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Effects of reactive and non-reactive counterion surfactants upon acid hydrolysis of hydroxamic acids

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ABSTRACT: Rates of acidic hydrolysis of hydroxamic acids of the type RCON(OH)R′ ($R = CH_3$, R′ = H, acetohydroxamic acid; $R = C_6H_5$, R′ = H, benzohydroxamic acid; $R = C_6H_5$, $R' = C_6H_5$, *N*-phenylbenzohydroxamic acid) were determined in perfluorooctanoic acid as a reactive counterion surfactant and also with sodium 1-dodecanesulphonate and sodium dodecyl sulphate. The pseudo-first-order rate constants increase with reactive and non-reactive surfactant concentrations. These kinetic results were explained by means of the pseudo-phase ion-exchange kinetic model. Activation parameters were also determined. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: hydroxamic acids; hydrolysis; micellar catalysis; reactive and non-reactive counterions

INTRODUCTION

Hydroxamic acids have been successfully used for a large variety of applications in the analytical, biological and medicinal fields, such as drug delivery systems, siderophores, iron transport and DNA cleavage.[1–10] The hydrolysis of hydroxamic acids to hydroxylamine is an important first step in the quantitative analysis of hydroxamate siderophores. It was our intention to investigate how the incorporation of hydroxamic acids in molecular assemblies can improve their interest in these fields. Studies in the presence of micelles would be of considerable relevance. We are interested[11–15] in the way in which self-assembling ionic colloids influence reaction rates and equilibria, and their relationship to colloidal structure. A study of hydrolysis in the presence of micelles may be a better model and medium than in water from which to draw conclusions concerning its biomedical applications. By using as reaction media the interfaces of direct or reverse cationic or anionic micelles and microemulsions, whose solvation properties are adjustable one can achieve and control the selectivities of these reactions. Many results[16–20] have been published showing different catalytic and inhibitory effects of various types of surfactants in chemical reactions such as acid- and base-catalysed hydrolysis of esters, amides, anilides, acetals, etc. Nevertheless, there appear to have been very few studies analysing the influence of fluorocarbon and hydrocarbon anionic micelles on hydrolysis reactions of hydroxamic acids.[21] Fluorocarbon surfactants behave in a similar way to hydrogenated surfactants in the formation of micellar aggregates, but they have some specific properties different from those of the corresponding hydrocarbon type.

Previous work by Berndt and co-workers[21] on the micellar catalysis of hydroxamic acid has shown that perfluorooctanoic acid is a potential reactive counterion surfactant for acid-catalysed reactions. some kinetic investigations of rates of hydrolysis of octano-, decano- and phenylacetohydroxamic acids employing reactive and non-reactive counterion surfactants have been reported.[21d] However, there appear to have been no kinetic studies of *N*-substituted hydroxamic acids in fluorocarbon micelles. We chose to study the hydrolysis of some carbon- and nitrogen-substituted hydroxamic acids (**I**) in perfluorooctanoic acid (PFOC) as a reactive counterion surfactant and in sodium dodecyl sulphate ($C_{12}H_{25}OSO_3{}^-Na^+$; SDS) and sodium 1-dodecanesulphonate ($C_{12}H_{25}SO_3{}^-Na^+$; SDOS) as non-reactive counterion surfactants.

The kinetic results can be explained by means of the pseudo-phase ion-exchange model.[22] One of its basic assumptions is that in systems containing two ions capable of acting as counterions to the micelle, their competition for micellar charges is governed by an equilibrium similar to that governing the behaviour of ion-exchange resins. In this model, water and micelles are regarded as distinct reaction regions. The overall reaction rate is the sum of the rates in each pseudo-phase and depends upon the rate constants and reactant concentrations in each pseudo-phase.

