SPECIFIC CATALYTIC ACTION OF LARGE MOLECULES CONTAINING IMIDAZOLE GROUPS

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INTRODUCTION

In recent years, studies of the reaction rates of small molecules in the presence of synthetic polymers containing catalytically active functions have contributed significantly to the understanding of the mechanism of enzyme behaviour[1]. Of particular interest in the field of polymeric catalysis have been the studies of the solvolyses of esters catalyzed by polymers containing pendent imidazole groups because the imidazole moiety has been shown to play a prolific role in enzymatic reactions[2-7].

In reactions catalyzed by poly-4(5)-vinylimidazole and by poly-5(6)-vinylbenzimidazole, three types of cooperative effects have been indicated.

(i) Cooperative interaction between two imidazole groups and substrate where neutral imidazole acts as a nucleophile on the substrate and anionic imidazole acts as a general base on the intermediate. This type of bifunctional catalysis was indicated in the poly-4(5)-vinylimidazole catalyzed solvolysis of PNPA (*p*-nitrophenyl acetate) and in the poly-5(6)-vinylbenzimidazole catalyzed solvolyses of PNPA, NABA (4-acetoxy-3-nitrobenzoic acid) and NABS (sodium 4-acetoxy-3-nitrobenzenesulphonate), all solvolyses occurring at high pH values[3, 4].

(ii) Cooperative interaction between two neutral, pendent imidazole groups and substrate where at intermediate pH the nucleophilic imidazole reaction is catalyzed by another neutral imidazole function acting as a general base[6].

(iii) Cooperative interaction between neutral and protonated imidazole groups in the solvolyses of NABA and NABS. The protonated sites on the polymer chain, which do not catalyze the solvolysis of PNPA, apparently serve as binding sites for the negatively charged esters, thereby facilitating a solvolytic attack from a neighbouring imidazole group. Because the solvolytic reactions are dependent on the concentrations of both protonated and neutral sites on the polymer chain, bell-shaped pH-rate profiles were obtained[3, 4].

A cooperative effect analogous to that described in (iii) (i.e., utilization of electrostatic attraction of substrate to the polymer chain) was observed in the solvolysis of the positively charged ester 3-acetoxy-*N*-trimethylanilinium iodide (ANTI) catalyzed by a copolymer of 4(5)-vinylimidazole and acrylic acid[5]. Although this copolymer was a less efficient catalyst than imidazole in solvolyzing PNPA and NABA, it exhibited marked selectivity towards ANTI at high pH values. The higher reactivity of the copolymer was rationalized

by the electrostatic attraction of the ester to the anionic carboxylate groups on the polymer, followed by a catalytic interaction from a neighbouring imidazole group. This is the first reported example of a copolymer capable of separating the roles of electrostatic attraction and catalytic action between two different functional groups on a polymer chain. A reaction of this type could be responsible for the high catalytic efficiency of acetylcholinesterase[8].

In order to substantiate the multifunctional catalysis displayed by poly-4(5)-vinylimidazole and poly-5(6)-vinylbenzimidazole, the activation parameters of reactions catalyzed by poly-4(5)-vinylimidazole, by poly-5(6)-vinylbenzimidazole and by poly-N-vinylimidazole were compared to the corresponding values for their respective monomeric analogues[6, 7]. In *Table 1*, the differences in enthalpy of activation $[\Delta(\Delta H_{\ddagger}^{\ddagger})]$ and in $T\Delta S_{\ddagger}^{\ddagger}$ $[\Delta(T\Delta S_{\ddagger}^{\ddagger})]$ for the solvolyses of PNPA catalyzed by polymeric and monomeric imidazole are listed. Particular attention was given to the poly-N-vinylimidazole catalyzed solvolysis of PNPA, since at high pH it was believed that the imidazole groups in this polymer could not participate in a multifunctional interaction with the substrate.

