the dynamic basicity of aqueous and mixed aqueous solutions (B = H_2O).[9a,c,10,11] Furthermore, electrolyte effects on the hydrolysis of **1** have been rationalized mainly in terms of electrostatic ion-water interactions affecting the dynamic basicity of water.[12]

Most reactions in which a water molecule is bound in the transition state of the rate-determining step (either as a base or as a nucleophile) seem to be little affected or are retarded by micelles.[13-15] These results have usually been explained in terms of the lower activity of water at the micellar surface. With this in mind it was deemed especially worthwhile to examine whether or not micelles affect the rate of the proton-transfer reaction from **1** to water. On one hand the availability of water at the micellar surface will be lower than in bulk water, but on the other hand the dynamic basicity of water at the micellar surface could be larger[12] and, moreover, the acidity of the substrate incorporated by the micelles could be enhanced appreciably.[16] The results of our study reveal that the rate of the pH-independent hydrolysis of **1** is enhanced by cationic micelles of CTABr. In addition, kinetic complexities not observed for hydrolysis in bulk solution have provided further insight into the micellar-catalyzed process.

Experimental Section

Materials. The preparations of tosylmethyl perchlorate (**1**) and *p*-nitrophenylsulfonylmethyl nitrate (**2**) have been described.[9] Hexadecyltrimethylammonium bromide (CTABr; Merck, p.a. quality) was purified by the method of Duynstee and Grunwald.[14] Sodium lauryl sulfate (Kochlight) and polyoxyethylene(20)nonylphenol (Igepal CO-850, General Aniline and Film Corp.) were used without further purification. The water was demineralized and distilled twice in an all quartz distillation unit. Deuterium oxide (99.75% D_2O; Merck, Uvasol quality) was used without purification. 1,4-Dioxane was filtered before use through active, neutral alumina in a nitrogen atmosphere.

Product Analysis. The UV spectrum after complete hydrolysis of **1** in 2.0×10^{-3} M CTABr was identical with that of *p*-toluenesulfinic acid. The formation of formic acid was easily ascertained in 0.05 M CTABr in D_2O by observation of the characteristic chemical shift of the formyl proton.[11]

Kinetic Measurements. The rate of hydrolysis of tosylmethyl perchlorate (**1**) and *p*-nitrophenylsulfonylmethyl nitrate (**2**) were measured by monitoring the change in the absorption at 235 and 245 nm, respectively. Pseudo-first-order kinetics were found for at least 3 half-lives. All reactions were performed in 2-cm quartz cells which were placed in the thermostated (±0.05 °C) cell compartment (equipped with a magnetic stirring device) of a Zeiss PMQ II spectrophotometer. About 5-20 μl of a concentrated solution of **1** in pure dioxane was added to the aqueous solution in the cuvette (10-12 ml) by means of a syringe under vigorous stirring. The conversions were followed to greater than 87% completion and infinity points were taken after approximately 10 half-lives.

Most rate measurements were performed at an initial pH of 5.5-5.7. During the reaction the pH decreased to ca. 4.0 for 4.7×10^{-5} M **1**. In the case of NaLS solutions, a drop of dilute hydrochloric acid was added to attain an initial pH of ca. 5.

Table I. Hydrolysis of **1** in the Presence of NaLS, Igepal CO-850, and CTABr at 25.0 °C

Surfactant, M	$k_{obsd} \times 10^5$, s^{-1}
	60.5
2.7×10^{-3} NaLS[a]	62.9
1.1×10^{-2} NaLS	47.0
1.6×10^{-4} Igepal[b]	69.3
8.4×10^{-4} Igepal	119
2.1×10^{-3} CTABr[c]	2420

[a] Cmc: 8.1×10^{-3} M. [b] Cmc: $(1.35–1.75) \times 10^{-4}$ M.[1a] [c] [**1**] = 4.7×10^{-5} M.

Table II. Activation Parameters for the Hydrolysis of **1** in Aqueous Solutions Containing CTABr or Igepal CO-850 at 25.0 °C

Medium	[**1**], M	$k_{obsd} \times 10^4$, s^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
H_2O[9]		6.05	19.1 ± 0.4	-9 ± 1
1.2×10^{-4} M CTABr		8.25	16.8 ± 0.4	-16 ± 1
2.1×10^{-3} M CTABr	4.7×10^{-5}	231	14.7 ± 0.4	-17 ± 1
2.1×10^{-3} M CTABr	9.4×10^{-5}	311	12.7 ± 0.4	-23 ± 1
1.0×10^{-2} M CTABr	4.7×10^{-5}	187	14.1 ± 0.4	-19 ± 1
1.0×10^{-2} M CTABr	9.4×10^{-5}	215	13.9 ± 0.4	-20 ± 1
8.4×10^{-4} M Igepal		11.2	15.7 ± 0.4	-19 ± 1
2.0×10^{-3} M CTABr + 0.1 M HCl		82	12.0 ± 0.4	-28 ± 1

Activation parameters were calculated from k_{obsd} values at at least four different temperatures in the range 25–45 °C.

