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Reactions within Association Complexes: The Reaction of Imidazole with Substituted Phenyl Acetates in the Presence of Detergents in Aqueous Solution

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The bimolecular rate constants for reaction of imidazole with phenyl acetates complexed with sodium dodecyl sulfate (SDS) or cetyltrimethylammonium bromide (CTAB) micelles obey Brønsted equations with β_{lg} similar to that of the reaction in aqueous solution. The dissociation constants of ester (K_S) and the hypothetical dissociation constant (K_{TS}) of the transition state of the micelle complexes obey Hansch equations with similar sensitivities (p) to π (−0.66 and −0.589 for K_S and −0.735 and −0.495 for K_{TS}, respectively). The slopes also indicate that the microsolvation environments associated with the transition state and the complexed ester have aqueous character. The relative values of K_{TS} and K_S indicate that the transition state of the reaction of imidazole with ester is more weakly complexed to both micelles than is the reactant ester. Log K_{TS} values are linear functions of log K_S for reactions with both CTAB and SDS; the slopes are, respectively, −0.893 and −1.19 consistent with a slightly more “water-like” medium for the transition state than for the site of binding of ester with CTAB-micelle and slightly less for the SDS-micelle. The results for ester and transition state are consistent with the location of the phenyl residue in a hydrophobic region that possesses water molecules. It is concluded that the acetyl group in the complexed transition state is located in an aqueous part of the Stern region, whereas the phenyl residue is in a part of the Stern region that possesses alkane components. The derived kinetic and complexation parameters in these experiments refer to micelles with Stern regions that have been maintained at constant ionic compositions.

Introduction

Micelles are self-organized aggregates of detergent molecules that contain both polar (often charged) hydrophilic groups and a hydrophobic group, usually a long-chain aliphatic component.[1−5] The polar headgroup of the detergent tends to associate with the bulk aqueous solvent, and the hydrophobic part aggregates with that of other detergent molecules to form a fluxional structure, the micelle. The shape of the micelle can be roughly spherical but at high detergent concentrations can take on more extended forms such as rods, tubes, or laminar forms. Whatever is the shape of a particular micelle, it has a hydrophobic region and a hydrophilic surface (interface with bulk solvent); the micelle can complex a reactive organic molecule thus lowering its concentration and inhibiting its reaction in the bulk aqueous phase. Reactions of complexed substrates could occur within the hydrophobic region of the micelle or at the interface with the bulk solvent. Reaction in the micellar pseudophase may be accelerated or decelerated depending on the nature of the headgroup and the reactant species.[5] The diameter of the roughly spherical micelle, which in the case of sodium dodecyl sulfate (SDS) and cetyltrimethylammonium bromide (CTAB) possesses between 80 and 90 detergent molecules, is up to 3 nm. There is sufficient space within the hydrophobic core to accommodate at least one substrate molecule without disrupting the overall structure of the micelle. Owing to the charged Stern region, the SDS and CTAB micelles are subject to ion-exchange phenomena; it is very important to keep the ion compositions of the bulk solutions constant throughout any concentration variations of the detergent in order that any derived kinetic and complexation constants are ascribed to a micelle with a Stern region of constant ionic atmosphere.

We present here a study of the effect of micelles on the first step of the reaction of imidazole with substituted phenyl acetates (Scheme 1); these esters do not possess long aliphatic side chains capable of binding in the interior of the micelle and able to force the phenyl component of the bound ester into the Stern layer. The hydrophobic effect of the substituent (π)[6,7] as well as the electronic effect[8] on the transition-state binding are studied to elucidate the possible location of the transition state of the reaction. Study of the bimolecular reaction between ester and imidazole has the advantage that the imidazole has a very small log P value and therefore has little propensity to partition into the hydrophobic core of the micelle. When hydroxide ion acts as a nucleophile the reaction is complicated by an ion-exchange component in CTAB and in SDS by a substantial electrostatic repulsion.

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Scheme 1. Reaction of Imidazole with Substituted Phenyl Acetates in Aqueous Solution

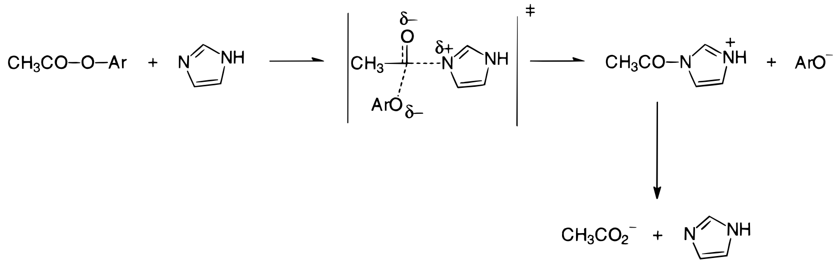

Table 1. Rate Parameters for Reaction of Imidazole with Substituted Phenyl Esters in the Presence of SDS at 25° [a]

