Micellar Inhibition of S_N1 Reactions of Sterically Hindered Compounds

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Aqueous cationic micelles of cetyltrimethylammonium surfactants (CTAX; X = Br, Cl, or $0.5SO_4$) and dodecyltrimethylammonium bromide, and anionic micelles of sodium lauryl sulphate (NaLS) inhibit S_N1 hydrolyses of sterically hindered arenesulphonates and chlorides. The substrates were 2-adamantyl *p*-bromobenzenesulphonate (brosylate) and *p*-nitrobenzenesulphonate, 1,2,2-trimethylpropyl (pinacolyl) tosylate, brosylate, benzenesulphonate, and *p*-methoxy- and *p*-nitrobenzenesulphonate, and 2,2-dimethyl-1-phenylpropyl chloride and tosylate. Micellar inhibition increases with increasing substrate hydrophobicity but is always larger with cationic than with anionic micelles by factors of between 2 and 5 for the arenesulphonate, and 10 for 2,2-dimethyl-1-phenylpropyl chloride. The difference is much larger for hydrolysis of diphenylmethyl chloride and bromide. For hydrolysis of 1-benzylbutyl tosylate, with nucleophilic participation by water, micellar inhibition is smaller than with the hindered substrates but greater with cationic than with anionic micelles. These micellar inhibitions are compared with those on deacylations which are dominated by bond-making and where reaction is faster in cationic than in anionic micelles. Micellar medium effects are related to the mechanisms of these spontaneous hydrolyses and to substrate structure. Substituent effects were examined for S_N reactions in water; $\rho \approx 1.5$ for hydrolyses of pinacolyl arenesulphonates, and is similar for hydrolyses in micelles.

Micellar effects upon the rates of thermal reactions in water have been extensively studied.[1-4] For bimolecular, non-solvolytic reactions the main effect depends upon the ability of a micelle to bring reactants together, and so speed reaction, or to keep them apart and so inhibit reaction. For many reactions of anionic nucleophiles second-order rate constants in the micellar pseudophase are similar to those in water,[1c,d,e,2-4] suggesting that for these reactions the medium effect of the micelles is similar to that of water. Aromatic nucleophilic substitution by azide ion is an exception to this generalization because reactivity in the micelle is much larger than expected.[5]

The situation is different for spontaneous unimolecular, and bimolecular, water-catalysed reactions where medium effects, and differences in the reactivity of water in the bulk and at the micellar surface, may be important. But rate and equilibrium constants for water addition are often similar to those in water,[6] in accord with the assumption of a highly aqueous micellar surface.[7]

Micellar rate enhancements of spontaneous decarboxylations[8] and hydrolyses of anionic phosphate[9] and sulphate esters,[10] and inhibition of S_N1 reactions,[11-13] are consistent with the polarity of the micellar surface being lower than that of water. Water nucleophilicity should not be important in these reactions, although water molecules may be intimately involved in solvating initial and transition states.

There also appears to be an effect dependent on micellar charge, even though net charge does not change in transition state formation. For example deacylations of micelle-bound substrates are faster in cationic than in anionic micelles[13,14] whereas the opposite is true for S_N reactions of phenylmethyl halides.

Our approach is to compare rate constants for hydrolyses of fully micelle-bound substrates in anionic and cationic micelles. This approach eliminates uncertainties due to partial incorporation of substrate in the micelle, which will depend on substrate hydrophobicity. The polarity of the micellar surface, and water activity, are believed to be insensitive to micellar charge, so that differences in rate constants in cationic and anionic micelles should be indicative of specific interactions between micellar head groups and reaction centres.

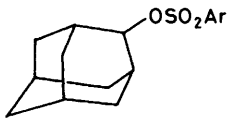
Micellar effects on reaction rate are analogous to solvent effects which depend on changes in the relative free energies of initial and transition states.[15] Micellar binding reduces the free energy of the initial state, which, of itself, will slow reaction, unless there is an offsetting stabilization of the transition state, or an acceleration due to increased concentration of a second reactant in the micelle.

It is difficult to define the precise role of solvent in solvolytic S_N reactions. The original definition of an S_N1 reaction required that the solvent (or other nucleophile) did not interact covalently with the reaction centre in the transition state, whereas this interaction was considered to be important in an S_N2 reaction.[16] However, it was recognized that solvent molecules could solvate both the cationic reaction centre and the leaving group, so that a distinction between solvation and nucleophilic interaction was implied in the definition. More recently the S_N1–S_N2 mechanistic spectrum has been described in terms of a mechanistic continuum, with varying degrees of bond-making and -breaking.[17] Bentley and Carter have provided evidence for solvation of the reaction centre in the solvolyses of t-butyl halide in nucleophilic solvents, hitherto regarded as archetypal S_N1 reactions.[18] The implications of this work are that participation by solvent may be important in solvolysis of any open-chain substrate, unless it is precluded by intervention of a neighbouring group, or hindered by a very bulky substituent.