Table 1. Differences in activation parameters for polymeric and monomeric imidazole catalyzed solvolyses of PNPA (in kcal/mole)

Catalysts		$\Delta(\Delta H_{\ddagger}^{\ddagger})$	$\Delta(T\Delta S_{\ddagger}^{\ddagger})$
Polymer	*Monomer*		
Poly-N-vinylimidazole	N-Methylimidazole	$-0\cdot4$	$-1\cdot1$
Poly-4(5)-vinylimidazole	Imidazole	$-3\cdot3$	$-2\cdot9$
Poly-5(6)-vinylbenzimidazole	Benzimidazole	$-2\cdot8$	$-1\cdot8$

Although there were only slight differences in the activation parameters for the solvolyses of PNPA catalyzed by poly-N-vinylimidazole and by N-methylimidazole, both poly-4(5)-vinylimidazole and poly-5(6)-vinyl-benzimidazole had marked decreases in enthalpy of activation relative to their respective monomeric analogues, imidazole and benzimidazole. These results were interpreted to be indicative of the existence of a higher functionality in reactions catalyzed by poly-4(5)-vinylimidazole and by poly-5(6)-vinylbenzimidazole than in reactions catalyzed by their respective monomeric analogues. The smaller reduction in $T\Delta S_{\ddagger}^{\ddagger}$ agrees with the anticipation that by transforming a third-order reaction into a lower order reaction of the same functionality (such as on a dimer or polymer), the $\Delta H_{\ddagger}^{\ddagger}$ of the third-order reaction is retained and the $T\Delta S_{\ddagger}^{\ddagger}$ term will be close to that of a second-order reaction[9]. As a result of this combination, multifunctional polymeric imidazole catalysis would be expected to show a greater catalytic efficiency than simple monomeric catalysis, as observed. Apparently, the high local concentration of pendent imidazole or benzimidazole groups on the polymer chain facilitates their action as multifunctional catalysts. This is analogous to an enzymatic reaction because the multifunctional attack by the groups of the active site of an enzyme on a substrate is believed to lead to a lowering of the enthalpy of activation for the solvolytic reaction[10-12].

Since the active sites of enzymes are usually comprised of several catalytic species, it was of interest to determine whether cooperative, catalytic interactions would occur between two different functional groups within a vinyl polymer chain and a substrate. Systems chosen for reporting here were two copolymers of 4(5)-vinylimidazole and vinyl alcohol and one copolymer of 4(5)-vinylimidazole and p-vinylphenol. It was believed that the copolymers with pendent imidazole and hydroxyl groups might serve as simple models for the active site of α-chymotrypsin[13], while the copolymer with pendent imidazole and phenol groups could be expected to enhance the overall polymeric nucleophilicity [relative to poly-4(5)-vinylimidazole]. The occurrences of any cooperative interactions between the functional groups in these copolymers could be ascertained by comparing the solvolytic rates of the substrates in the presence of the imidazole–alcohol and imidazole–phenol copolymers and in the presence of their respective monomeric and homopolymeric analogues.

Although previous studies had indicated that no cooperative interactions between imidazole and hydroxyl groups had occurred at intermediate pH[14, 15] it was believed that the study of several substrates over a range of pH would be more informative.

The two copolymers containing pendent imidazole and hydroxyl groups in ratios of 1 : 0·31 and 1 : 0·65 were prepared by free radically initiated solution and bulk copolymerizations of 4(5)-vinylimidazole and vinyl acetate, followed by rapid intramolecular hydrolyses of the acetate functions catalyzed by the neighbouring imidazole groups[15, 16].

The copolymer containing pendent imidazole and phenol groups in a ratio of 1 : 1·95 was prepared by a free radically initiated solution copolymerization of 4(5)-vinylimidazole and p-vinylphenol. Since the previously reported procedures for the preparation of p-vinylphenol were usually laborious and resulted in poor yields[17], an improved procedure was sought. It was found that p-vinylphenol could be prepared in one step from the pyrolysis of p-hydroxycinnamic acid. The yield obtained was 58 per cent based on recovered starting material. Poly-p-vinylphenol was obtained when p-vinylphenol was allowed to stand at room temperature[17].

