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Kinetic model for micellar catalysed hydrolysis of esters – biomolecular reactions

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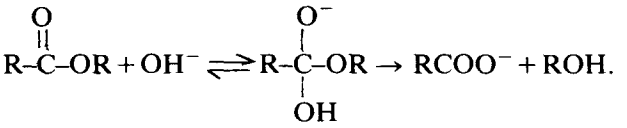
Abstract. The cationic micelles of cetyltrimethylammonium bromide, cetyldibenzylammonium chloride and cetylpyridinium chloride stabilize the tetrahedral intermediate formed in the hydrolysis of carboxylic esters (e.g. *p*-nitrophenylbenzoate) to a greater extent, preferring a B_{Ac2} mechanism, than the anionic intermediate formed in the hydrolysis of *m*-nitrophenyl-N-N-diphenylphosphorodiamidate, which prefers a E_{1cB} mechanism. The co-operative index, n_1, calculated for these reactions is greater than 1 indicating that the substrate induced micellation is responsible for the observed catalysis. Based on the present kinetic model for a bimolecular reaction, the fraction of substrate and nucleophile bound to the micelle have been calculated. The above results suggest that reaction occurs between the substrate solubilised into the micelle and the nucleophile residing at the Stern layer rather than at the micelle-water interface. The equilibrium constant, and critical micelle concentration, evaluated using the present model are in agreement with the values obtained by using earlier models, suggesting a method of evaluating these parameters from kinetic data only.

Keywords. Cationic micelles; catalysis in ester hydrolysis; kinetic model for bimolecular reaction; equilibrium constant; critical micelle concentration.

1. Introduction

The hydrolysis of esters generally involves an attack of the anion OH^- on the carboxyl carbon of the ester resulting in a negatively charged tetrahedral intermediate



Therefore, the acceleration or deceleration of the deacylation reactions in the presence of micelles can be rationalised by considering the forces that would stabilize or destabilize the tetrahedral intermediate.

In the present work, the micellar influences on the kinetics of the hydrolysis of carboxyl esters, viz., *p*-nitrophenylbenzoate (PNPB), *p*-nitrophenyl-*p*-nitrophenylacetate (PA), *p*-nitrophenyl-*p*-chlorobenzoate (PCB) and *p*-nitrophenyl-N-phenylcarbamate (PCM), sulphate esters – *p*-nitrophenyltoluene-sulphonate (PTS) and *p*-nitrophenylphenylmethanesulphonate (PMS), and a phosphate ester – *m*-nitro-

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phenyl-N–N-diphenylphosphorodiamidate (PDI), have been studied in detail. The cationic micelles, formed from cetyltrimethylammonium bromide (CTAB), cetyldimethylbenzylammonium chloride (CDBAC), and cetylpyridinium chloride (CPC), stabilize the tetrahedral intermediate and hence catalyse the hydrolysis of esters. In what follows, a concise account of the catalysis by each one of the cationic micelles in the hydrolysis of the above esters has been discussed.

2. Results and discussion

The influence of cationic-micelle-forming detergents, CTAB, CDBAC and CPC, has been investigated in the hydrolysis of esters in borax-buffer media at $30° \pm 0{\cdot}1°C$ and an ionic strength 0·10 mol dm^{-3}

2.1 *Effect of added CTAB, CDBAC and CPC on the hydrolysis of esters*

The cationic micelles of CTAB exhibit maximum rate enhancement in the case of PMS and exert minimum effect in the case of PDI. The rate constant (k_{obs}) versus [CTAB] profile for each ester exhibits a maximum which is characteristic of bimolecular reactions and the maximum rate benefit is observed at a particular concentration of CTAB for each one of the esters used (table 1). But with CDBAC, maximum rate acceleration is observed in the hydrolysis of PCB (100-fold) (table 2), while the rate enhancement observed in the hydrolysis of PTS is minimum (15-fold). The reaction of PA attains its maximum rate even at a concentration of CDBAC lower than its (critical micelle concentration) c.m.c. ($1{\cdot}20 \times 10^{-4}$ M under the present reaction conditions). Phenyl acetates have been shown to hydrolyse via E_{1cB} path in the presence of cationic micelles (Tagaki *et al* 1976; Yano *et al* 1979) and therefore, the observed higher rate maximum for PA even at low concentrations of CDBAC is not unexpected (Al-Lohedan and Bunton 1981).