We have extended earlier work on micellar effects upon S_N1 hydrolyses of open-chain substrates[13] to systems in which solvent attack from the rear of the substrate will be blocked sterically. We were restricted in our choice of substrates because, to avoid major substrate effects upon micellar structure, surfactant was in large excess over substrate. Thus spectrophotometry was the method of choice for following these reactions in ionic micelles. Therefore, our substrates were either arenesulphonates or had phenyl substituents in the alkyl groups.[13]

2-Adamantyl arenesulphonates, (1a—c) are convenient substrates because nucleophilic attack upon the reaction centre is precluded sterically.[17,19]

The other substrates were α-substituted neopentyl derivatives, *i.e.* pinacolyl (1,2,2-trimethylpropyl) arene sulphonates (2a—e), and we used 2,2-dimethyl-1-phenylpropyl tosylate and chloride (3a and b) to compare the effects of chloride and arenesulphonate as leaving groups.[20] Nucleophilic interactions with solvent should be unimportant in these reactions.[17-21]



(1)

a; Ar = p-MeOC$_6$H$_4$
b; Ar = p-BrC$_6$H$_4$
c; Ar = p-O$_2$NC$_6$H$_4$

Me$_3$C–CHMe–OSO$_2$Ar (2)

a; Ar = p-MeOC$_6$H$_4$
b; Ar = p-MeC$_6$H$_4$
c; Ar = C$_6$H$_5$
d; Ar = p-BrC$_6$H$_4$
e; Ar = p-O$_2$NC$_6$H$_4$

Me$_3$C–CHPhX (3)

a; X = p-MeC$_6$H$_4$SO$_3$ b; X = Cl

PhCH$_2$CHOSO$_2$–C$_6$H$_4$Me(p)
|
CH$_2$CH$_2$Me (4)

1-Benzylbutyl tosylate (4) should undergo hydrolysis with nucleophilic participation by water. We included it in our investigation because it has the same empirical formula as (3a), and the two compounds should have similar hydrophobicities and therefore bind similarly to micelles, but react by very different mechanisms.

We used sodium lauryl sulphate ($C_{12}H_{25}OSO_3Na$, NaLS) as the anionic surfactant, and cetyltrimethylammonium bromide ($C_{16}H_{33}NMe_3Br$, CTABr) was generally the cationic surfactant, but we also used dodecyltrimethylammonium bromide ($C_{12}M_{25}NMe_3Br$, DOTABr) to give information regarding the importance of the length of the alkyl group of the cationic surfactant. A problem is that CTABr is not very soluble in water, and at high [surfactant] we had to use CTACl or $(CTA)_2SO_4$. In addition Br^- is an effective nucleophile in a cationic micelle, although it does not trap diphenylmethyl carbocations,[13] but $(CTA)_2SO_4$ has a relatively non-nucleophilic counteranion.

The change of rate with added surfactant is greatest with hydrophobic substrates which bind strongly to the micelle,[1] but we were interested in the reactivity of substrates which were fully micelle-bound, and most of our rates were measured at surfactant concentrations for which substrate was largely in the micelle. Therefore we were not concerned with the extent of distribution of substrate between aqueous and micellar pseudophases, or the way in which this distribution depended on micellar charge or structure. Our major goal was to attempt to relate relative reactivities in cationic and anionic micelles to substrate structure and reaction mechanism, and to the postulated polarity and water activity at the micellar surface.[6,12,14,22,23]

Solvolyses of most of these compounds had been examined in the absence of surfactant, but not in water.[17,19,20,21,24] They are too insoluble to be studied in water, and we examined the non-micellar reactions in aqueous acetonitrile and extrapolated the rate constants to water. Acetonitrile is a convenient solvent because it is relatively inert and absorbs only at low wavelengths.

Results and Discussion

Hydrolyses in Water.—The first-order rate constants, k_ψ, for reaction in H_2O–MeCN at 25.0 °C are available in Supplementary Publication No. SUP 23764 (3 pp.),* and the values extrapolated to water, k'_w, are in Table 1. The extrapolation was made by plotting the observed first-order rate constants, k_ψ, against vol % MeCN. The plots were linear, except for some solutions of relatively low water content. We also plotted log k_ψ against vol % MeCN; the two sets of values of k'_w agreed reasonably well. The uncertainty in k'_w is largest for the more hydrophobic substrates for which we had to use most MeCN.

As control we estimated rate constants in water from rate constants which had been determined in organic or mixed solvents at 25 °C, or could be extrapolated to that temperature using the Arrhenius equation. The rate constants in water can then be calculated using the Grunwald–Winstein equation,[25] based on Y or Y_{OTs} values of solvent polarity [17a,c] by extrapolation, where possible, or assuming a sensitivity to solvent ionizing power (m value) of unity.