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Table 1. Dependence of k_ψ on fluorocarbon and hydrocarbon anionic micelles for the hydrolysis of hydroxamic acids

Surfactant (10^2 mol dm^{-3})	$k_\psi(10^5 s^{-1})$						
	Acetohydroxamic acid			Benzohydroxamic acid		*N*-Phenylbenzohydroxamic acid	
	PFOC[a,b]	SDS[a,c]	SDOS[a,c]	SDS[a,c]	SDOS[a,c]	SDS[a,c]	SDOS[a,c]
0	—	18.3	45.2	1.22	1.22	0.935	—
0.02	—	19.7	—	1.26	—	1.04	—
0.03	—	19.8	—	1.30	—	1.18	—
0.05	—	20.0	—	1.40	—	1.23	—
0.10	—	20.3	—	1.90	—	1.34	—
0.12	0.45	—	—	—	—	—	—
0.18	0.51	—	47.8	—	1.24	—	1.01
0.36	0.75	—	48.2	—	—	—	—
0.50	—	20.8	—	2.10	1.28	1.41	1.12
0.60	1.04	—	48.8	—	—	—	—
0.90	1.25	—	49.4	—	1.30	—	—
1.00	—	21.8	—	2.28	—	1.42	1.23
1.20	1.74	—	50.5	—	—	—	—
1.34	1.89	—	—	—	—	—	—
1.83	2.10	—	54.2	—	—	—	—
2.00	—	26.0	—	2.24	1.41	1.51	1.43
2.29	—	—	—	—	—	—	—
2.41	3.42	—	55.3	—	—	—	—
2.75	—	—	—	—	—	—	—
3.00	—	35.0	—	2.36	1.57	1.64	1.56
3.21	—	—	55.9	—	—	—	—
4.00	3.91	40.0	56.1	2.40	—	1.81	—
5.00	4.01	40.3	58.5	2.43	1.62	1.89	1.57
6.00	—	42.6	—	2.45		1.90	
10.0	—	54.1	—	2.47		2.03	
15.0	—	55.1	—	2.85		2.04	
17.0	—	55.5	—	2.88		2.06	
20.0		55.9	—	2.86		2.08	

[a] PFOC = perfluorooctanoic acid; SDS = Sodium dodecyl sulphate; SDOS = Sodium 1-dodecanesulphonate.

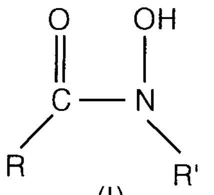
[b] At 65 °C in 1.91 M acetonitrile.

[c] At 55 °C in 5% (v/v) dioxane, 0.35 M HCl.

RESULTS AND DISCUSSION

Most hydroxamic acids are hydrolysed by an *A*-2 mechanism in which hydronium ion is transferred in the transition state and reactions are specifically hydrogen ion catalysed.[23] In the simplest description the first step is a pre-equilibrium protonation and the second step is rate-determining attack of water on the protonated substrate:

We are interested in the ability of aqueous micelles to

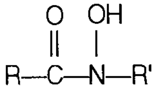


(I)

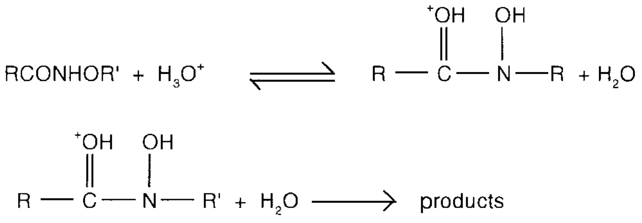
R = CH_3, R' = H: acetohydroxamic acid (AHA)
R = C_6H_5, R' = H: benzohydroxamic acid (BHA)
R = C_6H_5, R' = C_6H_5: *N*-phenylbenzohydroxamic acid (PBHA)

Scheme 1.