	phenyl ester	k_u/M^{-1}s^{-1} [m]	K_s/mM[b]	100k_c/ M^{-1} s^{-1} [c]	K_{TS}/M[d]	pK_a [j]	π[l]	[ester] × 10^4/M[p]	λ /nm[h]	N[e]	10^3k_{obs} /s^{-1} [g,n]	r[f]
				substituted phenyl acetates								
1	4-nitro	0.554 ± 0.010	33.1 ± 4.3	2.87 ± 0.16	0.639	7.14	0.22	0.442	400	6	27.7−5.34	0.9978
2	3-nitro	0.202 ± 0.004	70.6 ± 9.8	<1.1	>1.30	8.38	0.11	1.77	350	6	10.1−1.42	0.9975
3	4-cyano	0.264 ± 0.002	47.4 ± 0.002	<0.4	>3.12	7.95	−0.33	0.695	290	11	13.2−2.11	0.9991
4	3-cyano	0.127 ± 0.003	42.0 ± 5.9	<0.48	>1.11	8.61	−0.31	1.14	294	6	6.37−0.966	0.9973
5	4-acetyl	0.159 ± 0.002	45.1 ± 4.1	<0.43	>1.67	8.05	−0.39	0.288	330	6	7.96−0.834	0.9989
6	2-chloro	0.0577 ± 0.001	6.86 ± 0.54	0.58 ± 0.069	0.0682	8.48	0.76	1.69	290	7	2.89−0.40	0.9980
7	3-chloro	0.052 ± 0.001	11.5 ± 1.4	0.14 ± 0.01	0.427	9.02	0.77	1.97	280	8	2.58−0.237	0.9948
8	4-chloro	0.023 ± 0.0004	7.81 ± 0.98	0.200 ± 0.03	0.0898	9.38	0.73	2.44	280	7	1.15−0.116	0.9985
9	parent	$6.43 \pm 0.4 \times 10^{-3}$	22.2 ± 1.61	0.0325 ± 0.0084	0.439	9.99	0.00	5.99	260	6	0.24−0.0445	0.9995
10	2,5-dichloro	0.318 ± 0.002	3.00 ± 0.18	3.13 ± 0.12	0.0305	7.51	1.49	1.01	300	7	15.9−1.65	0.9998
11	2,3,4-trichloro	0.42 ± 0.004	1.58 ± 0.43	3.8 ± 0.37	0.0175	6.92	2.26	0.735	310	8	21.4−1.77	0.9992
12	3,4,5-trichloro	0.538 ± 0.002	0.855 ± 0.105	3.76 ± 0.13	0.0122	7.55	2.27	0.869	305	7	26.9−2.01	0.9999
13	2,3-dichloro	0.228 ± 0.002	2.81 ± 0.28	1.58 ± 0.14	0.0405	7.71	1.53	1.09	295	6	11.4−1.02	0.9999
14	3,4-dichloro	0.0938 ± 0.0022	2.1 ± 0.8	0.971 ± 0.162	0.0203	8.62	1.50	2.03	295	7	4.69−0.489	0.9987
				substituted phenyl hexanoate								
	4-nitro	0.346 ± 0.008	1.42 ± 0.2	1.99 ± 0.4	0.0247			0.539	400	9	17−1.2	0.9980

[a] Conditions of measurement: solution held at pH 8.92 ± 0.02 with borate buffer ($Na_2B_4O_7$) at 0.05 M, total [Na^+] = 0.22 M, free imidazole at 0.05 M. [b] Disssociation constant of the ester−micelle complex (in terms of detergent molecule concentration). [c] Second-order rate constant for reaction of imidazole with ester−micelle complex. [d] Dissociation constant of the transition state of the reaction between imidazole and ester−imidazole complex. [e] Number of data points not including duplicates. [f] Correlation coefficient of fit of k_{obs}/[free imidazole] to the concentration ([detergent] − cmc) according to eq 1. [g] Range of observed rate constants. [h] Wavelength of the kinetic studies. [j] pK_a of the leaving phenol from refs 37 and 38. [l] The value of π is taken from ref 39. [m] Ester concentration. [n] Refers to the SDS concentration range of 0−0.2 M.

Experimental Section

Materials. Sodium dodecyl sulfate was obtained from BDH and cetyltrimethylammonium bromide from Sigma. Substituted phenyl acetates were available from a previous study[9] or prepared by the method of Chattaway.[10] 3-Nitrophenyl acetate was donated by Dr. A. B. Maude. Imidazole was recrystallized from benzene. All solutions 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 with a diluent solution (identical in respect of imidazole concentration, pH and ionic strength) but without SDS. A similar protocol was employed for the variation of CTAB concentration (0−0.05 M). When the effect of imidazole concentration was being studied, the detergents were kept at a standard concentration in both buffers and imidazole was omitted from the diluent buffer. The component concentrations are recorded in Tables 1 and 2.

In the case of the SDS studies, the sodium ion concentration was maintained at 0.22 M, and in the case of CTAB, the bromide ion concentration was kept at 0.05 M. In the case of SDS, it is essential to keep the imidazolium ion concentration as low as possible so that as little as possible ion exchange occurs between the sodium ion in the Stern layer and the imidazolium ion in the bulk. The consequences of not paying due regard to these protocols are outlined in the Results.