Conductivity measurements were carried out with a Philips PW 9501 conductivity meter. For light scattering experiments a Cenco-TNO light scattering meter was used.

Results and Discussion

Kinetic Effect of Detergents. The hydrolysis of tosylmethyl perchlorate (**1**) is catalyzed strongly by cationic micelles of CTABr. The maximum catalysis is ca. 40 times at 2×10^{-3} M CTABr and a total substrate concentration of 4.7×10^{-5} M for **1** (vide infra). Igepal CO-850 induced only a small increase in rate (Table I). The small retarding effect of NaLS micelles is expected on electrostatic grounds for an anionic surfactant.[1-5]

The activation parameters for the uncatalyzed and CTABr and Igepal catalyzed reactions are given in Table II. The rate increase in the case of CTABr micelles is the result of a decrease in $\Delta H^{\ddagger}$, which is only partly compensated by a decrease in $\Delta S^{\ddagger}$.

As it will be shown below, the rate of hydrolysis of **1** in micellar solutions of CTABr is dependent on the total substrate concentration and involves important contributions of sulfinate, formate, and hydroxide ion as active Brönsted bases. Therefore the activation parameters in micellar solutions of CTABr are composites for at least four processes and consequently any detailed interpretation is precarious. However, the smaller $\Delta H^{\ddagger}$ observed in 2.0×10^{-3} M CTABr compared to the $\Delta H^{\ddagger}$ for the water-catalyzed reaction, as well as the smooth decrease of $\Delta H^{\ddagger}$ for the CTABr-catalyzed hydrolysis upon increasing substrate concentration are expected because the anions involved in the micellar-catalyzed process are all stronger bases than water.

Remarkably, we observed an even larger decrease of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in a solution of 0.1 N HCl and 1.0×10^{-3} M CTABr, where the contributions of these anions are negligible and the water reaction is predominantly involved in the hydrolytic process.[17] In this case the decrease in $\Delta H^{\ddagger}$ is explicable in terms of (i) an electrostatic stabilization of the partly negatively charged transition state,[1-5] or (ii) by an increase in the dynamic basicity of water at the micellar surface.[12]

The large decrease of $\Delta S^{\ddagger}$ (unstirred reaction) at a CTABr concentration (1.2×10^{-4} M) below the cmc (7.8-9.2×10^{-4} M)[1a,18] probably indicates that there is already substantial association of the substrate to either the detergent or small premicellar aggregates. Apparently this association has little effect on the rate. The same result is found for hydrolysis in the presence of 8.4×10^{-4} M Igepal (cmc: 1.35-1.75×10^{-4} M).[1a]

Furthermore, we note that interpretation of the activation parameters will be obscured by an unknown temperature effect on the association of **1** with the detergent. We feel, however, that this effect makes no dominant contribution to the observed changes in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, since *opposite* changes in the activation parameters have been observed for other reactions catalyzed by CTABr.[19]

Kinetics in the Presence of CTABr. A plot of the pseudo-first-order rate constant (k_{obsd}) for the hydrolysis of **1** vs. concentration of CTABr shows the characteristic pattern of a micellar-catalyzed reaction (Figure 1),[2] and is reminiscent of that for Michaelis-Menten kinetics. At low detergent concentration the rate is little affected, but close to the cmc (7.8-9.2×10^{-4} M)[1a,18] the rate rises sharply to a maximum value and then slowly decreases with increasing CTABr concentration.

Before engaging in an interpretation of the observed micellar catalysis, we first decided to affirm that no change in mechanism had occurred in the presence of the micellar aggregates. We therefore established the presence of sulfinic acid and formic acid as products of hydrolysis (see Experimental Section) and determined the primary kinetic and the solvent deuterium isotope effect of the CTABr-catalyzed reaction. The kinetic isotope effect in 2.6×10^{-3} M CTABr solution was $k_{CH_2}/k_{CD_2} = 5.3$ (at 4.7×10^{-5} M **1**), indicating that deprotonation is still the slow step in the micellar-catalyzed hydrolysis. Only the solvent isotope effect shows appreciable deviation from that of the reaction in the absence of CTABr ($k_{H_2O}/k_{D_2O} = 1.6$). We find $k_{H_2O}/k_{D_2O} = 0.9$ at 2.1×10^{-3} M CTABr, and 1.1 at 5.2×10^{-4} M CTABr for 4.7×10^{-5} M **1**. It should be noted, however, that D_2O lowers the cmc relative to that in H_2O, which will render k_{H_2O}/k_{D_2O} values determined in the vicinity of the cmc too low.[20,21]