Table 1. First-order rate constants for hydrolysis in water [a]

Compd.	Alkyl group [b]	Leaving group	$10^3k'_w/s^{-1}$
(1a)	2-Ad	$MeOC_6H_4SO_3$	0.18 (0.14 [c])
(1b)	2-Ad	$BrC_6H_4SO_3$	1.6 (1.3 [c])
(1c)	2-Ad	$O_2NC_6H_4SO_3$	9.5 (9.8 [c])
(2a)	Pin	$MeOC_6H_4SO_3$	2.0
(2b)	Pin	$MeC_6H_4SO_3$	4.5 (10,[d] 6.5 [d,e])
(2c)	Pin	$C_6H_5SO_3$	4.3
(2d)	Pin	$BrC_6H_4SO_3$	7.1 (30,[d] 6.8 [d,e])
(2e)	Pin	$O_2NC_6H_4SO_3$	70
(3a)	Me_3CCHPh	$MeC_6H_4SO_3$	1 000 (990 [f])
(3b)	Me_3CCHPh	Cl	0.5 (0.85,[f] 0.26 [e,f])
(4)	$PhCH_2CHPr$	$MeC_6H_4SO_3$	0.2

[a] Values in parentheses are calculated from rate constants of solvolysis in organic or aqueous organic solvents (see text). [b] Ad = adamantyl; Pin = pinacolyl. [c] Ref. 24a. [d] Ref. 24b. [e] Based on extrapolation using Y values. [f] Ref. 20.

The various rate constants calculated in terms of the Y_{OTs} (or Y) scale are in reasonably good agreement with our observed rate constants (Table 1) considering that experiments were carried out in very different solvents and sometimes at different temperatures. Most of our rate constants are within a factor of 2 of those calculated by extrapolation from other solvents.

For one substrate, 1-benzylbutyl tosylate (4), an estimated rate constant in water, $k_\psi = 2 \times 10^{-4}$ s^{-1}, is not very different from the value of k_ψ (3.7×10^{-4} s^{-1}) for hydrolysis of the chemically similar 1-benzylethyl tosylate extrapolated from the rate constant in formic acid using $m = 1$ and Y values.[26] This extrapolation is only a crude approximation because water probably participates nucleophilically in aqueous solvents, and there may be phenyl participation in formic acid.

Structural Effects upon Hydrolysis in Water.—Structural effects upon S_N reactions have been discussed in detail, largely on the basis of reactivities in organic or aqueous organic solvents.[16,27] For a series of pinacolyl arenesulphonates our values of k_ψ in water follow the electron-withdrawing effect of the p-substituent. A plot of log k_ψ against σ_p has a slope of 1.5, which is similar to that for ethanolysis of adamantyl arenesulphonates where $\rho = 1.76$ and 1.86 for the 1- and 2-

* For details of Supplementary Publications see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 2*, Issue 1, 1984.

Table 2. Hydrolysis of 2-adamantyl brosylate in surfactants [a]

[D]/M	NaLS	CTABr
0	160	
0.001		30
0.0075	29	
0.01	2.9	0.29
0.02	1.3	0.20
0.03		~0.15
0.04	0.89	
0.06	0.84	
0.08	0.84	

[a] Values of $10^5 k_\psi/s^{-1}$, at 25.0 °C.

Table 3. Hydrolysis of 2-adamantyl *p*-nitrobenzenesulphonate in surfactants [a]

[D]/M	NaLS	CTABr	DOTABr
0	950		
0.001		150 [b]	
0.002		20	
0.01	218	4.8	
0.02	5.9	3.4	
0.025	6.1		
0.03		2.3	
0.04	4.7	1.9	
0.06	4.0		
0.08	3.8		
0.10		1.2, 1.1 [c]	3.3
0.12	3.8		
0.20	3.7	1.2 [c]	2.6
0.40	3.0	1.0 [c]	2.1

[a] Values of $10^5 k_\psi/s^{-1}$, at 25.0 °C. [b] In 2 wt % MeCN. [c] In CTACl.

Table 4. Hydrolysis of pinacolyl *p*-methoxybenzenesulphonate in surfactants [a]

[D]/M	NaLS	CTABr	DOTABr
0	20		
0.0003		18.5	
0.0016	18.0	4.0	
0.005	15.3	1.2	
0.0075	8.9		
0.01	4.3	0.67	
0.02	0.83	0.43	
0.04	0.43	0.33	
0.05	0.43		
0.07		0.14	
0.1		0.13, 0.10 [b]	0.26
0.2	0.22	0.12 [b]	0.16
0.4	0.19	0.09 [b]	0.13

[a] Values of $10^4 k_\psi/s^{-1}$, at 25.0 °C. [b] In CTACl.

adamantyl derivatives respectively, and only slightly larger than ρ for solvolyses of primary and secondary alkyl arenesulphonates in alcoholic or aqueous alcoholic solvents.[24a,c] Substituent effects are similar for hydrolysis of 2-adamantyl arenesulphonates in water (Table 1), but here we only examined three compounds and cannot estimate ρ.