Reactions were initiated by the addition of an aliquot (0.01−0.05 mL) of a solution of the substrate (in acetonitrile) to 2.5 mL of buffered solution, contained in a 1 cm path length silica cuvette in the thermostated cell compartment of a Pye Unicam SP 8-200 UV/vis spectrophotometer. The pH's of the solutions were measured before and after each kinetic run using a Radiometer PHM62 pH meter with a Russell CMAWL combined electrode, calibrated with BDH buffers; data for experiments where the pH changed by more than 0.1 units were discarded. Wavelengths for studying the kinetics of the reactions were determined initially by repetitively scanning the spectrum during a reaction and are recorded in Tables 1 and 2. The reactions were followed kinetically by measuring the absorbance (A_t) at the optimal wavelength as a function of time.

Pseudo-first-order rate constants were obtained by fitting the value of A_t (which increases with time in these cases) to the equation $A_t = A_\infty - (A_\infty - A_o)\exp(-kt)$. Data were fit to theoretical equations by use of standard software.

Results

Monitoring the reaction between imidazole and substituted phenyl acetate in micellar solutions by UV-absorption spectrocopy demonstrated the release of a phenol and formation of the acetyl imidazole intermediate. In the case of the nonmicellar reactions, this reaction has been very well documented,[11,12] and there is no evidence that the micellar solutions are changing the nature of the reaction. The hydrolysis of the acetyl imidazole is not measured and it is therefore not a complicating feature. In the case of some esters, the UV-spectral changes demonstrated that acetyl imidazole

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Table 2. Rate Parameters for Reaction of Imidazole and Hydroxide Ion with Substituted Phenyl Esters in the Presence of CTAB at 25 °C

	ester	K_S/mM[b]	10^3k_c/M^{-1} s^{-1} [c]	K_{TS}/M[d]	N[e]	r[f]	10^3k_{obs}/s^{-1} [g,i]	λ/nm[h]
			substituted phenyl acetates with imidazole[a]					
1	4-nitro	19.6 ± 3.7	87.8 ± 3.2	0.124	6	0.9978	26.9−10.2	400
4	3-cyano	4.98 ± 0.23	20.8 ± 0.69	0.0304	6	0.99998	7.01−1.00	294
5	4-acetyl	25.0 ± 1.4	15.6 ± 3.6*	0.255	5	0.9900	7.68−3.3	330
6	2-chloro	4.26 ± 0.42	7.62 ± 1.1	0.0323	8	0.9992	3.14−0.554	280
7	3-chloro	3.15 ± 0.38	8.13 ± 0.98	0.0201	9	0.9964	2.8−0.531	280
8	4-chloro	5.25 ± 0.65	2.66 ± 0.49	0.0454	8	0.9976	1.12−0.220	260
9	parent	7.72 ± 1.2	1.33 ± 0.13	0.0373	6	0.9979	0.353−0.128	280
10	2,5-dichloro	2.33 ± 0.22	34.1 ± 5.2	0.0217	6	0.9989	15.3−1.98	300
11	2,3,4-trichloro	0.242 ± 0.031	42 ± 2.1	2.41 10^{-3}	9	0.9996	21.0−2.16	310
12	3,4,5-trichloro	0.513 ± 0.004	45.2 ± 4	6.11 10^{-3}	9	0.9989	24.5−2.11	295
			4-nitrophenyl acetate with hydroxide ion[k]					
		18 ± 0.68	219 ± 28	1 ± 0.01	7	0.9887	1.87−9.70	400
			4-nitrophenyl hexanoate with imidazole[a]					
	with imidazole[a]							
		0.303 ± 0.007	25.7 ± 0.3	4.08 × 10^{-3}	5	0.99999	22.1−1.91	400
			with hydroxide ion[m]					
		3.8 ± 0.29	198 ± 21	1.5 ± 0.33	8	0.9899	2.27−33.5	400

[a] Conditions of measurements: pH maintained at pH 7.04 ± 0.02 with imidazole buffer at a fraction of base = 0.5 (total imidazole concentration = 0.1 M). Bromide ion concentration maintained at 0.05 M with KBr. Ester concentrations, π, and pK_a values as given in Table 1. [b−h] Footnotes as in footnotes to Table 1. [i] Refers to concentration range from CTAB at 0−0.05 M. [k] pH 10.05 maintained with 0.025M borate buffer. Bromide ion concentration maintained at 0.005M with KBr. Value of k_u for hydroxide ion attack is 14.6 ± 1.6$M^{-1}s^{-1}$. [m] pH 10.45 maintained with 0.025M borate buffer. Bromide ion concentration maintained at 0.005M with KBr. Value of k_u for hydroxide ion attack is 8.2 ± 0.24$M^{-1}s^{-1}$.