Surprisingly, the magnitude of the catalysis by CTABr was found to increase with increasing concentration of **1** (Figures 1 and 2). In contrast, a dependence of the rate of hydrolysis on the total substrate concentration was not observed for the hydrolysis in water, in 0.05–0.8 M aqueous n-Bu_4NBr[10,12,22] or in aqueous solutions containing Igepal or NaLS. The results shown in Figures 1 and 2 for concentrations of **1** larger than 4.7×10^{-5} M were obtained by performing several subsequent hydrolysis experiments after each other in the same solutions. Rate constants obtained after two or three successive hydrolysis reactions, employing ca. 4.7×10^{-5} M **1**, were equal within experimental error to those found for starting concentrations of **1** of 9.4×10^{-5} or 14.1×10^{-5} M, respectively. This result rules out the possibility that the "concentration effect" is due to the changing concentration of the perchlorate iself.[23] In addition, control experiments revealed that the small amount of dioxane, used to introduce the substrate into the aqueous solution, did not significantly affect the rate of hydrolysis.[24]

Next, we examined the possibility of autocatalysis by p-

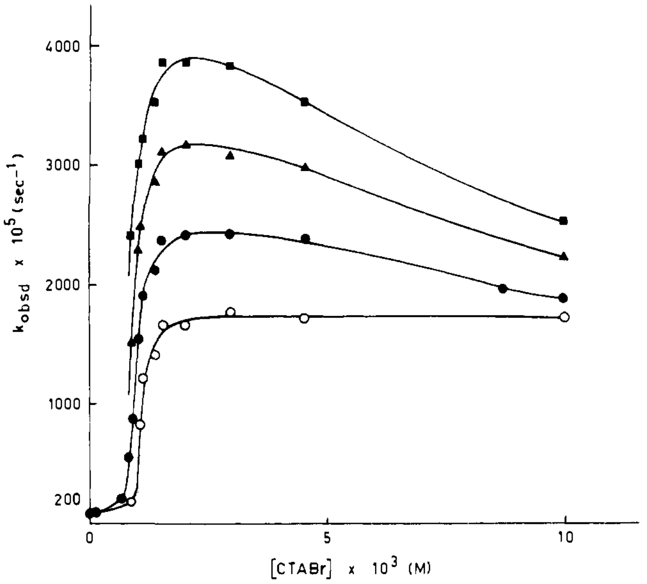


Figure 1. Variation of k_{obsd} for the hydrolysis of **1** at 25.0 °C, as a function of CTABr concentration: (●) [**1**] = 4.7 × 10^{-5} M; (▲) [**1**] = 9.4 × 10^{-5} M; (■) [**1**] = 14.1 × 10^{-5} M; (○) extrapolation to [**1**] = 0.

Table III. Effect of Some Electrolytes on the Rate of Hydrolysis of **1**[a] in 3.0 × 10^{-3} M CTABr at 25.0 °C

Electrolyte[b]	Concn of electrolyte, M	$k_{obsd} \times 10^4$, s^{-1}
		235
TsH	6.5 × 10^{-5}	334
TsNa	6.4 × 10^{-5}	362
HCOOH	8.7 × 10^{-5}	323
LiCl	1.3 × 10^{-3}	216
$NaClO_3$	5.1 × 10^{-4}	209
TsONa	3.6 × 10^{-4}	240
TsOH	1.5 × 10^{-3}	115
HCl	1.2 × 10^{-3}	132

[a] Initial concentration: 4.7 × 10^{-5} M. [b] Ts = *p*-$CH_3C_6H_4SO_2$.

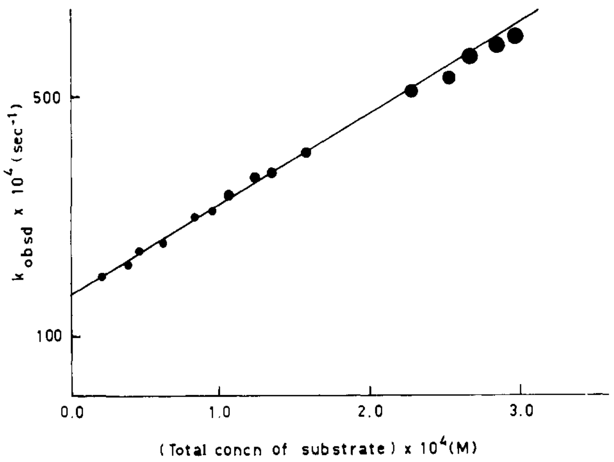


Figure 2. Effect of the total concentration of **1** on its rate of hydrolysis in 2.0 × 10^{-3} M CTABr at 25.0 °C.