Table 1. Effect of CTAB on the rate of hydrolysis of esters.

10^4[CTAB]M	PNPB[a]	PTS[b]	PMS[c]	PCB[a]	PDI[d,e]
0·00	5·5	5·0	3·4	5·2	1·06
0·50	6·8	8·4	4·6	7·1	—
1·00	7·4	8·4	3·3	15·1	—
2·5	9·1	10·6	10·5	—	—
5·0	12·1	35	25	41	—
10·0	12·3	25	41	37	2·3
20	—	25	48	—	2·3
50	—	—	45	—	2·7
100	—	—	—	—	2·8

[ester] = $1{\cdot}50 \times 10^{-5}$ M; pH = 9·2; [NaCl] = 0·10 M; temperature = 30°C.
[a] $10^4 k_{obs}$ s^{-1}; [b] $10^7 k_{obs}$ s^{-1}; [c] $10^3 k_{obs}$ s^{-1}; [d] $10^5 k_{obs}$ s^{-1}; [PDI] = $3{\cdot}0 \times 10^{-4}$ M in 20% aqueous CH_3CN.

Table 2. CDBAC influenced hydrolysis of esters.

10^4[CDBAC]M	PNPB[a]	PTS[b]	PMS[c]	PA[d]	PCB[e]
0·00	1·42	2·4	1·34	0·57	0·193
0·50	2·2	2·2	2·1	0·86	—
1·00	3·2	4·1	4·7	2·8	0·188
2·0	23	9·5	7·1	9·6	0·47
5·0	28	25	85	17·9	0·95
10·0	37	36	105	17·9	1·64
20	24	14·5	68	13·3	14·0
50	17·2	13·8	42	12·9	20
100	—	10·5	—	—	14·4

[ester] = $1{\cdot}50\times10^{-5}$ M; pH = 9·2; temperature = 30°C.
[a] $10^4\,k_{obs}\,s^{-1}$; [b] $10^7\,k_{obs}\,s^{-1}$; [c] $10^3\,k_{obs}\,s^{-1}$; [d] $10^2\,k_{obs}\,s^{-1}$; [e] $10^3\,k_{obs}\,s^{-1}$.

Table 3. Effect of CPC on the hydrolysis of esters.

10^4[CPC]M	PNPB[a]	PTS[b]	PMS[c]	PA[d]	PCB[d]	PDI[e,f]
0·00	1·42	2·4	1·34	5·7	0·193	1·64
0·050	2·8	—	—	36	—	1·77
0·100	3·1	—	2·1	60	—	—
0·50	3·6	2·1	2·2	116	1·02	2·5
1·00	5·6	4·0	7·9	134	2·2	2·9
2·0	9·5	6·2	21	108	4·7	—
5·0	12·2	8·0	58	—	11·7	2·1
10·0	19·4	11·1	109	—	14·6	—
20	30	50	132	—	29	—
50	22	50	108	—	15·0	—

[ester] = $1{\cdot}50\times10^{-5}$ M; pH = 9·2; temperature = 30°C.
[a] $10^4\,k_{obs}\,s^{-1}$; [b] $10^7\,k_{obs}\,s^{-1}$; [c] $10^3\,k_{obs}\,s^{-1}$; [d] $10^3\,k_{obs}\,s^{-1}$; [e] $10^4\,k_{obs}\,s^{-1}$ for the hydrolysis of [PDI] = $3{\cdot}0\times10^{-4}$ M by $1{\cdot}0\times10^{-2}$ M OH in 20% aqueous CH_3CN.

Cetylpyridinium chloride (CPC) catalyse the hydrolysis of these esters (table 3) even at submicellar concentrations and it is more effective in catalysing the hydrolysis of PCB (150-fold increase in rate) while it is less efficient with PDI (only 2-fold increase in rate).