The reactivities of tosylate and chloride as leaving groups [reactions of (3a) and (3b) in Table 1] differ by a factor of *ca.* 2 000, which is much smaller than the difference generally observed; for example a factor of 2×10^5 has been reported as typical of S_N1 reactions.[27] The lower value in water is probably due to differences in solvation of the leaving group. In water this hydration should favour chloride over tosylate, and the difference in solvation of these forming ions should be smaller in organic or aqueous organic solvents which were used earlier.

Table 5. Hydrolysis of pinacolyl tosylate in surfactant [a]

[D]/M	NaLS	CTABr	DOTABr
0	45		
0.03		0.27	
0.06	0.57		
0.07		0.14	
0.08	0.56		
0.10	0.50	0.11	0.36
0.12	0.49		
0.20	0.42	0.12 [b]	0.27
0.40	0.31	0.11 [b]	0.18

[a] Values of $10^4 k_\psi/s^{-1}$ at 25.0 °C. [b] In CTACl.

Table 6. Hydrolysis of pinacolyl benzenesulphonate in surfactant [a]

[D]	NaLS	CTACl	DOTABr
0	26		
0.10		0.61	
0.20	0.70	0.34, 0.15 [b]	0.7
0.40	0.57	0.2	0.5

[a] Values of $10^4 k_\psi/s^{-1}$ at 25.0 °C. [b] 0.2M-$(CTA)_2SO_4$.

Table 7. Hydrolysis of pinacolyl brosylate in surfactant [a]

[D]/M	NaLS	CTABr	DOTABr
0	71		
0.10		0.64	
0.20	1.5	0.66 [b]	1.3
0.40	1.3	0.56 [b]	0.9

[a] Values of $10^4 k_\psi/s^{-1}$ at 25.0 °C. [b] In CTACl.

The pinacolyl arenesulphonates are consistently more reactive than the corresponding 2-adamantyl derivatives (Table 1). The reactivity differences are not large (no more than a factor of 10), suggesting that nucleophilic assistance is not of major importance in hydrolyses of the pinacolyl arenesulphonates in water.[17]

The effect of replacing an α-methyl group in pinacolyl tosylate (2b) by a phenyl group, as in (3a), is relatively small (Table 1), as compared with that on the ethanolysis of isopropyl and 1-phenylethyl chloride where reactivities differ by a factor of *ca.* 10^5,[27,28] even though ethanolysis of isopropyl chloride may have extensive S_N2 character. Several factors may be responsible for these marked differences, and we do not have sufficient evidence to distinguish between them. (i) The β-methyl group in (2b) may be participating in its ionization, but not in ionization of (3a). This explanation is improbable, because there is little evidence for participation by neighbouring alkyl groups in open-chain systems.[17,24b] (ii) The bulk of the t-butyl group in (3a) may make it difficult for the α-phenyl group to be coplanar with a forming carbocation. (iii) Water may be so effective in assisting charge formation in S_N1 reactions that electron release by α-substituents becomes relatively unimportant. Comparison of parameters such as *m* and *l* for a variety of substrates provides no support for this argument,[17a,27] although the comparison is based on organic solvents which may be less effective than water in solvating anionic and cationic centres.

Micellar Inhibition.—All our hydrolyses are micelle-inhibited (Tables 2—11).[13] Rate effects of micelles in water are generally treated in terms of a distribution of reactants between aqueous and micellar pseudophases.[1-4,29] The distribution of substrate, S, between aqueous and micellar pseudophases (designated by subscripts W and M), and the reaction in each pseudophase, are illustrated in Scheme 1 and

Table 8. Hydrolysis of pinacolyl *p*-nitrobenzenesulphonate in surfactant [a]

[D]/M	NaLS	CTABr	DOTABr
0	700		
0.001		320	
0.005		37	
0.0075	340		
0.01	115	22	
0.02	30	13	
0.04	17	8.6	
0.05		7.4	
0.06	10		
0.07		8.8	
0.08	10		
0.1		5.5, 5.8 [b]	13.7
0.2	9.0		10.0
0.4	7.0	3.8 [b]	9.0

[a] Values of $10^4 k_\psi/s^{-1}$ at 25.0 °C. [b] In CTACl.

Table 9. Hydrolysis of 2,2-dimethyl-1-phenylpropyl tosylate in surfactants [a]

[D]/M	NaLS	CTABr	DOTABr
0	1 000		
0.03		0.64	
0.05		0.61	
0.07		0.66	
0.08	7.0		
0.10	5.9	0.59	1.9
0.12	6.1		
0.20	5.0	0.6, 0.60 [b]	1.3
0.40	3.9		1.0

[a] Values of $10^3 k_\psi/s^{-1}$ at 25.0 °C. [b] In CTACl.

