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Influence of imidazole and bifunctional nucleophiles on the micellar catalysed hydrolysis and hydroxylaminolysis of esters

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Abstract. Though 2- and 3-hydroxypyridines, structurally resemble imidazole, 2-hydroxypyridine seems to function as a nucleophile in the hydrolysis of *p*-nitrophenylbenzoate as it can acquire a pyridine form (Mosher 1959) while the latter cannot. The bifunctional activity of benzamidine has also been enhanced by anionic micelles of sodium laurylsulphate. The anionic micelle formed by sodium laurylsulphate retards the rate of hydroxylaminolysis of *p*-nitrophenylbenzoate, while the cationic micelle formed from cetyltrimethylammonium bromide enhances the rate in H_2NOH-$H_2NOH \cdot HCl$ buffer at pH = 6·14. Such behaviour is in favour of the anion, H_2NO^-, acting as a nucleophile to some extent. On the contrary, hydroxylaminolysis of *p*-nitrophenylphenylmethane sulphonate (PMS) proceeds at a slower rate and imidazole catalysis is observed as these esters at pH = 6·14 possibly prefer a $B_{Ac}2$ mechanism, which is absent at pH = 9·2 as the same reactions proceed by a E_1cB path.

Keywords. Catalysis; imidazole; 3-hydroxypyridine; 2-hydroxypyridine; benzamidine; hydrolysis; hydroxylaminolysis.

1. Introduction

As bifunctional nucleophiles can concertedly attack the carbonyl carbon of an ester and deliver a proton to the carbonyl oxygen, an intermediate will be formed without the creation of charge. In this communication we report the effect of benzamidine, 2-hydroxypyridine and 3-hydroxypyridine on the hydrolysis of *p*-nitrophenylbenzoate (PNPB) in micellar media.

Also, hydroxylamine can function as an ambient nucleophile, which can attack at the carbonyl carbon of an ester either from the oxygen or the nitrogen end, yielding acetohydroxymic acid as a final product, as proposed in the case of a thiol ester (Bruice and Fedor 1964) as well as in the reaction of amides and hydroxylamine (Alburn and Grant 1965). This communication also includes a study of the micellar influence on the hydroxylaminolysis of carboxylic, sulphate and phosphate esters, which is used to decide the mode of attack by NH_2OH. The imidazole catalysis of the hydroxylaminolysis of these esters at this pH = 6·15 points to the operation of a different mechanism.

2. Results and discussion

2.1 *Catalysis by 2- and 3-hydroxypyridines*

The catalysis of the hydrolysis of several esters by added imidazole (Bender and Turnquest 1957; Bruice and Schmir 1957; Jencks 1969) and by a number of micelles

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bearing an imidazolyl group (Brown and Bunton 1974; Moss *et al* 1975; Tagaki *et al* 1979) have been documented in literature. Though imidazole catalyses many hydrolytic reactions, it lacks the bifunctional activity exhibited by related compounds. The present work is on the effect of 2- and 3-hydroxypyridines, which are structurally similar to imidazole, on the hydrolysis of PNPB. 2-Hydroxypyridine is known to function as a bifunctional catalyst (Swain and Brown 1952).

In the present study both 2- and 3-hydroxypyridines alter the rate of hydrolysis of PNPB only in the presence of micelles (table 1). The rate enhancement observed in the rate of hydrolysis of PNPB due to added 2-hydroxypyridine both in cationic and anionic micellar phase may be due to 2-hydroxypyridine (2-HP) acquiring a pyridone form (Mosher 1959) and hence possessing a reduced phenolic character. But the added 3-hydroxypyridine (3-HP) accelerates the rate in the presence of sodium lauryl sulphate (SLS) and retards the rate in the presence of cetyl trimethylammonium bromide (CTAB) possibly due to its inability to acquire the pyridone form. As the catalysis by 2-HP is observed only in the micellar phase, the results possibly suggest that the proximity and proper orientation of 2-HP in the micellar phase assist the bifunctional nature of this compound (figure 1) as ketones are most likely to be solubilised near the surface or in the head group region with the carbonyl oxygen pointing towards the surface (Balasubramanian *et al* 1982).

Table 1. Influence of hydroxypyridines on the rate of hydrolysis of PNPB in the presence and absence of micelles[a].

	3-HP			2-HP		
	b	c	d	b	c	d
[Hydroxypyridine]* M	$10^4 k_{obs}\, s^{-1}$			$10^4 k_{obs}\, s^{-1}$		
0·00	5·5	0·61	12·3	5·5	0·61	12·3
0·25	5·6	0·73	11·2	4·8	0·72	12·4
0·50	5·6	0·85	10·2	4·6	0·72	13·8
1·00	5·3	1·03	9·3	4·8	0·78	14·5
1·50	5·5	1·98	9·1	5·3	0·99	—
2·0	5·3	2·0	9·0	5·3	1·16	16·5

* The values in this column refer to 10^2[3-HP] or 10[2-HP]; [a] reactions were carried out at 30°C at pH = 9·2 and [PNPB] = $1·50 \times 10^{-5}$ M at μ = 0·10 mol dm^{-3}; [b] in the absence of micelles; [c] in 0·010 M SLS; d in 0·0010 M CTAB.