toluenesulfinate and formate anions, the products of hydrolysis of **1**. A priori, this effect seemed unlikely in view of the fact that the expected deviation from pseudo-first-order kinetics was not observed (vide infra). However, the observation that the maximum in the plot of k_{obsd} vs. [CTABr] becomes more pronounced upon increasing total substrate concentration (Figures 1 and 2) may be indicative for the contribution of one or more second-order terms to the overall rate equation.[1a] This assumption is supported by the finding that extrapolation to zero concentration of **1** leads to disappearance of the maximum, and the observation of a "plateau" rate, as normally found for pseudo-first-order kinetics (Figure 1).[1,2] Furthermore, experiments conducted in the presence of small amounts of *p*-toluenesulfinic acid (pK_a = 2.80),[25] sodium *p*-toluenesulfinate, formic acid (pK_a = 3.75), and sodium formate (Table III) clearly revealed that the conjugate anions of both acids strongly accelerate the hydrolysis of **1** in a 3.0 × 10^{-3} M solution of CTABr. Salts of strong acids, like sodium *p*-toluenesulfonate, lithium chloride, and sodium chlorate did not significantly alter the rate of hydrolysis. Low concentrations of *p*-toluenesulfonic acid and hydrochloric acid suppress the rate of hydrolysis, apparently because of protonation of part of the sulfinate and formate anions formed upon hydrolysis. In an aqueous solution containing 2.0 × 10^{-3} M CTABr and 0.1 M HCl, the "concentration effect" had almost completely disappeared. This also applies to solutions containing high concentrations of CTABr (0.1 M), most likely as a result of the decrease in the effective concentrations of the substrate and anionic bases at the micellar surface.

Second-order rate constants for $HCOO^-$ and *p*-toluenesulfinate (Ts^-) were obtained from plots of k_{obsd} vs. concentrations of these anions at 2.0 × 10^{-3} M CTABr (Figure 3). At each concentration of Ts^- or $HCOO^-$ several experiments were performed with different amounts of **1**. If a dependence of the rate on the total substrate concentration was observed, as found for the lower parts of the plots, the rates were extrapolated to zero substrate concentration to give $k_{obsd}{}^0$ values. Good linear relationships were found up to ca. 1 × 10^{-3} M $HCOO^-$ and 6 × 10^{-4} M Ts^- (Figure 3). Above 1 × 10^{-3} M $HCOO^-$ the reaction was too fast to be measured accurately with our kinetic technique. The downward curvature at Ts^- concentrations above 6 × 10^{-4} M may originate from a lowering of the charge at the micellar surface, resulting in a decreased catalytic activity.[26] It is noteworthy that the measured k_{HCOO^-} = 174 M^{-1} s^{-1} is 3000 times larger than that in water ($k_{HCOO^-}{}^{H_2O}$ = 5.96 × 10^{-2} M^{-1} s^{-1}).[9] Since k_{Ts^-} in water could not easily be determined, this rate constant was estimated from the Brönsted plot for carboxylic acids[9] to give a $k_{Ts^-}{}^{H_2O}$ of ca. 2 × 10^{-2} M^{-1} s^{-1}. Combining this value with k_{Ts^-} = 279 M^{-1} s^{-1} for the CTABr-catalyzed reaction, the cationic micelles are found to enhance the rate by a factor of even ca. 10^4. The more efficient catalysis by the sulfinate as compared with that by the formate anion presumably arises from the larger hydrophobicity of this anion, leading to a stronger association with the micellar pseudo phase.[27]

From k_{Ts^-} and k_{HCOO^-} and the change in pH measured during the reaction, we can calculate the contributions of Ts^- and $HCOO^-$ to the overall rate constant for hydrolysis (Table IV). In this approach, we assume that (i) both anions do not affect each others reactions, (ii) the pK_a of HCOOH and pK_{H_2O} are not changed by micelles, and (iii) the pK_a of *p*-toluenesulfinic acid decreases by ca. 0.5 pK_a unit.[28]

$$k_{obsd} = k_{H_2O}[H_2O] + \underbrace{k_{Ts^-}[Ts^-] + k_{HCOO^-}[HCOO^-]}_{A} + k_{OH^-}[OH^-]$$

This analysis clearly reveals that the contributions of *p*-toluenesulfinate- and formate-catalyzed hydrolysis should increase rapidly during a run and should lead to a substantial deviation from first-order kinetics. Since this is not borne out in practice we are led to suggest that an additional contribution is involved of a species whose concentration diminishes during a kinetic run, i.e., OH^-.[29] Unfortunately, even in the absence of the detergent, k_{OH^-} is too high to be measured by our ex-