2.2 *Co-operativity index in micellar catalysed reactions*

Binding of additional substrate to oligomeric enzymes may increase or decrease the observed reaction rate and by analogy the co-operativity between the surfactant molecules and the substrate may account for micellar catalysis. For such a reaction, a co-operativity model has been proposed by Piskiewicz (1977) and the equation arrived at from such a model is

$$\log\,[(k_{obs}-k_0)/(k_m-k_{obs})] = n\,\log\,[D]-\log\,K_D. \qquad (1)$$

From the data in tables 1, 2 and 3, $\log\,[(k_{obs}-k_0)/(k_m-k_{obs})]$ versus log [detergent] graphs have been drawn. Fairly linear correlations are observed and the values of co-operativity index, n, and $\log\,[D]_{50}$ derived therefrom are summarised in table 4.

Table 4. Piskiewicz's co-operativity values.

Substrate	Detergent	n	$\log [D]_{50}$	$[D]_{50}$	K_D
PNPB	CTAB	1·6	−3·8	$1{\cdot}70\times10^{-4}$	$1{\cdot}04\times10^{-6}$
PTS	CTAB	0·63	−2·6	$2{\cdot}7\times10^{-3}$	$2{\cdot}5\times10^{-2}$
PMS	CTAB	2·3	−3·3	$5{\cdot}2\times10^{-4}$	$3{\cdot}1\times10^{-8}$
PCB	CTAB	2·1	−3·7	$2{\cdot}1\times10^{-4}$	$1{\cdot}39\times10^{-8}$
PDI	CTAB	0·39	−3·4	$3{\cdot}6\times10^{-4}$	$4{\cdot}6\times10^{-2}$
PNPB	CDBAC	1·28	−3·7	$1{\cdot}92\times10^{-4}$	$1{\cdot}75\times10^{-5}$
PTS	CDBAC	2·3	−3·5	$3{\cdot}6\times10^{-4}$	$1{\cdot}78\times10^{-8}$
PMS	CDBAC	0·87	−4·0	$9{\cdot}2\times10^{-5}$	$3{\cdot}1\times10^{-4}$
PA	CDBAC	2·8	−4·7	$2{\cdot}0\times10^{-5}$	$6{\cdot}3\times10^{-14}$
PCB	CDBAC	2·2	−3·7	$2{\cdot}0\times10^{-4}$	$7{\cdot}4\times10^{-9}$
PNPB	CPC	0·64	−3·0	$9{\cdot}5\times10^{-4}$	$1{\cdot}16\times10^{-2}$
PTS	CPC	1·19	−2·7	$1{\cdot}94\times10^{-3}$	$5{\cdot}9\times10^{-4}$
PMS	CPC	1·89	−3·3	$5{\cdot}0\times10^{-4}$	$5{\cdot}7\times10^{-7}$
PA	CPC	1·06	−4·8	$1{\cdot}52\times10^{-5}$	$9{\cdot}8\times10^{-6}$
PCB	CPC	1·28	−3·1	$8{\cdot}5\times10^{-4}$	$1{\cdot}18\times10^{-4}$
PDI	CPC	1·04	−4·2	$6{\cdot}1\times10^{-5}$	$4{\cdot}2\times10^{-5}$

The values of n are in keeping with the earlier observations (Piskiewicz 1977) and a value $n > 1$ predicts substrate induced micellisation which would have been responsible for the observed catalysis in the presence of detergents at submicellar concentrations. $[D]_{50}$ is also in good agreement with the experimental observations. From the intercept, the decomposition constant, K_D, has been evaluated. Although this treatment predicts that the number of surfactant monomers in each aggregate is of the order of 1–5, making the size of the micelle considerably smaller than typical micelles, the approach may be useful in indicating the way in which substrates may assist micellisation or comicellisation.