EFFECTS OF IMIDAZOLE–ALCOHOL COPOLYMERS ON THE SOLVOLYTIC RATES OF ESTERS

In order to determine whether the pendent imidazole and hydroxyl groups were involved in any cooperative catalytic interactions with the substrates, the catalytic activities of the imidazole–alcohol copolymers, poly-4(5)-vinylimidazole and imidazole were compared over a range of pH utilizing the esters PNPA, NABA and NABS.

The first-order observed rate constants (the differences in reaction rate constants in the presence and absence of catalysts) for the solvolyses of PNPA catalyzed by 1 : 0·31 and 1 : 0·65 imidazole–alcohol copolymers, by poly-4(5)-vinylimidazole and by imidazole are listed in *Table 2*. All catalyst solutions utilized in this study were prepared in 28·5 per cent ethanol–water buffered solutions at an ionic strength[3] of 0·02. The first-order observed rate constants were calculated for concentrations of 2·5 × 10^{-4} M in imidazole.

The observed rate constants in *Table 2* are plotted against pH in *Figure 1*

and against α_1 (the fraction of neutral imidazole) in *Figure 2*. The pK_1 values for the imidazole groups at half neutralization were determined to be 5·45 for the 1 : 0·31 imidazole–alcohol copolymer, 5·55 for the 1 : 0·65 imidazole–alcohol copolymer, and 6·10 for poly-4(5)-vinylimidazole at an ionic strength of 0·02 in 28·5 per cent ethanol–water.

Table 2. First-order observed rate constants for 1 :0·31 imidazole-alcohol copolymer, 1 :0·65 imidazole-alcohol copolymer, poly-4(5)-vinylimid-azole and imidazole catalyzed solvolyses of PNPA

pH	$k_{obs} \times 10^3$ (min^{-1})			
	1:0·31 Im–OH	*1:0·65 Im–OH*	*Homopolymer*	*Imidazole*
6·02	1·47	1·33	1·17	0·78
7·14	4·07	3·34	2·76	2·87
8·04	6·40	4·64	4·56	—
9·14	9·35	6·60	5·56	4·23

It is apparent from inspection of *Figures 1* and *2* that the homopolymer is a more efficient catalyst than imidazole in catalyzing the solvolysis of PNPA as the pH of the solution is increased. This effect can be rationalized by the terfunctional interaction of neutral and anionic imidazole groups on the polymer with PNPA. Furthermore, both imidazole–alcohol copolymers are more reactive than poly-4(5)-vinylimidazole in the pH region investigated, and this enhancement cannot be rationalized on the basis of the lower apparent pK_1's of the imidazole groups in the copolymers. It would be
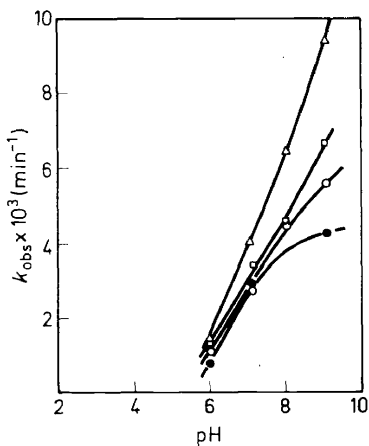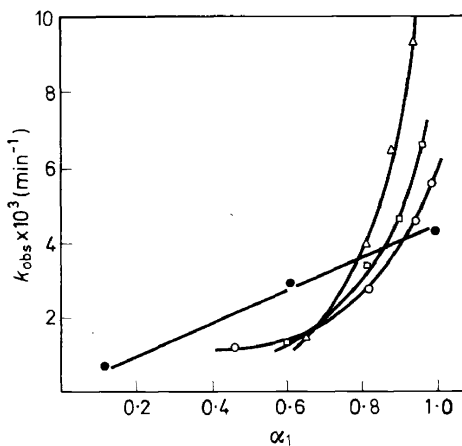

Figure 1   *Figure 2*

Figure 1. pH–rate profiles for the solvolysis of PNPA catalyzed by 1 : 0·31 imidazole–alcohol copolymer ($\triangle$), by 1 : 0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinyli-midazole ($\bigcirc$), and by imidazole ($\bullet$).