Table IV. Contributions of *p*-Toluenesulfinate (Ts^-) and Formate Catalysis to the Rate of Hydrolysis of **1**, as Calculated from pH and Extinction (E_1) in 2.0 × 10^{-3} M CTABr at 25.0 °C

t, s	$E_1{}^a$	pH	$[Ts^-]^b \times 10^5$, M	$[HCOO^-]^c \times 10^5$, M	$k_{Ts^-}[Ts^-] \times 10^4$, s^{-1}	$k_{HCOO^-}[HCOO^-] \times 10^4$, s^{-1}	$A^d \times 10^4$, s^{-1}	$(k_{obsd} - A)^e \times 10^4$, s^{-1}
14.4	0.645	4.58	1.30	1.13	36.2	19.7	56	178
26.4	0.537	4.29	2.02	1.56	56.3	27.1	83	151
38.4	0.461	4.25	2.54	1.93	70.9	33.6	104	130
50.4	0.399	4.22	2.95	2.20	82.3	38.3	121	113
62.4	0.351	4.19	3.28	2.41	91.5	41.9	133	101
74.4	0.314	4.15	3.52	2.52	98.2	43.9	142	92
86.4	0.283	4.13	3.73	2.63	104	45.8	150	84
98.4	0.264	4.12	3.86	2.71	108	47.2	155	79
110.4	0.249	4.11	3.96	2.76	110	48.1	158	76
122.4	0.231	4.10	4.08	2.82	114	49.1	163	71

[a] Extinction at 235 nm. [b] Assuming that all TsH is dissociated. [c] If K_{HCOOH} (1.78×10^{-4}) is unchanged by CTABr. [d] $A = k_{Ts^-}[Ts^-] + k_{HCOO^-}[HCOO^-]$. [e] $k_{obsd} = 234 \times 10^{-5}\ s^{-1}$.

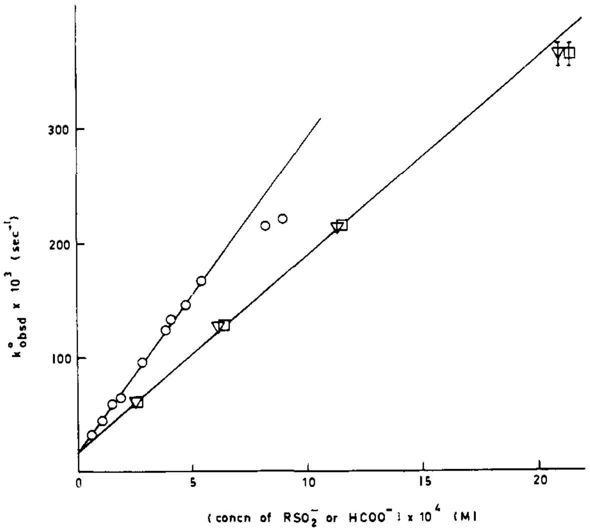


Figure 3. Plots of $k_{obsd}{}^0$ as a function of the concentration of sodium *p*-toluenesulfinate (○) and sodium formate (▽, $[HCOO^-]_{calcd}$; □, $[HCOO^-]_{from\ pH}$) in 2.0 × 10^{-3} M CTABr at 25.0 °C, $k_{Ts^-} = 279\ M^{-1}\ s^{-1}$, $k_{HCOO^-} = 174\ M^{-1}\ s^{-1}$.

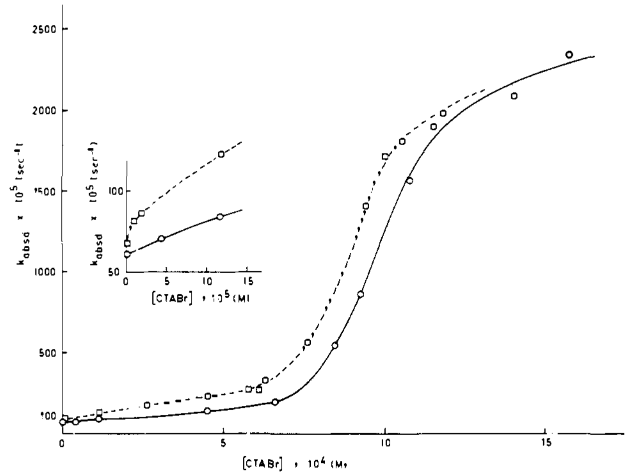


Figure 4. Effect of stirring on the rate of hydrolysis of **1**, as a function of CTABr concentration, at 25.0 °C and [**1**] ≈ 4.7 × 10^{-5} M; (□) with stirring; (○) without stirring.

perimental technique. Nevertheless, a strong indication that catalysis by OH^- (at a pH of ca. 5) plays an important role in the hydrolysis of **1** in micellar solutions of CTABr (at 2.0 × 10^{-3} M) is provided by our observations that (i) a decrease of the initial pH of the solution from 5.6, as normally used, to 4.0 by addition of HCl, leads to a *negative* deviation from pseudo-first-order kinetics in the first stages of the reaction and (ii) an increase of the initial pH to 6.6 gives rise to a *positive* deviation in the first stages of the reaction. These observations may be rationalized by assuming that catalysis by OH^- plays an important role in the first reaction stages when concentrations of sulfinate and formate anions are still small.