2.3 *Model for bimolecular micellar catalysed reactions*

The acceleration of reaction rates in the presence of micelles have been attributed on most occasions to the increase in concentration of reactants on the micellar phase, and the association in micellar phase has been explained quantitatively in terms of the binding constants. Earlier models in vogue for the evaluation of binding constants in micellar catalysed reactions require a parameter such as volume of the Stern layer or the micellised nucleophile concentration etc., which is difficult to determine kinetically. Therefore, this paper attempts to evaluate the binding constants of reactants with the micelle from the kinetically accessible parameters above. According to the following simplified scheme (I),

$$nD + S \overset{K_1}{\rightleftharpoons} D_nS$$

$$D_nS + N \overset{K_2}{\rightleftharpoons} D_nSN$$

$$D_nSN \overset{k_m}{\rightleftharpoons} \text{Products}$$

$$S + N \overset{k_0}{\rightleftharpoons} \text{Products}.$$

where D, S and N refer to the detergent monomer, substrate and the nucleophile while D_nS and D_nSN refer to the binary and ternary complexes. The products are assumed to result from the reaction between the substrate and the nucleophile, in aqueous medium as well as in the miceller phase, by the decomposition of ternary complex. The rate-law for this scheme is,

$$\text{rate} = k_0[S]_f[N]_f + k_m[D_nSN], \tag{1}$$

where f refers to free species. As

$$[D_n\text{SN}] = K_2[D_nS][N]_f,$$

$$[D_n\text{S}] = K_1[D]^n[S]_f, \text{ and}$$

free substrate concentration $[S]_f = [S]_{\text{total}} - [D_nS]$, the concentration of D_nS and D_nSN can be given as,

$$[D_n\text{S}] = K_1[D]^n[S]_T/(1 + K_1[D]^n),$$

$$[D_n\text{SN}] = K_1K_2[D]^n[S]_T[N]_f/(1 + K_1[D]^n).$$

Assuming $[N]_f = [N]_{\text{total}} - [D_nSN]$, the concentration of ternary complex, D_nSN, $[N]_f$ and $[S]_f$ are evaluated. On introducing these in 1, it becomes

$$\text{rate} = \frac{k_0[S]_T[N]_T + k_mK_1K_2[D]^n[S]_T[N]_T}{1 + K_1[D]^n\{1 + K_2[S]_T\}},$$

or

$$k_{\text{obs}} = \frac{k_0 + k_mK_1K_2[D]^n}{1 + K_1[D]^n\{1 + K_2[S]_T\}} \tag{2}$$

This form of equation is identical to those derived by Martinek *et al* (1977) and Bunton *et al* (1978). This model also predicts constancy in k_{obs} values at high detergent concentrations.

Equation 2 takes the form

$$\frac{k_{\text{obs}} - k_0}{k_{\text{obs}}} \frac{1}{[D]^n} = K_1K_2 \frac{k_m}{k_{\text{obs}}} K_1\{1 + K_2[S]_T\}, \tag{2}$$

which predicts a linear relationship between $(k_{\text{obs}} - k_0)/k_{\text{obs}} \cdot (1/[D]^n)$ with k_m/k_{obs} and it is realised in various systems. Using the value of n obtained from Piskiewicz's co-operativity model, with the help of the present model, K_1 is calculated without recourse to the c.m.c. value which is a variable parameter. However, this model does not consider the effect of counter ions nor the interaction of products with the micelles. When the proposed model is applied to several systems, the value of K_1 and the intercept in all the cases are almost the same in magnitude as $K_2[S]_T \ll 1$ (table 5). The evaluated K_1 values are also in good agreement with those obtained from the Piskiewicz model and an abnormal value of K_1 from both the models would be due to the assumption that the substrate induces micellisation in which case there should be very strong association of the substrates with the micelles.

Table 5. Evaluation of binding constants using present model.