Figure 2. Solvolysis of PNPA catalyzed by 1 : 0·31 imidazole–alcohol copolymer ($\triangle$), by 1 : 0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinylimidazole ($\bigcirc$), and by imidazole ($\bullet$).

expected that if the hydroxyl groups did not participate in the solvolytic process, a reduction in the copolymer reactivity [in comparison to poly-4(5)-vinylimidazole] would ensue because of a dilution of the local concentration of catalytic imidazole groups on the polymer chain. Such reductions in polymeric imidazole activity have been previously observed when the local concentration of pendent imidazole groups were diluted with other functional groups[5, 18].

The enhanced activities of the imidazole–alcohol copolymers at high pH toward PNPA could be due to either the cooperative interaction of imidazole and hydroxyl groups, such as occurs in α-chymotrypsin catalyzed hydrolyses[13], or to the separate catalytic action of imidazole (neutral and anionic) and alkoxide groups. On the copolymer chain it is possible that the apparent pK_a of the hydroxyl groups is decreased and that the alkoxide residues could participate in the catalytic process[19].

The imidazole–alcohol copolymers also exhibited enhanced activities in the catalyzed solvolyses of the negatively charged esters NABA and NABS. The first order observed rate constants for the solvolyses of NABA catalyzed by the imidazole–alcohol copolymers, by poly-4(5)-vinylimidazole and by imidazole appear in *Table 3*.

Table 3. First-order observed rate constants for 1:0·31 imidazole–alcohol copolymer, 1:0·65 imidazole–alcohol copolymer, poly-4(5)-vinylimidazole and imidazole catalyzed solvolyses of NABA

pH	$k_{obs} \times 10^2$ (min^{-1})			
	1:0·31 Im–OH	*1:0·65 Im–OH*	*Homopolymer*	*Imidazole*
4·08	0·57	0·50	0·43	—
6·02	4·58	3·60	2·76	0·15
7·14	4·38	3·11	2·93	0·51
8·04	2·65	1·60	1·57	—
9·14	—	—	—	0·77
10·30	0·98	0·62	1·00	—

Plots of pH *vs.* k_{obs} and α_1 *vs.* k_{obs} for the data in *Table 3* appear in *Figures 3* and *4*, respectively. The bell-shaped pH- rate profiles obtained for the polymeric reactions are analogous to those previously reported for the solvolyses of negatively charged substrates catalyzed by polymers that contain both protonated sites and catalytically active functions[3, 4, 20]. It is also apparent that the imidazole–alcohol copolymers are more efficient catalysts than poly-4(5)-vinylimidazole for the solvolysis of NABA. The enhanced copolymer activities cannot be explained on the basis of the lower apparent pK_1's of the imidazole groups in the copolymers at half neutralization, since the copolymers are shown to be more reactive than the homopolymer in the plot of α_1 *vs.* k_{obs} (*Figure 4*).

Results analogous to those mentioned above were obtained when NABS was employed as the substrate. In *Table 4*, the first-order observed rate constants for the solvolyses of NABS catalyzed by the imidazole–alcohol copolymers, by poly-4(5)-vinylimidazole and by imidazole, are listed. The
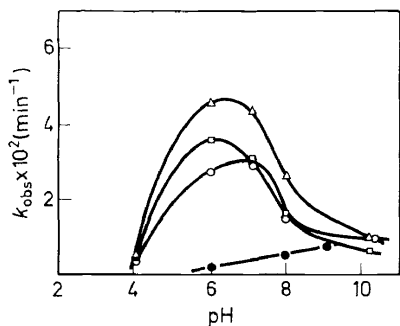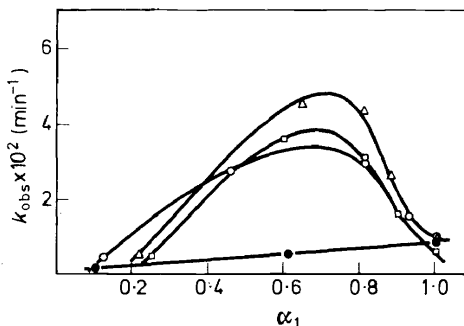
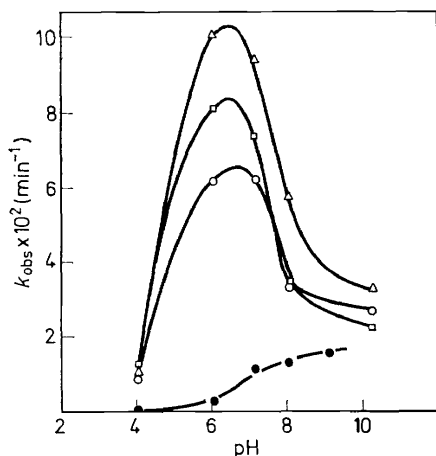Figure 3   Figure 4