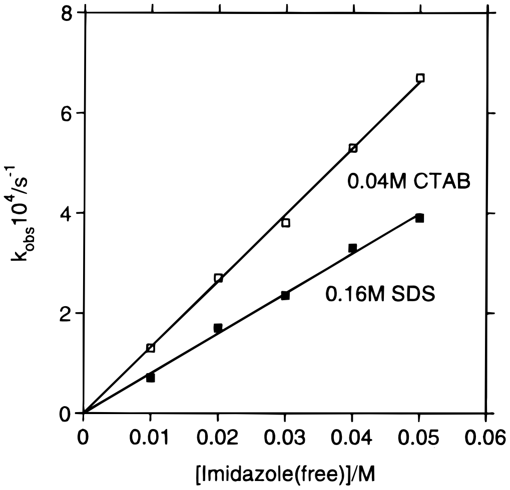

Figure 1. Dependence of k_{obs} on free imidazole concentration for the reaction with 2-chlorophenyl acetate in the presence of SDS at 0.16 M or CTAB at 0.04 M. Lines are least-squares fits.

intermediate was formed and was starting to hydrolyze during the experiments. The wavelengths were chosen so that the decay of the acetylimidazole did not interfere with the measurement of accurate kinetics of its formation.

The reactions of imidazole with substituted phenyl acetates to yield acetyl imidazole give good pseudo-first-order kinetics up to about 90% of the total reaction. At a given concentration of detergent, the observed first-order rate constants are proportional to the free imidazole concentration, and examples of this relationship are illustrated for the 2-chlorophenyl acetate reacting in the presence of SDS and CTAB (Figure 1). The reaction of imidazole with substituted phenyl acetates is inhibited by the detergents (Figure 2). The observed pseudo-first-order rate constants for the inhibition reaction of imidazole with substituted phenyl acetates in a series of detergent concentrations follow eq 1.

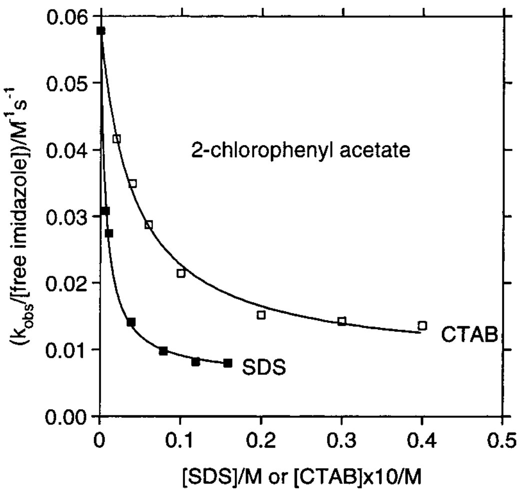

Figure 2. Reactivity of 2-chlorophenyl acetate (k_{obs}/[free imidazole]) in the presence of SDS and imidazole(0.05 M free) at pH 8.92 and in the presence of CTAB and imidazole (0.05 M free) at pH 7.03. Lines are theoretical, calculated from the parameters in Tables 1 and 2.

Equation 1 is predicted by Scheme 2,[13] and the conditions employed for the experiments are given in Tables 1 and 2. We have treated the partitioning of ester into micelle as if it were a regular one to one complexation process; this is acceptable if the overall detergent concentration far exceeds that of the ester (see Tables 1 and 2). It is reasonable to assume that only a very small number of ester molecules is absorbed in one micelle particle at the concentration levels of detergent employed in this study, that cmc values are not significantly perturbed, and that there is little intermolecular interaction between ester molecules complexed in a single micelle. The values of the critical micelle concentrations (cmc's) for SDS and CTAB are taken as 1.35 × 10^{-3} M and 0.8 × 10^{-3} M, respectively, and the aggregation

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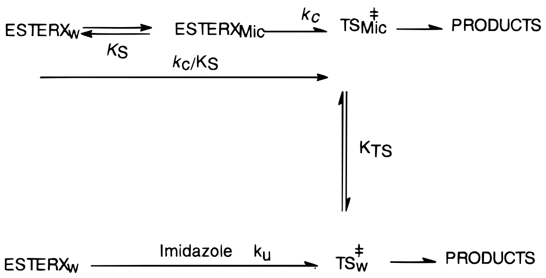
Scheme 2. Mechanism for Reaction of Imidazole with Substituted Phenyl Acetates in the Presence of Detergent Molecules (w = Bulk Aqueous Phase; Mic = Micelle Pseudophase)



numbers are 93 and 85.[14–17]

$$k_{obs}/[\text{imidazole}]_{free} = (k_u[K_S] + k_c[\text{detergent} - \text{cmc}])/(K_S + [\text{detergent} - \text{cmc}]) \quad (1)$$

Neglect of the cmc term in eq 1 introduces differences in the resultant kinetic parameters less than the standard deviations. This was noted previously for similar systems by Tee and Fedortchenko[18] and by us;[19,20] it is a useful point as cmc's and aggregation numbers vary with the conditions and it is likely that small variations will occur within the ranges of detergent concentrations employed. Further, it is not clear how much the increasing concentrations of micelle will alter the concentration of free, unaggregated detergent molecules.