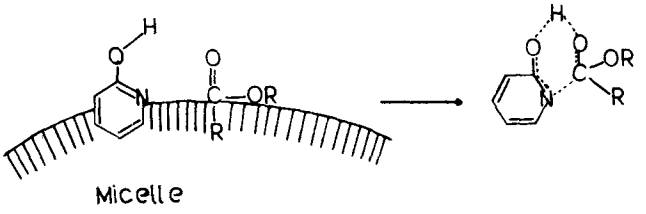


Figure 1. Bifunctional catalysis by 2-hydroxypyridine in micellar phase.

The observed catalysis by 2-HP may also be partly due to a smaller change in pK_a value in micellar media wherein the presence of the anionic form may increase the nucleophilicity of 2-HP (pK_a value for 2-HP is 10·6 at 30°C and it is 10·0 in 0·0010 M CTAB and 9·4 in SLS; pK_a value for 3-HP is 4·3 at 30°C and 4·2 in 0·0010 M CTAB and 4·4 in 0·010 M SLS).

2.2 *Catalysis by benzamidine*

Menger (1966) observed 15 000 fold rate enhancement in the reaction of benzamidine with PNPBin chlorobenzene at 25°C, which has been attributed to its bifunctional nature. In the present study also the benzamidine added catalyses the hydrolysis of PNPB both in the presence and absence of micelles (table 2). Benzamidine, because of its bifunctionality, may favour the formation of a tetrahedral-like intermediate through a six-membered transition state (figure 2). The catalytic efficiency of benzamidine is enhanced in a anionic micellar phase compared to the cationic micellar phase probably due to partial reduction in the nucleophilicity of benzamidine on the cationic surface. Nevertheless, the catalysis by benzamidine observed in presence of both anionic and

Table 2. Effect of added benzamidine on the rate of hydrolysis of PNPB in the presence and absence of micelles*.

	$10^4\ k_{obs}\ s^{-1}$				
	PNPB				
[Benzamidine]	a	b	c	PDI[d]	PMS[e]
0·00	5·5	0·61	12·3	2·3	21
0·0040	—	1·58	16·0	—	—
0·0086	—	2·5	—	—	—
0·016	6·4	3·4	18·4	—	—
0·050	8·4	5·0	31·	—	23
0·10	13·2	—	38	—	25
0·20	29	—	62	0·78	20
0·38	—	—	—	0·77	—

* Reactions were carried out at 30°C at pH = 9·2 and μ = 0·10 mol dm^{-3} and [PNAB] = 1·50 × 10^{-5} M; [a] in the absence of micelles; [b] in 0·010 M SLS; [c] in 0·0010 M CTAB; [d] for PDI in 0·0010 M CTAB; [e] for PMS in 0·0010 M CTAB.

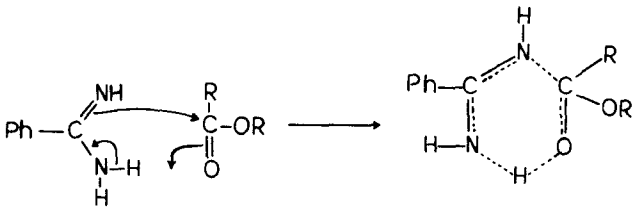


Figure 2. Transition state in benzimidinolysis of esters.

cationic micelles seem to be very much like that of 2-HP. Also such catalysis has not been observed in the case of PMS and PDI which prefer the E_1cB path at pH = 9·2 (table 2).

2.3 *Hydroxylaminolysis of esters and imidazole catalysis*

The rate of hydroxylaminolysis of PNPB depends on the first power of concentration of the ester both in the presence and absence of SLS or CTAB. In the concentration range of 0·010 M to 0·50 M, the reaction exhibits a first order dependence on hydroxylamine concentration. Hence the rate-law for the reaction can be given as

$$\text{rate} = k[\text{ester}][H_2NOH]. \quad (1)$$

Cationic detergents CTAB, CDBAC (cetyldibenzylammonium chloride) or CPC (cetylpyridinium chloride) added increase the rate marginally at lower concentrations of detergent but retard the rate at higher concentrations (table 3). The catalytic effects of cationic surfactants on the reaction seems to be less significant, probably because the reactions have been carried out at acidic pH = 6·14 where there is only a slight difference in the structures of the transition state and the initial ester (Geneste *et al* 1976).

There is considerable retardation in rate with an increasing concentration of SLS (table 4), which is generally observed for reactions involving a nucleophilic attack on the carbonyl carbon of esters. Coupled with the rate enhancement observed in the

Table 3. Effect of added cationic detergent on the rate of hydroxylaminolysis of PNPB.

	$10^3 k^*_{obs}\ s^{-1}$		
10^4 [Detergent] M	CTAB	CDBAC	CPC
—	1·12	1·12	1·12
0·050	—	—	2·3
0·50	1·61	2·1	2·4
1·000	1·70	2·3	2·8
5·0	0·76	1·90	1·87

* At 30°C, pH = 6·15, [buffer] = 0·10 M, in 2·5% CH_3CN and 97·5% H_2O (v/v) and [PNPB] = $3·0 \times 10^{-5}$ M.