Reaction	n*	intercept**	K_1*	K_2**	
Electron transfer from *n*-butyl ferrocene to Fe^{3+} in presence of NaIS	1·07	$-9{\cdot}4\times10^{2}$	$9{\cdot}4\times10^{2}$ ($5{\cdot}7\times10^{2}$)	0·69	(Bunton and Cerichelli 1980)
Hydrolysis of *o*-nitrophenyl acetate in presence of CTAB	1·72	$-1{\cdot}48\times10^{4}$	$1{\cdot}48\times10^{4}$ ($3{\cdot}8\times10^{4}$)	1·35	(Beheme *et al* 1965)
Hydrolysis of *p*-nitrophenylhexanoate in presence of CTAB	2·8	$-2{\cdot}3\times10^{8}$	$2{\cdot}3\times10^{8}$ ($1{\cdot}3\times10^{8}$)	0·90	(Beheme *et al* 1965)
Hydrolysis of methyl-ortho benzoate in presence of NaIS	3·0	$-1{\cdot}15\times10^{8}$	$1{\cdot}15\times10^{8}$ ($4{\cdot}4\times10^{7}$)	0·43	(Beheme *et al* 1965)
Hydrolysis of *p*-nitrophenylhexanoate in presence of TDTACI	4·9	$-5{\cdot}5\times10^{12}$	$5{\cdot}5\times10^{12}$ ($6{\cdot}3\times10^{12}$)	1·09	(Romsted and Cordes 1968)
Hydrolysis of *p*-nitrophenyl acetate in presence of TDTACl	2·5	$-9{\cdot}3\times10^{5}$	$9{\cdot}3\times10^{5}$ ($1{\cdot}14\times10^{6}$)	1·05	(Romsted and Cordes 1968)
Acid hydrolysis of *N*-(trifluoroacetyl)indole in presence of NaIS	4·1	$-4{\cdot}3\times10^{9}$	$4{\cdot}3\times10^{9}$ ($6{\cdot}1\times10^{9}$)	1·06	(Cipicianni *et al* 1981)

* From Piskiewicz's co-operativity equation; ** using (2) derived from present model; values in parantheses are obtained from the intercept of Piskiewicz's equation.

The low values of K_2 ($K_2 \ll K_1$) suggest that $[N]_f = [N]_{\text{total}}$, and therefore, the nucleophile is present almost in full in the bulk phase – an idea which parallels the assumptions of Romsted (1977) and the opinion of Reeves (1975).

In the light of the above conclusion we have to conjecture that the reaction takes place between the substrate solubilised into a micelle and the nucleophile residing at the Stern layer of the micelle without being bound strongly to it at the micelle-water interface. This also gains support from Menger's (1971) work.

Therefore, the observed catalysis of reactions by cationic micelles might have been the result of a proper orientation of the substrate the carbonyl group being polar residing at the Stern layer with the non-polar portions adsorbed into the cone for facile reaction with the nucleophile. However, this conclusion cannot be proved beyond doubt with the data available.

The micelle-substrate binding constant has been separated from other equilibrium constants by modifying the scheme as

$$D_n + S \rightleftharpoons D_nS,$$

$$nD + S \rightleftharpoons D_nS.$$

This leads to the modified expression

$$\frac{k_{\text{obs}} - k_0}{k_{\text{obs}}}\frac{1}{[D_n]} = K_1K_2\frac{k_m}{k_{\text{obs}}} - K_1\{1 + K_2[S]_T\}. \tag{3}$$

Table 6. Comparison of binding constants (K/N) from Menger's equation and the present model.

Reactions	a*	b
Hydrolysis of		
PNPB in presence of CTAB	$7{\cdot}4 \times 10^3$	$1{\cdot}04 \times 10^4$
PMS in presence of CTAB	$1{\cdot}36 \times 10^2$	62
PNPB in presence of CDBAC	$2{\cdot}1 \times 10^4$	$2{\cdot}2 \times 10^4$
PCB in presence of CDBAC	$7{\cdot}8 \times 10^4$	$7{\cdot}7 \times 10^4$
PTS in presence of CDBAC	$2{\cdot}3 \times 10^3$	$3{\cdot}0 \times 10^3$
PA in presence of CDBAC	$4{\cdot}1 \times 10^3$	$3{\cdot}6 \times 10^3$
PMS in presence of CDBAC	$1{\cdot}0 \times 10^5$	$2{\cdot}2 \times 10^3$
PNPB in presence of CPC	$6{\cdot}8 \times 10^3$	$9{\cdot}4 \times 10^3$
PCB in presence of CPC	$2{\cdot}3 \times 10^2$	$1{\cdot}56 \times 10^3$
PMS in presence of CPC	$4{\cdot}5 \times 10^3$	$5{\cdot}1 \times 10^3$