The derived kinetic parameters for the reaction of imidazole with substituted phenyl acetates in the presence of the detergents are shown in Tables 1 and 2 together with the experimental conditions. Second-order rate constants for the reaction of imidazole with acetates (k_u) correlate with the pK_a of the leaving phenol (eq 2) and agree with those from previous studies.[11,12] Second-order rate constants for the reaction of imidazole with acetates in the presence of micelles (k_c) also obey Brønsted-type equations (3) and (4) (Figure 3). The units of K_S quoted in Tables 1 and 2 are in molar concentration of detergent rather than the molar concentration of the micellar particles because this would require an accurate knowledge of the aggregation numbers. Even if the aggregation number were known for a detergent, variation of its concentration is likely to cause a change in this number. If the micelle were to be treated as a molecule the molar dissociation constant would be given by the term K_S/N, where N is the aggregation number of the micellar particle. The use of the molar concentrations of detergent does not introduce the ambiguity that could arise due to a possible change in shape of the micelles as the concentration of detergent is decreased. It is not possible to compare the results with much of the previous work because of the general lack of cation or anion control generally obtained in the literature. In studies of the alkaline hydrolysis of 4-nitrophenyl acetate where the ionic atmosphere *was* controlled,[18,21] K_S values agree with those of the present report. Dissociation constants of the ester from the ester-micelle complexes (K_S) fit Hansch equations (5) and (6) against π and are illustrated in Figures 4 and 5.

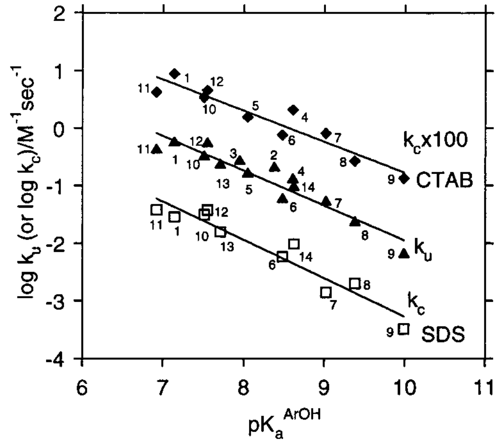


Figure 3. Brønsted correlations for k_u, k_c (CTAB), and k_c(SDS). Data are taken from Tables 1 and 2, and the lines are calculated from the parameters in eqs 2, 3, and 4, respectively. Identities of the ester points are from Table 1.

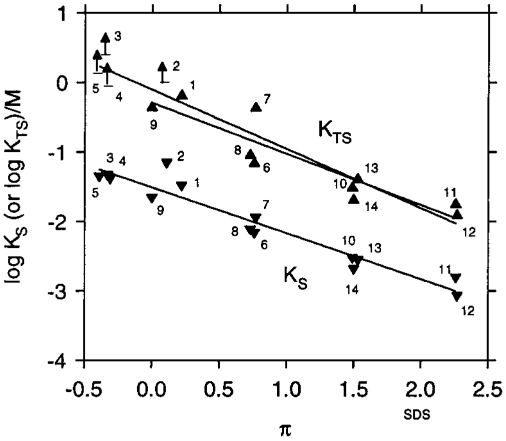


Figure 4. Hansch correlations of K_S and K_{TS} for SDS. Data are taken from Table 1, and lines are calculated from the parameters in eqs 5 and 7, respectively. Identities of the ester points are from Table 1.

Hypothetical dissociation of the transition state in the micelle complex to give free micelle and "free" transition state gives rise to the apparent dissociation constant ($K_{TS} = k_uK_S/k_c$).[22–24] Log K_{TS} correlates with Hansch π-parameters (eqs 7 and 8) as illustrated in Figures 4 and 5. Log K_{TS} is also linearly related with log K_S for both SDS- and CTAB-mediated reactions of ester with imidazole (eqs 9 and 10, Figure 6).

In the case of CTAB, the total bromide ion concentration was maintained constant; the effect on the kinetics of not doing this was reported earlier for CTAB[19] and it was shown how to obtain rate constants that referred to a standard ionic composition. In the case of SDS at pH's in the region of 7, ion exchange between the imidazolium

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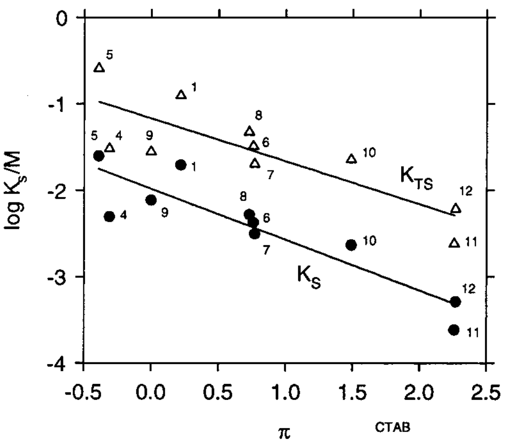

Figure 5. Hansch correlations of K_S and K_{TS} for CTAB. Data are taken from Table 2, and lines are calculated from the parameters in eqs 6 and 8, respectively. Identities of the ester points are from Table 1.