Table 4. Influence of SLS on the rate of hydroxylaminolysis of PNPB.

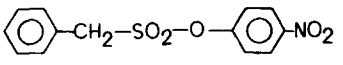
10^2 [SLS] M	$10^3 k^*_{obs}\ s^{-1}$
—	6·0
0·25	4·0
0·50	2·2
1·00	1·58
2·5	0·90
5·0	0·68
10·0	0·60

* At pH = 6·15, [buffer] = 0·10 M, 30°C, in 2·5% CH_3CN and 97·5% H_2O (v/v) and [PNPB] = $3·0 \times 10^{-5}$ M.

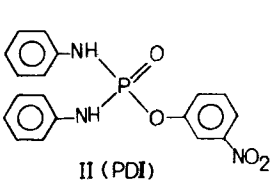
cationic micelle in the hydroxylaminolysis of esters, the above rate-retarding effect of SLS suggests an attack on the carbonyl carbon of esters by the oxygen end of H_2NO^- at this pH.

Using Menger and Portnoy's treatment (1967), the substrate-micelle binding constant (K_s/N) has been evaluated from this data to be $2{\cdot}9 \times 10^2$ M^{-1} (where N is the aggregation number). The cooperativity index, n, calculated using the Piskiewicz's equation (1977) is 1·4, indicating a positive interaction between the anionic micelle and the substrate.

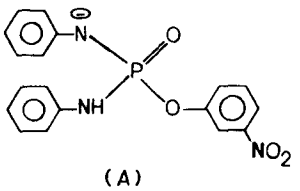
The rate of hydroxylaminolysis of PMS(I) and PDI(II) is slow at pH = 6·15 and the specific rate of hydrolysis of these esters at pH = 9·2 is least affected by added imidazole. As the hydrolysis of PMS and PDI preferably follows the E_1cB path at this pH, imidazole has no effect on these reactions. As the sulphur and phosphorus centres involved in the E_1cB path seem to deter the nucleophilic attack by imidazole, similar reactivity is expected for the nitrogen end of H_2NOH. But the formation of a such an anion (A) is not favoured at pH = 6·15 and the E_1cB path will be less favoured at this pH. As the added imidazole does catalyse the hydroxyaminolysis of sulphate and phosphate esters at pH = 6·15, these esters probably prefer the $B_{Ac}2$ path at this pH. From the above results on the hydroxylaminolysis of esters, coupled with imidazole catalysis, E_1cB or $B_{Ac}2$ mechanisms have been assigned to the reactions.



I (PMS)



II (PDI)



(A)

Chart 1.

3. Experimental

3.1 *Materials*

PNPB was prepared following the procedure in Vogel (1978). *p*-Nitrophenylphenylmethane sulphonate (PMS) was prepared by the procedure of Davy *et al* (1977). The ester, *m*-nitrophenyl-N,N-diphenylphosphorodiamidate was prepared by refluxing a mixture of aniline, $POCl_3$ and *m*-nitrophenol in the ratio 2:1:1 in the presence of catalytic amounts of pyridine. The refluxing was continued for 4 hrs and then the mixture was cooled and the solid compound which separated, recrystallised from chloroform–hexane mixture. The purity of the compound was checked by the TLC technique (m.p. 172°C).

The surfactants were of extra pure variety (BDH/Aldrich) and were further purified by crystallization from dry ether until the critical micelle concentration agreed with the

reported value (Fendler and Fendler 1975). Acetonitrile was purified by distillation over P_2O_5 and the fraction distilling out at 80°–81°C was collected and stored in air-tight bottles. Borex, used as buffering agent was of analytical grade (BDH) and was used without further purification. The hydroxypyridines, benzamidine and imidazole obtained from Aldrich were used as such.

All the hydrolytic reactions were carried out at pH = 9·2, maintaining the pH with borax buffers while the kinetics of hydroxylaminolysis of PNPB was studied at pH = 6·15 in 2·5% CH_3CN–97·5% H_2O (v/v) at 30°C at an ionic strength of 0·50 maintained by using 0·50 M NaCl. A solution of the required pH was prepared by titrating a solution of the buffer agent of known concentration against NaOH (carbonate free), pH being measured with a digital pH meter (of 0·010 accuracy). Whenever surfactants were employed the pH of the buffer solution was adjusted in the presence of the required concentration of surfactant.

3.2 *Rate measurements*

The reactions were studied by monitoring the increase in absorbance due to the release of the *p*-nitrophenoxide ion at 400 nm or *p*-nitrophenol at 320 nm on a Carl-Zeiss VSU2-P spectrophotometer provided with a thermostatic cell compartment. All the hydrolytic reactions were conducted at 30°C and at 0·10 ionic strength, maintained by using 0·10 M NaCl, unless otherwise mentioned. The reactions were studied for at least four half-lives and the rate constants were evaluated from the slopes of the regression lines for correlation of $\log(A - A_t)$ versus time. The linear regression analysis was performed on a micro 2200 programmable calculator (Hindustan Computers, India).

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