Figure 3. pH–rate profiles for the solvolysis of NABA catalyzed by 1:0·31 imidazole–alcohol copolymer ($\triangle$), by 1:0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinyl-imidazole ($\bigcirc$), and by imidazole ($\bullet$).

Figure 4. Solvolysis of NABA catalyzed by 1:0·31 imidazole–alcohol copolymer ($\triangle$), by 1:0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinylimidazole ($\bigcirc$), and by imidazole ($\bullet$).

Table 4. First-order observed rate constants for 1:0·31 imidazole-alcohol copolymer, 1:0·65 imidazole–alcohol copolymer, poly-4(5)-vinylimidazole and imidazole catalyzed solvolyses of NABS

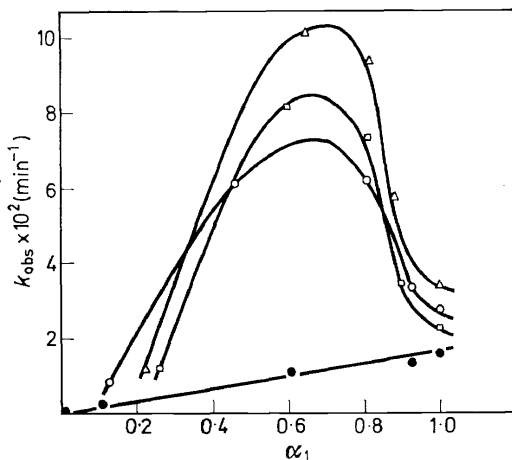| pH	$k_{obs} \times 10^2$ (min^{-1})			
	1:0·31 Im–OH	*1:0·65 Im–OH*	*Homopolymer*	*Imidazole*
4·08	1·20	1·25	0·89	0·01
6·02	10·10	8·16	6·12	0·29
7·14	9·40	7·39	6·22	1·17
8·04	5·77	3·42	3·37	1·33
9·14	—	—	—	1·58
10·30	3·30	2·23	2·69	—

Figure 5. pH–rate profiles for the solvolysis of NABS catalyzed by 1:0·31 imidazole–alcohol copolymer ($\triangle$), by 1:0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinylimidazole ($\bigcirc$), and by imidazole ($\bullet$).

Figure 6. Solvolysis of NABS catalyzed by 1 : 0·31 imidazole–alcohol copolymer ($\triangle$), by 1 :0·65 imidazole–alcohol copolymer ($\square$), by poly-4(5)-vinylimidazole ($\bigcirc$), and by imidazole ($\bullet$).

first-order constants are plotted against pH in *Figure 5* and against α_1 in *Figure 6.*

It is again noted that the imidazole–alcohol copolymers are more efficient catalysts in the pH region investigated than are either poly-4(5)-vinyl-imidazole or imidazole, and that the 1 : 0·31 imidazole–alcohol copolymer was in each instance a better catalyst than the 1 : 0·65 imidazole–alcohol co-polymer. The latter effect may be due to the arrangement of groups on the polymer chain and/or to the greater proportion of imidazole groups in the 1 : 0·31 copolymer.