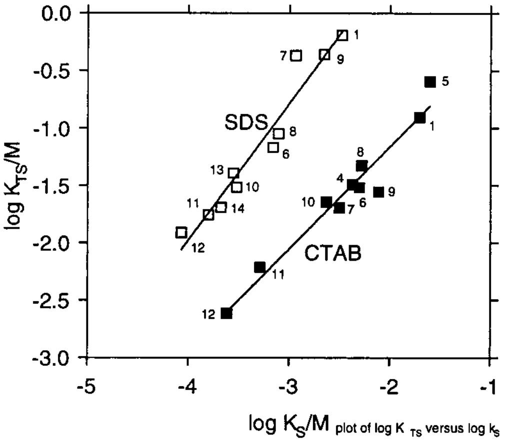

Figure 6. Relationships between log K_{TS} and log K_S for the ester reaction with imidazole in the presence of SDS and CTAB. Lines are calculated from eqs 9 and 10, respectively. Identities of the ester points are from Table 1. For clarity, the SDS line is shifted 1 log K_S unit to the left.

ion and sodium ion at the Stern layer gives rise to a variant ionic composition at the Stern layer; this is overcome by using a pH (~9.0) where there is little free imidazolium ion and also by compensating for the change in sodium ion concentration by the use of sodium chloride in the diluent used in making up solutions of different SDS concentrations. It was found that, as the concentration of SDS is increased without compensating for the sodium ion in the presence of 0.1 M total imidazole (FB = 0.5), the pH rises substantially (typically from 7 up to 8) due to the ion exchange of the imidazolium ion into the Stern layer reducing its concentration in the bulk water and increasing the fraction of base. A further manifestation is that k_{obs} is not necessarily proportional to the free imidazole concentration unless the ionic composition of the micelle's Stern layer is maintained constant. Arranging the experimental conditions so that ion exchange is constant also simplifies the mathematical equations for the kinetics so that fewer disposable parameters (such as degree of cation binding or ion-exchange constants) need be included; the consequence of this is that the accuracy of the resultant kinetic and dissociation constants is improved.

Perusal of Table 1 indicates that it has proved impossible to measure k_c accurately for esters with low or negative π values because of the relatively large K_S values. In view of the necessity of keeping the sodium ion concentration constant, it is not possible to use SDS concentrations in excess of the chosen molarity of the sodium ion. It would be possible to use a higher sodium ion concentration but it would then not be possible to compare the results with those for the lower concentration. The lower limits obtained for K_{TS} may be obtained from the errors in determining k_c. It is interesting that these values, when incorporated with the accurately measured K_{TS} values, do not significantly alter equations (7) and (9) (Table 3). Scheme 3 illustrates the effective charge map for the systems.

Discussion

Rate constants for the reaction of hydroxide ion with substituted phenyl dodecanoates in CTAB solutions are independent of Hansch π parameters for the substituents on the aromatic ring of the phenyl esters[19] consistent with a transition state where the undecanyl side chain of the ester substrate lies within the hydrophobic interior of the micelle and the phenolate leaving residue and ester function are located in the Stern region. Calculations show that the log P value of 4-nitrophenyl acetate is some five units smaller than that of 4-nitrophenyl dodecanoate.[25a] When there is no long-chain alkyl group attached to the reacting substrate, the only binding available is that for the leaving group, and there is therefore less hydrophobic force available for complexation than in the dodecanoate case. It is likely that the phenyl component of the complexed acetate lies in a hydrophobic region at the surface in the Stern region. Tee and Fedortchenko[18] showed that there is a monotonic increase in transition state binding as a function of the acyl group chain length in a series of 4-nitrophenyl alkanoate substrates in agreement with these conclusions. Broxton and co-workers also concluded that compounds with single phenyl groups complex at the interface in positively charged micelles.[25b,c]

The values of log K_S for CTAB- and SDS-mediated reactions of acetate esters correlate with Hansch's π values (eqs 5 and 6) rather than with the pK_a of the leaving phenol; this indicates that the complexation of ester with micelle is governed only by partitioning interactions and has no significant component due to the polarity of the substituent. The slopes of the Hansch correlations are less than unity and therefore indicate that the microscopic medium of the complexed ester is more water-like than *n*-octanol[26] consistent with a binding region that possesses both alkane chain as well as water molecules. 4-Nitrophenyl hexanoate binds with both SDS and CTAB much more efficiently than the corresponding acetate and this is ascribed to the extra hydrophobic character of the pentyl chain of the ester lending extra components to the overall log P value. The low value of log P for imidazole (−0.08)[29] indicates that it would be reluctant to complex with a micelle and this explains why there is no observable curvature in the plot of k_{obs} against free imidazole.