We now turn our attention to the question of whether or not the rate of the water-catalyzed reaction is also enhanced at the micellar surface. We therefore performed the hydrolysis of **1** in a solution containing 0.1 N HCl and 2.0 × 10^{-3} M CTABr, assuming that catalysis by hydroxide and formate ions is negligible under these conditions. Since there was still a small "concentration effect", probably owing to sulfinate ion catalysis, we performed rate measurements at several substrate concentrations. Upon extrapolation to zero concentration we obtained $k_{obsd}{}^0 = 72 \times 10^{-4}\ s^{-1}$, while in pure water $k_{H_2O} = 61 \times 10^{-5}\ s^{-1}$ and in 0.1 N $HClO_4$ (without CATBr) $k = 56 \times 10^{-5}\ s^{-1}$.[9a,c] This moderate acceleration (ca. 12 times) of the water reaction might be attributed to the same factors as mentioned above to explain the decrease in $\Delta H^{\ddagger}$, i.e., either an increase in the dynamic basicity of water at the micellar surface, or an electrostatic stabilization of the transition state by the cationic micelle.

Effect of Mechanical Agitation. Quite unexpectedly, it was found that the rate of perchlorate hydrolysis was two- to threefold enlarged upon stirring of the solution (Figure 4).[30] Shaking, although difficult to quantify, appeared to accelerate the reaction even more efficiently than stirring. These effects were most easily observed at CTABr concentrations below the cmc. Above the cmc the effect becomes overshadowed by the rapid increase of the efficiency of micellar catalysis, and the effect is hidden between 1 and 2 × 10^{-3} M CTABr. That the stirring effect also may occur above this concentration region is supported by the following observations: (i) a 10–15% increase in rate upon stirring in 2.0 × 10^{-3} M CTABr for tosyldideuteriomethyl perchlorate (**1**-d_2), which hydrolyzes 5.3 times more slowly than **1**; (ii) a twofold acceleration of the rate of hydrolysis of *p*-nitrophenylsulfonylmethyl nitrate (**2**) upon stirring in 2.0 × 10^{-3} M CTABr. This compound hydrolyzes by a mechanism analogous to that for **1**, but much more slowly.[9b]

No effect of stirring was observed for hydrolysis of **1** in pure water or in aqueous n-Bu_4NBr.[22] In order to test whether the stirring effect also affects other micellar-catalyzed reactions, we examined the reaction between hydroxide ion and 2,4-dinitrochlorobenzene[18] and the decarboxylation of 6-nitrobenzisoxazole-3-carboxylate anion,[6] both in the presence of CTABr. In neither of the two cases, however, was the rate affected by stirring.

Table V. Effect of HCl on the Hydrolysis of **1** in 1.2 × 10^{-4} M CTABr at 25.0 °C

[HCl], M	[**1**] × 10^5, M	Stirring	$k_{\text{obsd}} \times 10^5$, s^{-1}
		−	82
	3.3	+	136
63 × 10^{-5}	4.1	−	71
71 × 10^{-5}	3.5	+	89
0.10	9.8	−	101
0.10	9.8	+	101

We also found that relatively small amounts of hydrochloric acid did attenuate the effect of stirring markedly and in CTABr solutions containing 0.1 N HCl, the effect was completely absent (Table V). An increase in substrate concentration also suppressed the effect, probably owing to the decrease of the pH during the reaction. These results suggest that the effect is possibly linked to the hydroxide ion catalyzed reaction postulated in the previous section. The influence of substrate concentration was rather small for **1**, but larger for *p*-nitrophenylsulfonylmethyl nitrate (**2**), which is known to be more sensitive to hydroxide ion catalysis than **1** (Table VI).[9b,c]

To the best of our knowledge, effects due to mechanical agitation on rates of micellar-catalyzed reactions have not been reported previously.

Several explanations for this peculiar effect can be advanced: (**a**) **Heterogeneity**. Initially the effect was ascribed to the presence of an impurity or to precipitation of the substrate and/or reaction products.[19] However, the following evidence strongly indicates that the effect does not find its origin in the presence of a heterogeneity: (i) Extensive purification of the substrate and surfactant did not influence the effect. (ii) The aqueous solution remains perfectly clear after addition of the solution of **1** in dioxane. Light scattering experiments only showed an increase in turbidity during addition of **1** to the reaction mixture, but this initial turbidity disappeared rapidly. (iii) The solubility of **1** is about 50 times higher than the concentration of **1** used for the rate measurements.[22] (iv) The effect is present over the whole temperature range of 25-45 °C. (v) Filtration even through a 0.2-μm membrane filter did not change the effect.