Table 2. Kinetic parameters and binding constants obtained in the presence of fluorocarbon and hydrocarbon micelles [Eqn. (1)]

 $R-C(=O)-N(OH)-R'$		Perflurooctonoic acid[a]					Sodium dodecyl sulphate[a]					Sodium 1-dodecanesulphonate[a]				
R	R′	10^5 k_m (s^{-1})	K_s (M^{-1})	$C_D \times 10^2$	r[b]	n	10^5 k_m (s^{-1})	K_s (M^{-1})	$C_D \times 10^2$	r[b]	n	10^5 k_m (s^{-1})	K_s (M^{-1})	$C_D \times 10^2$	r[b]	n
CH_3	H (AHA)	481	54.7	0.12 to 5.0	0.970	8	5.66	12.89	0.02 to 20	0.970	11	68.8	28.4	0.12 to 5.0	0.981	6
C_6H_5	H (BHA)	—	—	—	—	—	2.98	37.2	—	0.970	7	172	33.7	—	0.970	5
C_6H_5	C_6H_5(PBHA)	—	—	—	—	—	2.27	40.9	—	0.990	9	1.81	70.3	—	0.991	5

[a] cmc: PFOC, 2.5×10^{-3}; SDS, 1.0×10^{-3}; SDOS, 1.32×10^{-3} mol dm^{-3}.
[b] r = Correlation coefficient.



Scheme 2.

control reaction rates and equilibria. The kinetic data for acetohydroxamic acid with perfluorooctanoic acid are reported in Table 1. Although perfluorooctanoic acid serves as a source of hydrogen ions, it does not initiate BHA and PBHA for hydrolysis. In non-micellar acidic hydrolyses of hydroxamic acids, pseudo-first-order rate constants increase with acid concentration at low to moderate acidity. For AHA a pseudo-first-order rate constant surfactant profile is observed with a rise in rate constant occurring. For reactive counterion surfactants, the pseudo-phase ion-exchange model is expressed[21a] as

$$k_\psi = \frac{k_w[N_t] + \beta(k_m K_s - k_w)(C_t - \text{cmc})}{K_s(C_t - \text{cmc}) + 1} \quad (1)$$

where k_ψ, k_w and k_m are the observed pseudo-first-order, aqueous phase and micellar phase rate constants, respectively, K_s (M^{-1}) is the substrate–micelle binding constant, β is the degree of counterion binding to the micelle, C_t is the total surfactant concentration and cmc is the critical micelle concentration. N_t is the total concentration of surfactant counterion and is equal to C_t with no added salts. Equation (1) can be rewritten and rearranged in the form

$$k_\psi = \frac{k_w C_t - k_\psi}{K_s(C_t - \text{cmc})} + b \quad (2)$$

where $b = \beta\ (k_m K_s - k_w)/K_s$.

A graph of k_ψ vs (k_w C_t-k_ψ)/(C_t-cmc) is a good linear plot, within experimental error. Evaluation of the slope and intercept for PFOC yields $K_s = 37.2\ \text{M}^{-1}$ and $b = 6.46 \times 10^{-5}\ \text{s}^{-1}$. With sufficiently large K_s, $k_m K_s \gg k_w$ and $b = \beta\ k_m$. The reaction was carried out at 65 °C in aqueous acetonitrile. The reaction of aromatic hydroxamic acids (no hydrolysis) in perfluorooctanoic acid micelles is considerably less than for aliphatic compounds.[24] Perhaps at higher surfactant concentrations a micellar effect on the rates for the aromatic hydroxamic acids might be observable.

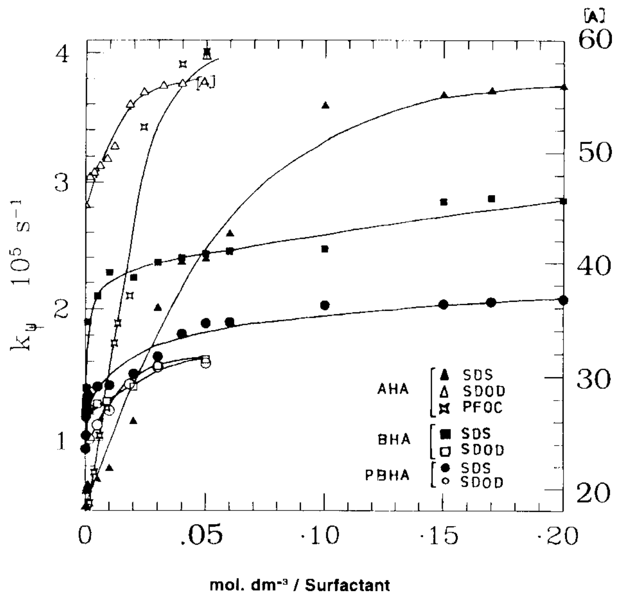


Figure 1. Pseudo-first-order rate constants for the acidic hydrolysis of hydroxamic acids in surfactants