Table 10. Hydrolysis of 2,2-dimethyl-1-phenylpropyl chloride in surfactants [a]

[D]/M	NaLS	CTABr
0	50	
0.0075	25	
0.01	7.4	0.54
0.02		0.19
0.025	2.0	
0.03		0.10
0.04	1.1	
0.06	1.6	
0.08	0.78	
0.12	0.63	

[a] Values of $10^5 k_\psi/s^{-1}$ at 25.0 °C.

equations (i)—(iii), where D_n is micellized surfactant, and cmc is the critical micelle concentration.

$$[D_n] = [D] - \text{cmc} \quad \text{(i)}$$

$$K_s = [SD_n]/[S_W]([D] - \text{cmc}) \quad \text{(ii)}$$

$$k_\psi = \{k'_W + k'_M K_s([D] - \text{cmc})\}/\{1 + K_s([D] - \text{cmc})\} \quad \text{(iii)}$$

Equation (iii) can generally be applied to micelle-inhibited reactions and to spontaneous reactions. But there is a problem when reactants are very hydrophobic, because they may induce micellization, or react in submicellar aggregates, so that equation (i) does not give the concentration of micellized surfactant.[30] This situation applies in some of our experiments where we see inhibition at surfactant concentrations below the cmc (Table 4 and ref. 13).

However, we are concerned with the rate constants, k'_M for fully micelle-bound substrate, and these values can be determined by following the reaction in relatively concentrated surfactant, so that essentially all the substrate is micelle-bound, or by extrapolation. At high surfactant concentration equation (iii) reduces to (iv), so that a plot of

$$k_\psi = k'_M + k'_W/K_s([D] - \text{cmc}) \quad \text{(iv)}$$

k_ψ against $1/([D] - \text{cmc})$ should extrapolate to k'_M at high [D]. Under these conditions [D] ≫ cmc, so that uncertainties in the cmc are relatively unimportant and we used this method to calculate the values of $k_{rel} = k'_M/k'_W$ in Table 12 for most of the compounds. For a few compounds we can only quote upper limits for k_{rel}, and for some compounds we used CTACl or $(CTA)_2SO_4$ instead of CTABr at high surfactant concentrations, because of the relatively low solubility of CTABr at 25 °C [on a molar basis $(CTA)_2SO_4$ contains twice as much surfactant as CTACl or CTABr].

Plots of log k'_M against σ for hydrolysis of pinacolyl arenesulphonates give values of ρ which are similar to that for reaction in water (ρ = 1.5), with ρ ≈ 1.6, 1.65, and 1.8 in NaLS, CTABr, and DOTABr, respectively. Qualitatively, leaving-group effects upon hydrolyses of the 2-adamantyl derivatives are similar to those in water. (Hydrolysis of the *p*-methoxybenzenesulphonate is too slow to be followed in micelles.)

Table 12 includes values of k^+/k^- where k^+ and k^- are respectively values of k'_M (for fully bound substrate), typically in CTABr and NaLS respectively, and also values of $k_{rel} = k'_M/k'_W$ which give the overall micellar rate retardation. Values of k'_W, k_{rel} and k^+/k' for other S_N reactions are also in Table 12.[13]

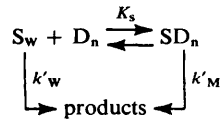
Effects of Micellar Structure.—It is convenient first to consider reactions of the 2-adamantyl and pinacolyl compounds, where there should be no nucleophilic participation by water. The micelle can affect reaction in two ways. (i) It can exert medium effects, because of a lower polarity than water, or inability of micelle-bound water to stabilize forming ions.[7,12-14,23] (ii) The micellar charge may affect the rate of a reaction in which the charge distribution changes during transition state formation. It is this second effect which may lead to rate differences for substrates bound fully to cationic or anionic micelles.[1b]

Substrate hydrophobicity affects micellar inhibition in two ways.[1-4] First, the sharpness of the decrease of rate constant with increasing [surfactant] depends upon the extent to which substrate is transferred from aqueous to micellar pseudophase, which depends upon substrate hydrophobicity.

Table 11. Hydrolysis of 1-benzylbutyl tosylate in surfactant [a]

[D]/M	NaLS	CTACl	DOTABr
0	210		
0.1	7.3		9.1
0.2	7.2	4.4	
0.4	6.8	2.0 [b]	9.2

[a] Values of $10^6 k_\psi/s^{-1}$ at 25.0 °C. [b] In $(CTA)_2SO_4$.



Scheme 1.