(**b**) **Gas Absorption**. We also checked the possibility of gas (O_2) absorption upon stirring. This possibility was rendered unlikely by the observation that the effect was still present in a deoxygenated solution under a nitrogen atmosphere, and in a totally filled and stoppered cuvette.

(**c**) **Induction of Micellization by Stirring**.[31] This possibility was carefully tested using conductivity measurements. However the conductivity of CTABr solutions in the concentration range 10^{-5}-10^{-3} M was found to be independent of mechanical agitation. In addition, light scattering experiments failed to detect changes in turbidity upon stirring in 1.2 × 10^{-4} and 2.0 × 10^{-3} M CTABr. The observation that under certain conditions the effect of stirring can still be observed at CTABr concentrations well above the cmc is also difficult to reconcile with induction of micellization by stirring of the solution.

A negative influence of stirring on micellar size has been assumed by Brown et al.[32] They observed a lowering of surface tension by stirring a solution of sorbitan monostearate in *o*-xylene, and suggested that micelles are partially broken down by shear forces.

(**d**) **Transport Phenomena.** Transport phenomena may clearly account for the observed effect of stirring and could involve catalysis by hemimicelles at the quartz-water or water-air interface. Lin and Somasundaran[33] established that hemimicellization does occur above a certain critical concentration (hmc),[33] far below the cmc. We were unable to find any literature data for the hmc of CTABr, but by comparison with dodecylammonium acetate,[33,34] which has a cmc close to that of CTABr, the hmc of CTABr was estimated to be ca. 2 × 10^{-6} M. As can be seen from Figure 4, the rate profile for the stirred solutions has a much steeper slope at CTABr concentrations in the region up to 10^{-5} M than at higher CTABr concentrations up to the cmc. It is felt that hemimicelles could be invoked to explain this observation. One could consider at least two different mechanisms. First the role of stirring may be attributed to the transport of reagents to and from the surface.[35] Stirring could also favor the formation of hemimicelles,[32] or the formation of (pre)micelles in the vicinity of the surface. Since the effect of stirring is attenuated upon lowering of the pH, we suggest[36] that the phenomenon may find its origin in a strong acceleration of the hydroxide ion catalyzed hydrolysis by hemimicelles,[37] just as found for micelles at higher detergent concentrations.

Table VI. Hydrolysis of *p*-Nitrophenylsulfonylmethyl Nitrate (**2**) in Aqueous Solutions of CTABr at 25.0 °C

[CTABr], M	E_{∞}[a]	Stirring	k_{obsd}[b] × 10^5, s^{-1}
		−	~5
2 × 10^{-3}	0.232	+	183
2 × 10^{-3}	0.232	−	107
2 × 10^{-3}	0.479	+	152
2 × 10^{-3}	0.479	−	89
2 × 10^{-3}	0.680	+	99
8.3 × 10^{-4}	0.315	+	102
8.3 × 10^{-4}	0.470	+	92
8.3 × 10^{-4}	1.342	+	42.8
8.3 × 10^{-4}	0.398	−	26.1

[a] Final extinction at 245 nm due to *p*-nitrobenzenesulfinic acid. [b] At an initial pH ~4.4.

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Supplementary Material Available: tables of the data used in the graphs of Figures 1-4 (4 pages). Ordering information is given on any current masthead page.

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V. A. Motsavage and H. B. Kostenbauder, *J. Colloid Sci.*, **18**, 603 (1963); C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J. Chem. Soc., Perkin Trans. 2*, 1900 (1973); or (b) the catalysis is due to a "solvent effect", e.g., M. D. Bentley, S. E. Bowie, and R. D. Limogenes, *J. Phys. Chem.*, **75**, 1763 (1971); the neutral hydrolysis of tosylmethyl perchlorate in water (without CTABr) is rather independent of the dielectric constant of the medium.[10a]

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(17) It is questionable how much the strong decrease of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in 0.1 N HCl + 2.0 × 10^{-3} M CTABr could be the result of an electrolyte effect on the formation of micelles or on the micellar catalysis. Electrolyte effects generally decrease the magnitude of the catalysis.[1-5]

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(23) Addition of small amounts (10^{-5}–10^{-4} M) of compounds structurally related to the substrate, e.g., tosylmethyl nitrate or tosylmethane, which did not hydrolyze appreciably under the reaction conditions employed, had no effect on the rate.

(24) Acetonitrile or methanol also can be used with the same results.