It can be concluded that the presence of hydroxyl groups on a polymeric imidazole chain has caused a significant enhancement of the polymeric reactivity with negatively charged substrates at intermediate pH. The enhanced activities of the imidazole–alcohol copolymers can be rationalized by the electrostatic attraction of the negatively charged substrates to the protonated sites on the polymer chain such that either cooperative inter-actions between imidazole and hydroxyl groups or separate interactions of imidazole and hydroxyl groups (from neighbouring positions[21]) can occur in the solvolytic process. Evidence which favours more strongly the effect of bifunctional catalysis involving pendent imidazole and —OH functions was indicated in the imidazole–phenol copolymer catalyzed solvolyses of esters.

EFFECT OF IMIDAZOLE–PHENOL COPOLYMER ON THE SOLVOLYTIC RATES OF ESTERS

The effect of the imidazole–phenol copolymer on the solvolytic rates of esters was investigated in a manner analogous to that employed for the imidazole–alcohol copolymers, i.e. the observed rate constants for the solvolyses of esters in the presence of the imidazole–phenol copolymer, poly-4(5)-vinylimidazole, imidazole, phenol and poly-*p*-vinylphenol were compared at several pH values.

The solvent system used in this investigation was methanol–water (80:20), since both the imidazole–phenol copolymer and poly-p-vinylphenol were insoluble in systems containing lower percentages of alcohol. The first order observed rate constants were determined for concentrations of $2 \cdot 5 \times 10^{-4}$ M (in either imidazole or phenol).

Table 5. First-order observed rate constants for $1:1 \cdot 95$ imidazole–phenol copolymer, poly-4(5)-vinylimidazole and imidazole catalyzed solvolyses of PNPA

pH	$k_{obs} \times 10^4$ (min^{-1})		
	1:1·95 Im–φOH	*Homopolymer*	*Imidazole*
7·38	3·02	2·10	2·62
8·22	5·12	3·00	2·39
9·12	28·60	3·15	2·70

In *Table 5* are listed the first-order observed rate constants for the solvolyses of PNPA catalyzed by $1:1 \cdot 95$ imidazole–phenol copolymer, by poly-4(5)-vinylimidazole and by imidazole. These values are plotted against pH in *Figure 7*. It was observed that neither phenol nor poly-p-vinylphenol affected the solvolytic rate of PNPA in the pH region investigated.

It is apparent from inspection of *Figure 7* that the imidazole–phenol copolymer greatly increased the solvolytic rate of PNPA as the pH of the solution was increased. This strong enhancement of the solvolytic rate was not observed with either poly-4(5)-vinylimidazole or imidazole, both of which had nearly identical reactivities in the pH region and solvent system investigated.

In comparing the reactivities of the imidazole–phenol copolymer and the imidazole–alcohol copolymers towards PNPA in the pH range 7–9 in their respective solvent systems, it is evident that the imidazole–phenol copolymer is a much more efficient catalyst than either imidazole–alcohol copolymer. The enhanced activity of the imidazole–phenol copolymer appears to be a consequence of the interaction of both neutral imidazole and anionic phenol with the substrate. The fraction of anionic phenol in the copolymer was determined by spectrophotometric titration to be *c.* 0·1 at pH 9. Since neither phenol nor poly-p-vinylphenol, with fractions of anionic phenol at pH 9 of 0·14 and 0·04, respectively, catalyzed the solvolysis of PNPA to a detectable extent in the pH region investigated, the occurrence of a terfunctional interaction among imidazole, anionic phenol and substrate is strongly indicated for the imidazole–phenol copolymer catalyzed reaction.