To test for possible specific interactions between substrate and surfactant and to elucidate the effect of non-reactive counterion surfactants, AHA, BHA and PBHA acid hydrolysis with sodium dodecyl sulphate and sodium 1-dodecanesulphonate as surfactants with HCl (0.35 M) was studied. Table 1 and Fig. 1 present the data. In all the cases the pseudo-first-order rate constants increase with increasing [SDS] and [SDOS] and slow at higher concentrations of surfactant. SDOS is more reactive than SDS. The hydrolysis mechanism in the micellar environment can be explained by two functions. The first function is an orientation effect in which the micelles attract the neutral substrate and a reagent, such as H_3O^+ of charge opposite to the charge of the micelle. The other function is micellar stabilization of a transition state of charge opposite to that of the micelle relative to its stabilization of the reagent, in turn relative to stabilization by water, leading to rate enhancement. At high concentrations of surfactant, small changes relative to the micellar effect on reaction were observed. The fraction of organic substrate incorporated into the micelle increases more rapidly with increasing surfactant concentration than the fraction of hydrogen ion incorporated.

Table 3. Kinetic parameters and binding constants obtained in the presence of SDS [Eqn. (2)]

Substrate	k_w (10^5 s^{-1})	10^5 k_m (s^{-1})	K_s (M^{-1})	*n*	r^a
Acetohydroxamic acid	18.3	5.86	56.2	10	0.934
Benzohydroxamic acid	1.22	2.90	104.6	7	0.880
N-Phenylbenzohydroxamic acid	0.935	2.17	116.0	8	0.978

[a] *r* Correlation coefficient.

Table 4. Activation parameters for acetohydroxamic acid in different surfactants

Surfactant	Concentration (10^2 mol dm^{-3})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J K^{-1} mol^{-1})
None	—	86.1	102.5	−56.0
Perfluorooctonoic acid	0.18	70.0	112.4	−129.0
	1.83	65.3	107.5	−142.0
Sodium 1-dodecanesulphonic acid	0.18	69.7	100.5	−104.0
	1.83	63.9	99.4	−120.0
Sodium dodecyl sulphate	0.18	70.5	108.8	−102.0

Values for K_s were obtained from the slope and intercept of the linear relationship between $1/k_w$-k_ψ and $1/(C_D$-cmc) using the following equation, and are given in Table 2:

$$\frac{1}{k_w - k_\psi} = \frac{1}{k_w - k_m} + \left(\frac{1}{k_w - k_m}\right)\left[\frac{1}{K_s(C_t - \mathrm{cmc})}\right] \quad (3)$$

As one can see, both SDS and SDOS micelles produce a catalytic effect over the entire concentration range used, but the effect is different depending on the hydroxamic acid.

The kinetic results can be explained by means of the micellar pseudo-phase ion-exchange model.[22] This model considers the micelle to be separate from the aqueous phase and that the reaction occurs in both phases. The concentration of H^+ at the micellar surface of SDS and SDOD depends upon competition with the inert counterion, Na^+, and this competition can be treated quantitatively by the ion-exchange equilibrium:

$$H^+{}_m + Na^+{}_w \overset{K^H{}_{Na}}{\rightleftharpoons} H^+{}_w + Na^+{}_m$$

where $H^+{}_m$, $Na^+{}_w$, $H^+{}_m$ and $Na^+{}_m$ denote the reactive ions and micellar counterions in the aqueous and micellar phases, respectively. The value of $K^H{}_{Na}$= 0.82, which is nearly 1, indicates there is no difference between specific absorption of these ions in the micellar surface, and the ions can be considered to be statistically distributed between the aqueous and micellar phase, $H_m{}^+$, given by the following quadratic equation:

$$\left(\frac{[H^+{}_m]}{[D_n]}\right)^2 + \left(\frac{[H^+{}_m]}{[D_n]}\right)\left\{\frac{[H^+{}_T] + K^H{}_{Na}[Na^+{}_T]}{(K^H{}_{Na} - 1)[D_n]} - \beta\right\} + \frac{[H^+{}_T]}{(K^H{}_{Na} - 1)[D_n]} = 0 \quad (4)$$

which depends on $K^H{}_{Na}$ and the fraction of micellar head groups neutralized, $\beta = ([H^+{}_m] + [Na^+{}_m])/[D_n]$, or for the expression in the case $K_{Na}{}^H$= 1

$$[H^+{}_m] = \frac{[H^+{}_T]\beta[D_n]}{[H^+{}_T][Na^+{}_T]} \quad (5)$$

This variation in $K^H{}_{Na}$, between 0.82 and 1, does not produce any significant variation in the fitting of the kinetic results. β values were obtained by conductivity measurements as the ratio of the slopes above and below the cmc. The concentration of micellized surfactant, $[D_n]$, can be represented as $[D_n] = [D_T] - \mathrm{cmc}$, where $[D_T]$ is the stoichiometric surfactant concentration and the cmc is that obtained under the experimental reaction conditions. $[H^+{}_T]$ and $[Na^+{}_T]$ are the total concentration of hydrogen and sodium ions, respectively.

The first-order rate constant for the overall reaction, k_ψ, is given by the following equation, and data are given in Table 3:

$$k_\psi = \frac{k_2{}^w[H^+{}_w] + (k_2{}^m K_s - k_2{}^m)[H^+{}_m]}{1 + K_s[D_n]} \quad (6)$$

where $k_2{}^w$ and $k_2{}^m$ are the second-order reaction rate constants in the aqueous and micellar phases, respectively. Experimental kinetic values can be adapted to this model. The experimental data were fitted to the model to estimate the best values of K_s, $K_{Na}{}^H$ and $k_2{}^m$ by using constant values of β and cmc. We found that values of $K_{Na}{}^H$ in the range 0.82–1.0 all gave good fits to the experimental points, yielding similar values of the optimized parameters in Fig. 1. The values are given in Table 3.

Effect of temperature

We studied the influence of temperature on the reaction rate in the presence and absence of surfactant in the range 55–75 °C. Variations of k_ψ with temperature in water and in surfactants follow the Eyring equation and values are given in Table 4. The conclusion to be drawn from Table 1 is that the reaction is slower in water than micelles as a result of the entropy difference. The enthalpies of activation and free energies of activation are not very different. This is evidence that (i) the proton is in the same state in both media because there is no indication of specific interaction with the micellar surface and (ii) in the micelle the reaction takes place in a highly hydrated region, i.e. the Stern layer. The difference in activation entropy between the aqueous and micellar phase can be attributed in terms of the mobility of the transition state. The mobility of the transition state at the micellar surface is restricted by interaction between the negatively charged micelle head and the positive charge. The restriction of mobility lowers the entropy of the transition state.

EXPERIMENTAL

N-Phenylbenzohydroxamic acid, acetohydroxamic acid and benzohydroxamic acid were prepared by the standard method.[25] The surfactants were commercial samples (PFOC, Fluka; SDS, BDH; SDOS, Fluka) and used without further purification. The acids used were of analytical-reagent grade. Dioxane (Qualigens-AR) and acetonitrile (Merck) were used as received. All solutions were prepared with doubly distilled water. Reaction kinetics were followed spectrophotometrically with a Systronics Type 108 UV–VIS spectrophotometer, measuring the change in absorbance of the iron(III)–hydroxamic acid complex at 520 nm due to the disappearance of hydroxamic acid. Beer's law is obeyed by the system. The cmcs were determined under the reaction conditions by conductivity measurements using a Systronics Type 304 conductivity meter with a cell constant 1. Least-squares analysis was carried out on a WIPRO Pentium Acer computer under MS-DOS.

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