(25) D. de Filippo and F. Momicchiolo, *Tetrahedron*, **25**, 5733 (1969).

(26) The $HCOO^-$-catalyzed hydrolysis of **1** in CTABr micelles was performed at an initial pH of ca. 4 and a constant ion strength of 4.1 × 10^{-3} M (by addition of NaCl). Further experiments without NaCl revealed, however, that k_{HCOO^-} and k_{Ts^-} were not influenced by the differences in ionic strength.

(27) We assume that the association constants of **1** and *p*-toluenesulfinic acid are large, due to the hydrophobicity of the tolyl group.[6] Unfortunately, the complexity of the CTABr-catalyzed reaction strongly hampers the determination of a reliable binding constant for **1** from the kinetic data.

(28) C. A. Bunton and M. J. Minch, *J. Phys. Chem.*, **78**, 1490 (1974).

(29) (a) A plot of (k_{obsd} − *A*) vs. concentration of hydroxide ions during the reaction shows almost a linear correlation. From the slope of this plot we tentatively conclude that pseudo-first-order kinetics may be expected if k_{OH^-} is about 10^8 M^{-1} s^{-1}. In water in the absence of CTABr, k_{OH^-} has recently been determined as 6.4 × 10^4 M^{-1} s^{-1}.[22] If the acceleration of the hydroxide ion catalyzed reaction is comparable to that for formate and *p*-toluenesulfinate, a value of 10^8 is reasonable indeed. There are strong indications, however, that the use of k_{Ts^-} and k_{HCOO^-} as determined in separate experiments is questionable. We found that at substrate concentrations >7–8 × 10^{-5} M the sum of the calculated contributions of sulfinate and formate exceeds k_{obsd}. Therefore the actual contributions of these species are smaller than calculated, which points to a competition of these anions for "active sites" (see also ref 19a). (b) A referee has pointed out that the situation is further complicated by the unknown distribution of acid and anion between water and the micelle. We feel, however, that this complexity (reflected in k_{Ts^-} and k_{HCOO^-}) does not affect our explanation in terms of compensatory kinetic effects.

(30) The effect of stirring on the rate depends on the stirrer and the rate of stirring. Absolute values of reaction rate with stirring have therefore little meaning. The fluctuations in the effect are in the order of ca. ±10%, probably due to uncontrolled variations in stirring speed. The effect also was observed if the reaction was performed in a glass vessel and followed by conductivity measurements. A similar effect of stirring was found also for *p*-nitrophenylsulfonylmethyl perchlorate.

(31) It is well known that aggregation of polymers may be assisted by orientation of the molecules in a hydrodynamic field. See, for example: S. Frenkel, *J. Polym. Sci., Polym. Symp.*, **No. 44**, 49 (1974). Micellization might be induced likewise by orientation of the surfactant molecules in the direction of the stirring stream.

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Kinetics and Mechanisms of the 1,5-Dihydroflavin Reduction of Carbonyl Compounds and the Flavin Oxidation of Alcohols. 4. Interconversion of Formaldehyde and Methanol

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Abstract: The mechanism of the kinetically biphasic reduction of formaldehyde by dihydroflavin (ref 9) has been elucidated. In the first and rapid phase, dihydroflavin and formaldehyde yield, via two competing reactions: (a) oxidized flavin plus methanol; and (b) the *N*(5)-hydroxymethyl derivative plus the corresponding imine. In the slower second phase of reaction the oxidized flavin produced in the first phase acts as a catalyst in the conversion of the *N*(5)-hydroxymethyl derivative to reduced flavin plus formaldehyde, and these reactants reenter the reactions of the first phase. Concentration and pH dependencies have been investigated and the appropriate rate constants determined. 1,5-Dihydro-3-methyllumiflavin is proposed to form an *N*(1)-hydroxymethyl adduct as has been shown (ref 25) for uracils. Methanol has been shown to reduce oxidized flavin at alkaline pH providing as products 1,5-dihydroflavin and formaldehyde in a 1:1 ratio. Previous studies are reviewed (Introduction) and a general radical mechanism presented (Discussion).

Introduction

The elucidation of the mechanisms of flavin mediated oxidation–reduction reactions in simple chemical systems is of prime importance to the understanding and appreciation of the mechanisms of catalysis by flavoenzymes. In those examples of enzymatic reactions where an organic cofactor is required, physical organic studies of the mechanism of reaction of the cofactor with substrate (sans apoenzyme) have proved invaluable to the understanding of the enzyme catalytic process. Even appreciation of the differences in the mechanisms of model reactions and enzyme reactions are of importance since they explicitly describe the role of the apoenzyme. The present study is the fourth[2-4] in a series dealing with the kinetics and mechanisms for the overall reactions of eq 1.

In the two-electron oxidation (or reduction) of one organic