Table 12. Effects of substrate structure and micellar charge upon hydrolysis in surfactants

[Compd.]	[Alkyl group]	[Leaving group]	$[10^3k'_w/s^{-1}]$	10^3k_{rel} NaLS	CTABr	DOTABr	k^+/k^-
(1b)	2-Ad	$BrC_6H_4SO_3$	1.6	4	0.7	2	0.2
(1c)	2-Ad	$O_2NC_6H_4SO_3$	9.5	4	1	4.5	0.3
(2a)	Pin	$MeOCH_4SO_3$	2.0	8.5	3.5	2.5	0.4
(2b)	Pin	$MeC_6H_4SO_3$	4.5	6	2.5	6	0.4
(2c)	Pin	$C_6H_5SO_3$	4.3	10	2 [c]	8	0.2
(2d)	Pin	$BrC_6H_4SO_3$	7.1	15	7.5	11	0.5
(2e)	Pin	$O_2NC_6H_4SO_3$	70	10	5	0.7	0.5
(3a)	Me_3CCHPh	$MeC_6H_4SO_3$	1 000	3	0.6		0.2
(3b)	Me_3CCHPh	Cl	0.5	7	0.6		0.1
(4)	$PhCH_2CHPr$	$MeC_6H_4SO_3$	0.2	~30	~10		0.3
	Ph_2CH	Cl [a]	~990	~500	~7 [c]		~0.01
	PhCHMe	Cl [a]	51	54	7 [c]		0.15
	$PhCH_2$	Br [a]	0.16	130	90		0.7
	Me	$PhSO_3$ [a]	0.011	390	700 [d]		1.8
	PhCO [b]	Cl [a]	860 [e]	60	40		0.7

[a] Ref. 13. [b] Acyl group. [c] In CTACl. [d] In CTAOMs. [e] The value was estimated by extrapolation of data in aq. MeCN, and was reported incorrectly as 86×10^{-3} s^{-1} in ref. 13. Dr. T. W. Bentley has informed us that he estimates the rate constant as $1\,500 \times 10^{-3}$ s^{-1} conductimetrically.

Secondly, although most polar solutes, such as our substrates, seem to reside, on the average, close to the water–micelle interface,[1] the more hydrophobic substrates may spend more time away from the surface in a less polar region. For example micellar inhibition, as given by k_{rel} (Table 12), tends to be larger for the adamantyl and 2,2-dimethyl-1-phenylpropyl arenesulphonates than for the pinacolyl arenesulphonates, which should be less hydrophobic, and therefore less likely to go deeply into the micelle. However, the differences are not large, consistent with evidence that polar organic solutes bind in clefts at the micellar surface.[6-8,14,31]

There are a variety of estimates of the polarity of micellar surfaces, generally based on comparison of spectral shifts of indicators bound to the micelle and in bulk solvents.[7,22,23] For example, effective dielectric constants at the surface of ionic micelles have been estimated to be in the range 30—40,[14,22] and for several micelles Kosower's $Z \approx 85$. This value is similar to that of methanol (83.6). Comparison of the Z and Y scales, based on aqueous methanol,[32] suggests that $Y \approx -1$ at a micellar surface, assuming that one can apply parameters based on properties of bulk solvents to a submicroscopic micelle–water interface.

Micellar inhibition of S_N1 reactions by ionic micelles is much less than that expected on the basis of these polarity estimates. For example, cationic micelles inhibit hydrolyses of 2-adamantyl arenesulphonates by factors of less than 2 000, and inhibition by anionic micelles is even less (Table 12), but based on $Y = 3.49$ for water [25] and $m \approx 1$, equation (i), the rate should be reduced by a factor of 3×10^4. The predicted rate decrease would be even larger if the comparison was based on Y_{OTs}.

Added electrolytes exert specific positive salt effects on S_N1 reactions,[16,17a,33] and their effect should be very large at the surface of an ionic micelle where the ionic concentration is very high; for example it is estimated to be *ca.* 4M on a micelle of NaLS.[34] (Although common ion inhibition is observed with halide ions in aqueous acetone,[16] there is no such inhibition in cationic micelles,[13] consistent with the micellar reaction occurring in a water-rich environment.)

An effect related to micellar charge is superimposed upon those related to ' micropolarity,' or water activity, at the micellar surface, because, except for hydrolysis of methyl benzenesulphonate, all the S_N reactions are faster in anionic than in cationic micelles, *i.e.* $k^+/k^- < 1$ (Table 12 and ref. 13). However, the magnitude of this ' charge ' effect depends upon substrate structure, and is much larger for hydrolyses of diphenylmethyl halides than for the other substrates, and we must consider interactions between the micellar head groups, or counterions, and the forming cationic and anionic centres in the transition state.