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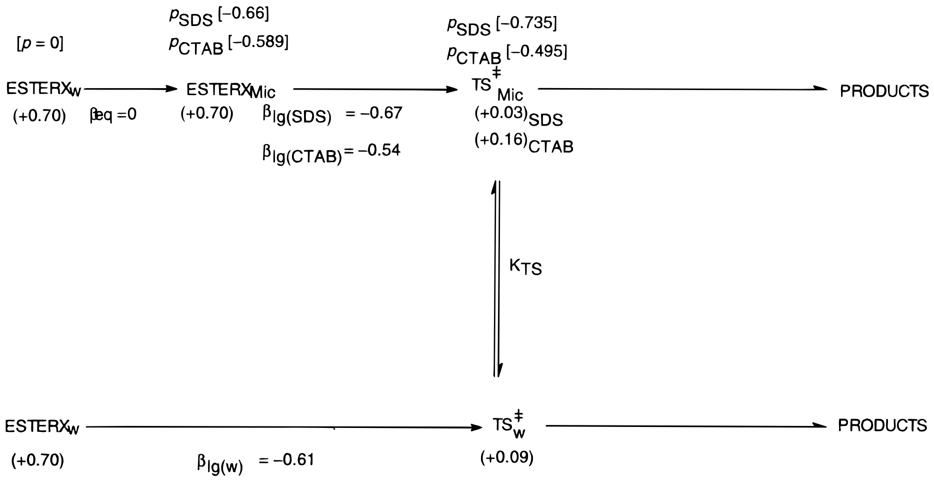
(25) (a) The fragmentation technique described by Leo[27] was employed to calculate log P values for 4-nitrophenyl acetate (1.26), 4-nitrophenyl hexanoate (3.61), and 4-nitrophenyl dodecanoate (6.55). (b) Broxton, T. J.; Christie, J. R.; Sango, X. *J. Org. Chem.* **1987**, *52*, 4814. (c) Broxton, T. J.; Christie, J. R.; Chung, R. P. T. *J. Org. Chem.* **1988**, *53*, 3081.

Table 3. Linear Free Energy Relationships for the Kinetic and Binding Parameters of the Reaction of Imidazole with Phenyl Acetates in Water and Aqueous Solutions of CTAB or SDS

reaction in water:	$\log k_u = -0.606(\pm0.058)\mathrm{p}K_a + 4.11(\pm0.48)$	$(r = 0.9488;\ n = 14)$	(2)
reaction in solution of SDS:	$\log k_c = -0.666(\pm0.071)\mathrm{p}K_a + 3.38(\pm0.59)$	$(r = 0.9575;\ n = 10)$	(3)
reaction in solution of CTAB:	$\log k_c = -0.540(\pm0.066)\mathrm{p}K_a + 2.63(\pm0.55)$	$(r = 0.9453;\ n = 10)$	(4)
dissociation constant of the ester−SDS micelle complexes:	$\log K_S = -0.660(\pm0.053)\pi - 1.51(\pm0.06)$	$(r = 0.9639;\ n = 14)$	(5)
dissociation constant of the ester−CTAB micelle complexes:	$\log K_S = -0.589(\pm0.097)\pi - 1.98(\pm0.12)$	$(r = 0.9074;\ n = 10)$	(6)
dissociation constant of the transition state−SDS micelle complexes:	$\log K_{TS} = -0.735(\pm0.117)\pi - 0.293(\pm0.16)$	$(r = 0.9120;\ n = 10)$	(7)
	$[\log K_{TS} = -0.852(\pm0.083)\pi - 0.106(\pm0.097)$	$(r = 0.9476;\ n = 14)]$[a]	
dissociation constant of the transition state-CTAB micelle complexes:	$\log K_{TS} = -0.495(\pm0.117)\pi - 1.17(\pm0.14)$	$(r = 0.8297;\ n = 10)$	(8)
relationship between K_S and K_{TS} for the SDS micelle reaction:	$\log K_{TS} = -1.19(\pm0.11) \log K_S - 1.60(\pm0.25)$	$(r = 0.9695;\ n = 10)$	(9)
relationship between K_S and K_{TS} for the CTAB micelle reaction:	$\log K_{TS} = -0.893(\pm0.077) \log K_S + 0.62(\pm0.19)$	$(r = 0.9713;\ n = 10)$	(10)

[a] This regression includes the lower limits for K_{TS} determined by employing the upper limits of k_c for 3-nitro-, 4-cyano-, 3-cyano-, and 4-acetylphenyl acetates (see Table 1).

Scheme 3. Effective Charge Map and Hansch *p* Map for the Reaction of Imidazole with Substituted Phenyl Acetates in the Presence of CTAB and SDS Micelles[a]



[a] Values of *p* (given in square brackets) are the slopes of the Hansch correlation against π; the Hansch *p* value for water is defined as zero and that for *n*-octanol as unity.

The values of k_c for reaction of imidazole with 4-nitrophenyl hexanoate and acetate are similar within an order of magnitude (Tables 1 and 2) for both micellar species. Since the reaction of the hexanoate involves attack when the ester residue is in the Stern region it is likely that the same goes for the acetate reaction. The conclusion that reaction of the acetate occurs in the Stern region is also supported by the observation[18] of only a small decrease in k_c (which mirrors that in k_u) for the alkaline hydrolysis of 4-nitrophenyl alkanoates in CTAB micelles and by the low value of log *P* for imidazole.

The present data do not favor any particular micelle model but could be interpreteted according to a Dill−Flory lattice-type model[30] where the location of both transition state and reactant ester binding site would be in the surface where alkane side chain and headgroups exist side by side.