* in calculating the binding constants, c.m.c. values from present model have been used;
a) binding constant (K/N) using equation 3
b) binding constant (K/N) calculated using the equation of Menger and Portnoy (1967)

This equation has also been applied to different systems and the derived data have been collected in table 6. The consequence of the much lower values of K_2, i.e. the binding of the nucleophile with micelles is negligible, conveys that only the substrate is distributed between micellar and aqueous phases. In such case, the earlier treatment of Menger and Portnoy (1967) for unimolecular reactions should also hold good for bimolecular reactions. Table 6 includes data obtained by using the equation by Menger and Portnoy (1967). A fairly good agreement between the values in columns *a* and *b* of table 6, upholds the applicability of (3) to bimolecular micellar catalysed reactions.

3. Experimental

A detailed procedure for the preparation of the esters used in the present work is included in our early paper (Raghavan and Srinivasan 1984). The detergents were purified till the c.m.c. agreed with the reported value (Fendler and Fendler 1975).

All the reactions were carried out at pH = 9·2 in 0·050 M borax buffer in 0·10 M NaCl at 30°C unless otherwise mentioned. Small amount of H_3CCN was used in making up the substrate solution and pure water was generally used as the solvent. The pH of the buffer solution was adjusted in the presence of detergent with a digital pH meter. The critical micelle concentrations were measured for these detergents spectrophotometrically, using the dye eosine (λ_{max} = 540 nm), as probe. (c.m.c. value for CTAB, CDBAC and CPC in borate buffer at pH = 9·2 is around $1{\cdot}0 \times 10^{-4}$ M.) Reactions were monitored by following the release of *p*- (or) *m*-nitrophenoxide ion at 400 nm using a Carl-Zeiss VSU 2P spectrophotometer. From the infinite values determined after nine half-lives, specific rates were evaluated from the slopes of the regression lines for correlations of log $[A_\infty - A_t]$ vs. time. The linear regression analysis was performed on a micro-programmable calculator (Hindustan Computers).

References

Al-Lohedan H and Bunton C A 1981 *J. Org. Chem.* **46** 3929
Behme M T A, Fullington J G, Noel R and Cordes E H 1965 *J. Am. Chem. Soc.* **87** 266
Bunton C A, Rivera F and Sepulveda L 1978 *J. Org. Chem.* **43** 1166
Bunton C A and Cerichelli G 1980 *Int. J. Chem. Kinet.* **12** 519
Cipicianni A, Linda P, Savelli G and Bunton C P 1981 *J. Org. Chem.* **46** 911
Fendler J H and Fendler E J 1975 *Catalysis in micellar and macromolecular systems* (New York: Academic Press)
Martinek K, Yatsimirski A K, Lavashor A V and Berezin I V 1977 in *Micellisation, solubilisation and microemulsions* (ed.) K L Mittal (New York: Plenum Press) p. 489
Menger F M and Portnoy C E 1967 *J. Am. Chem. Soc.* **89** 4698
Menger F M 1971 *J. Am. Chem. Soc.* **92** 5965
Piskiewicz D 1977 *J. Am. Chem. Soc.* **99** 1550
Raghavan P S and Srinivasan V S 1984 *Proc. Indian Acad. Sci. (Chem. Sci.)* **93** 1305
Reeves R L 1975 *J. Am. Chem. Soc.* **97** 6019, 6025
Romsted L R and Cordes E H 1968 *J. Am. Chem. Soc.* **90** 4404
Romsted L S 1977 in *Micellisation, solubilisation and microemulsions* (ed.) K L Mittal (New York: Plenum Press) p. 309
Tagaki W, Kobayashi S, Kurihara A, Kurashima A, Yoshida Y and Yano Y 1976 *J. Chem. Soc., Chem. Commun.* 843
Yano Y, Yoshida Y, Kurashima A, Tamura Y and Tagaki W 1979 *J. Chem. Soc. Perkin II* 1128