Most of our substrates are arenesulphonates, and our only comparison between chloride and tosylate is for the 2,2-dimethyl-1-phenylpropyl system (3a and b). Values of k^+/k^- are 0.1 and 0.2 for chloride and tosylate respectively (Table 12), and this difference is probably due to interactions between the forming tosylate ion and the quaternary ammonium ion head groups in a CTABr micelle. The binding between cationic micellar head groups and arenesulphonate ions is very much stronger than that with Cl^-, and depends on interactions between the ammonium ions and the π-rich arene group.[8,35]

This difference between leaving groups is, however, insufficient to account for the value of $k^+/k^- \approx 0.01$ in hydrolyses of diphenylmethyl halides, and values of 0.1—0.5 for hydrolyses of the sterically hindered substrates (Table 12 and ref. 13). We believe that this difference must be due to an electrostatic interaction between the forming carbocation centre in a diphenylmethyl halide and the sulphate ion head group of an anionic micelle, which assists reaction. Neighbouring group participation by carboxylate ions in S_N reactions has been ascribed by various workers to either coulombic or covalent interactions,[16,36] and our proposed effect is analogous to the electrostatic description. However, interaction between a sulphate ion head group and a forming carbocation should be much more effective with a diphenylmethyl halide, where the rear of the reaction centre is open, than with sterically hindered substrates where the rear of the reaction centre is blocked.

For hydrolysis of a diphenylmethyl halide in a cationic micelle the leaving halide ion will be solvated by water, and interactions between the carbocationic centre and the micellar head groups will be coulombically unfavourable, but will be favourable in an anionic micelle. In this context we note that in polar protic solvents low charge density anions, such as perchlorate, are much more effective than small high charge density anions in speeding S_N1 reactions.[33]

Interactions between the sulphate moiety in an anionic micelle and the reaction centre should be relatively unimportant for substrates whose hydrolysis involves nucleophilic

participation by water, as with the primary and unhindered secondary alkyl compounds (Table 12).

Reactions are slightly faster in micelles of DOTABr as compared with CTABr (Table 12). Also, regardless of micellar charge, micellar inhibitions, as given by k_{rel}, are larger for S_N1 reactions with the more hydrophobic substrates. These (small) effects suggest that, on average, substrates are located more deeply in the micelles, and away from the micelle–water interface, with increasing chain length of the surfactant, and increasing substrate hydrophobicity. Pinacolyl *p*-nitrobenzenesulphonate (3b) behaves differently from the other substrates in that hydrolysis is slightly faster in DOTABr than in NaLS. (Nitro-compounds may behave differently from the other substrates because hydrolysis of *p*-nitrophenyl chloroformate is faster in CTABr than in water, whereas all the other deacylations are micellar inhibited, *cf.* ref. 13.) Comparison of the behaviour of pinacolyl and 2,2-dimethyl-1-phenylpropyl tosylates [(2b and 3b), Table 12] suggests that substrate hydrophobicity is not very important, because a phenyl group should markedly increase interaction with the micelle.

1-*Benzylbutyl Tosylate*.—Nucleophilic interactions between water and the alkyl group should be important in hydrolysis of 1-benzylbutyl tosylate (4). This substrate was used because it is more hydrophobic than benzyl and benzoyl chlorides, which should be hydrolysed by S_N2-like mechanisms,[37] but for which reaction is faster in anionic than in cationic micelles.[13]

Most spontaneous bimolecular deacylations, and hydrolysis of methyl benzenesulphonate, are faster in cationic than in anionic micelles, whereas the opposite is observed with S_N hydrolyses of other primary and secondary alkyl halides or arenesulphonates,[13] even though there is extensive covalent interaction with water in the transition state. These differences suggest that in spontaneous S_N2-like hydrolyses in water the transition states are ' loose,' except for hydrolyses of methyl derivatives. This conclusion is consistent with analyses based on Jencks–More O'Ferrall free energy diagrams which suggest that there is extensive bond-breaking and limited bond-making in the transition state, which would therefore have considerable ionic character.[38] On the other hand formation of tetrahedral intermediates in deacylation involves no bond-breaking, but extensive bond-making, in the transition state. Hydrolysis of methyl benzenesulphonate is different, in this respect, from the other S_N hydrolyses, and the energetics of formation of a methyl cation are so unfavourable that bond-making, rather than bond-breaking, should be important in this reaction.[39]

Relation between Reaction Rate and Micellar Micropolarity and Water Activity.—The overall factors which influence reactivity in normal micelles are reasonably well understood. In particular, both water reactivity and polarity at the micellar surface seem to be somewhat lower than in bulk water. But we feel that it is difficult to quantify micellar effects upon chemical reactivity in terms of the properties ascribed to bulk solvents, *e.g.* dielectric constant, or polarity based on Y,[25] Z,[23] or E_T,[40] if only because micellar effects upon spontaneous reactions seem to depend upon micellar charge and substrate structure and upon the nature of the reaction. However, the qualitative effects are readily understandable in terms of micellar structure and reaction mechanism, with polar substrates binding largely in clefts at the micellar surface, and therefore in an aqueous environment.[7,14,31,41]

Experimental

Materials.—The surfactants were prepared or purified by standard methods and there were no minima in plots of surface tension against concentration,[30] and the critical micelle concentrations (cmc) agreed with literature values.[42]