The Brønsted dependence for the second-order rate constants of the reaction in water (k_u) (eq 2) and the micelle (k_c) (eqs 3 or 4) measures the change in effective charge[8] on the leaving oxygen of phenolate from the ground state to the transition state in water and the micelle, respectively, as illustrated in the effective charge map (Scheme 3). The Brønsted slopes for the reaction in the micelles are approximately the same as that in water, indicating similar charge development in the transition states and a near normal water activity at the interface. Previous workers came to the same conclusion by showing that the extent of hydration of counterions incorporated into the Stern region is about the same as that in bulk aqueous solvent.[31−33] The insensitivity of k_c to π

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(26) The slope of a linear Hansch correlation with π may be employed as a measure of the nature of the complexation medium by comparing it with the slopes for complexation into standard media. Thus, the plot of log *P* versus π will have a slope of unity that is the standard for partitioning into the *n*-octanol phase from aqueous solution; a zero slope is obtained for the identity partitioning from water into water. The approach is the same as that employed by Leffler (see ref 24, p 52), who compared α values for rate constants with those for equilibrium constants to measure the progress of reaction as a function of reactant and product. A Hansch *p* value of zero for transfer between two states (such as complexed ester and complexed transition state) indicates that there is no change in microsolvation environment between the two states. A value for *p* of unity for transfer from water to the complexed system indicates that the medium in the complex has the attributes toward hydrophobic interactions such as *n*-octanol. A value of *p* of zero for such a system indicates that the part of the substrate where π varies resides in an aqueous environment in the complexed system.

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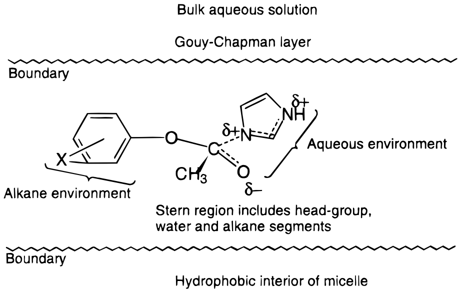
indicates that there is no *change* in hydrophobic complexing capacity in the medium between reactant state and the transition state. Although the transition state may be in the Stern region, for the reasons already given the results indicate that the substituted phenyl group must have substantial hydrophobic interactions with the micelle and that its locus in the transition state has similar polarity to that of the ester binding.

The dissociation constants (K_{TS}) for both SDS and CTAB reactions (Tables 1 and 2) indicate weaker binding of the transition state to the micelle than that of the ester substrate. The values of the transition-state dissociation constants provide an alternative way of indicating the micro-solvation environment of the locus of the transition state. The values of log K_{TS} are linearly related to the corresponding log K_S value (Figure 6 and eqs 9 and 10). The slope is significantly less than unity for CTAB, indicating that the site of the transition state is more aqueous-like than that for ester binding. In the SDS case the slope is slightly greater than unity indicating that the binding of the phenyl residue of the substrate in the transition state is slightly more hydrophobic than the locus of binding of binding the reactant state.

The inhibition caused by the SDS micelles is undoubtedly due to the preferential complexation of the ester compared with that for the reactant imidazole, although the observation of a significant k_c parameter indicates that the imidazole is not completely excluded from the micellar pseudo phase. The results of this study refer to limited ranges of ester, imidazole, and detergent concentrations. When these ranges are greatly exceeded, there is little doubt that the rate laws will change due to the likely massive changes in the structures of the micelles. The lower value of k_c compared with that of k_u would also be expected due to the greater steric requirements for nucleophilic attack at the complexed ester.

A Hansch dependence has been observed for the dissociation constant between esters of substituted phenyl acetates and the micelle of the imidazolyl containing detergent, dimethyl[2-(4-imidazolyl)ethyl]octadecylammonium chloride (DIEODC).[34] The values of K_S for the acetates and of (*p*) compare with those found here and for the dissociation constants of aromatic substrates and inhibitors from chymotrypsin.[35] The results of this study enable an effective molarity to be determined for the intramolecular reaction of imidazolyl group with the complexed ester in the DIEODC micelle. Division of the first-order rate constant for reaction of the complexed ester in DIEODC by the second-order rate constant for reaction of imidazole with CTAB complexed ester gives an average value of 4.9 for the acetates (1, 5, 8, and 9). This is a relatively low effective molarity for an intramolecular reaction of an acyl function with a nucleophile[36] and is similar to those values found for intramolecular proton-transfer reactions. Low effective molarities are consistent with a high degree of disorder in the intramolecular reaction between complexed ester and the imidazolyl group of the detergent; this might be expected for micelle-catalyzed reactions.

Scheme 4. Schematic of the Location, in the Interface of an SDS-Micelle, of the Transition State for Acetyl Imidazole Formation



The conclusions that can be made from this study that the location of the transition state is close to the Stern layer of the micelle are reasonable as it would prove difficult for the imidazole to penetrate into the hydrophobic interior. The Hansch and Brønsted dependencies also indicate that the orientation of the ester part of the transition state in both micellar types is such that the substituted phenyl component resides in the Stern region. We represent this conclusion in the schematic structure of Scheme 4. The conclusions agree with those of Tee and Fedortchenko[18] for the reaction of hydroxide ion with 4-nitrophenyl esters mediated by CTAB where there is even more reason for the reagent, hydroxide ion, not to enter the core region of the micelle.

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