The arenesulphonates were prepared, following standard procedures,[17,19,24] by allowing the alcohol to react with purified arenesulphonyl chloride in dried pyridine at 5 °C, generally for 1–2 weeks until there was a copious precipitate of pyridine hydrochloride. Most of the arenesulphonates were solids and were recrystallized from light petroleum (b.p. 35—60 °C). Two arenesulphonates would not crystallize. Their ethereal solutions were dried (K_2CO_3) and ether was removed under high vacuum. All the esters had the expected n.m.r. spectra and equivalent weights (by quantitative hydrolysis), and with one exception [20] m.p.s agreed with literature values. M.p.s were: (1a), 74; (1b) 114; (1c) 144—145; (2c) 39; (2d) 53—54, (2e) 92—93 °C.

The preparation of 2,2-dimethyl-1-phenylpropyl tosylate (3a) had been reported by Winstein and Morse, who had allowed the alcohol to react with tosyl chloride in pyridine for 1 week at 4 °C. The material had m.p. 75—76 °C and was obtained in *ca.* 10% yield.[20] We followed this general procedure, but saw little evidence of reaction in 1 week; however, pyridine hydrochloride crystallized after 5 weeks at 5 °C. 2,2-Dimethyl-1-phenylpropyl tosylate was recrystallized (light petroleum, b.p. 35—60 °C) and had m.p. 89 °C (Found: C, 67.8; H, 7.1. Calc for $C_{18}H_{22}O_3S$: C, 67.9; H, 6.9%).

1-*Benzylbutyl tosylate* (4), prepared in the usual way, had m.p. 49.5—50.5 °C (Found: C, 67.6; H, 6.95. $C_{18}H_{22}O_3S$ requires C, 67.9; H, 6.9%).

2,2-Dimethyl-1-phenylpropyl chloride was prepared from the alcohol and $SOCl_2$.[20] Its b.p. (90 °C at 7 mmHg) agreed with the literature, and it had the expected n.m.r. spectrum and equivalent weight (by quantitative hydrolysis).

Kinetics.—All hydrolyses were followed spectrophotometrically at 25.0 °C unless otherwise specified.[13] It was necessary to use low substrate concentrations ($2.5—5 \times 10^{-5}$M) because some of the substrates were only sparingly soluble in dilute surfactant, and also we wished to avoid excessive perturbation of the micellar structure by these hydrophobic substrates. The absorbance changes during reaction were small, *ca.* 0.03 units, and we had to use the most sensitive setting of a Gilford spectrophotometer (0.1 units full scale). The following wavelengths were used: (1a) 255, (1b) 245, (1c) 255, (2a) 254, (2b) 231, (2c) 235 or 230, (2d) 243, (2e) 250, (3a) 231, (3b) 230, (4) 231 nm. Most reactions were followed to completion, and the first-order rate constants, k_ψ, were then calculated in the usual way, from experimentally determined absorbances at complete reaction. This procedure could not be followed for reactions of the less reactive substrates at high [surfactant]; we then followed the reaction for at least 3 half-lives and calculated k_ψ by curve fitting using a simple computer program.

Hydrolyses could not be followed in water in the absence of surfactant or added organic solvent, in part because of the low solubilities of the substrates, but also because hydrolyses of the more reactive substrates would have been too fast to be followed by conventional methods. We therefore followed the hydrolyses in H_2O–MeCN, in the range 2—40% MeCN (see Supplementary Publication).

The rate constant for hydrolysis of pinacolyl *p*-methoxybenzenesulphonate (2a) determined conductimetrically in 5 vol % MeCN was 1.31×10^{-3} s^{-1}, in good agreement with a value of 1.35×10^{-3} s^{-1} estimated by interpolation from rate constants measured spectrophotometrically in other H_2O–MeCN mixtures.

We also determined the rate constant for solvolysis of pinacolyl brosylate (2c) in EtOH–H_2O (50 : 50 v/v). Our

spectrophotometric value of 9.7×10^{-5} s^{-1} is in reasonable agreement with the literature value of 10.1×10^{-5} s^{-1}.[24b]

Initially it appeared that hydrolysis of 2-adamantyl *p*-nitrobenzenesulphonate (1c) was speeded by dilute surfactant at submicellar concentrations [42] ([NaLS $< 8 \times 10^{-3}$M, [CTABr] $< 8 \times 10^{-4}$M). However, some of these solutions were turbid to the eye, and good first-order rate plots were not obtained. Substrate concentrations were too low for reaction to be followed by acid–base titration, and conductivity experiments gave erratic results in dilute surfactant. Rate effects at submicellar concentrations are often observed, and good first-order rate plots were obtained for hydrolysis of pinacolyl *p*-methoxybenzenesulphonate (2a) at [surfactant] < cmc (Table 4).

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