The cooperative interaction of pendent imidazole and phenol groups on a polymer chain is also indicated in the imidazole–phenol copolymer catalyzed solvolyses of NABA and NABS. The observed rate constants for the imidazole–phenol copolymer, for poly-4(5)-vinylimidazole and for imidazole catalyzed solvolyses of NABA and NABS are summarized in *Tables 6* and *7*, respectively. Plots of pH *vs.* k_{obs} for NABA and NABS appear in *Figures 8* and *9*, respectively. Neither phenol nor poly-p-vinylphenol were observed to catalyze the solvolyses of NABA and NABS in the pH region studied.
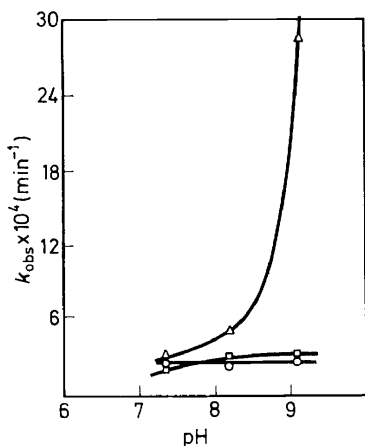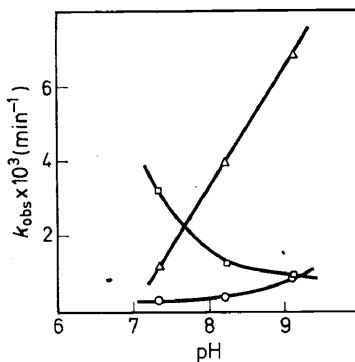
Figure 7   Figure 8

Figure 7. pH–rate profiles for the solvolysis of PNPA catalyzed by 1 : 1·95 imidazole–phenol copolymer ($\triangle$), by poly-4(5)-vinylimidazole ($\square$) and by imidazole ($\bigcirc$).

Figure 8. pH–rate profiles for the solvolysis of NABA catalyzed by 1 : 1·95 imidazole–phenol copolymer ($\triangle$), by poly-4(5)-vinylimidazole ($\square$), and by imidazole ($\bigcirc$).

Table 6. First-order observed rate constants for 1 : 1·95 imidazole–phenol copolymer, poly-(45)-vinylimidazole and imidazole catalyzed solvolyses of NABA

pH	$k_{obs} \times 10^3$ (min^{-1})		
	1:1·95 Im–ϕOH	Homopolymer	Imidazole
7·38	1·27	3·29	0·32
8·22	3·99	1·37	0·44
9·12	6·90	0·96	0·98

Table 7. First-order observed rate constants for 1 : 1·95 imidazole–phenol copolymer, poly-4(5)-vinylimidazole and imidazole catalyzed solvolyses of NABS

pH	$k_{obs} \times 10^3$ (min^{-1})		
	1:1·95 Im–ϕOH	Homopolymer	Imidazole
7·38	4·13	6·92	0·52
8·22	9·54	3·79	1·14
9·12	17·48	1·27	2·48

Striking differences between the imidazole–phenol copolymer and poly-4(5)-vinylimidazole are noted in *Figures 8* and *9*. Although the homopolymer exhibits its characteristic decrease in reactivity towards negatively charged esters with increasing pH, the imidazole–phenol copolymer exhibits an enhanced reactivity with increasing pH (compare *Figures 3* and *8* for NABA

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and *Figures 5* and *9* for NABS). Since neither phenol nor poly-*p*-vinylphenol were effective catalysts for the solvolyses of the negatively charged substrates, the enhanced reactivity of the imidazole–phenol copolymer suggests that as the fractions of neutral imidazole and anionic phenol increase, the co-operative catalytic interactions of these groups also increase.
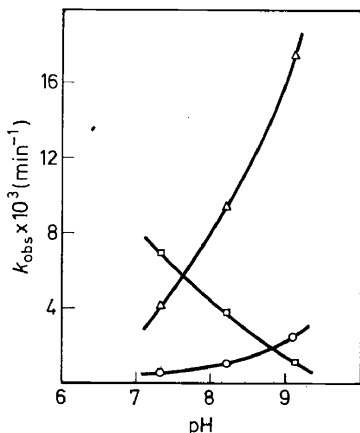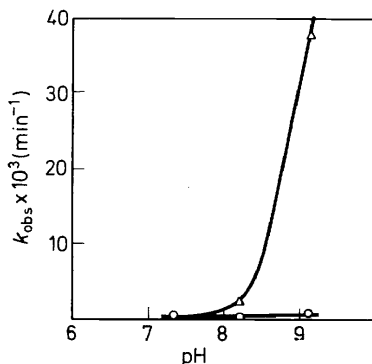

Figure 9   Figure 10

Figure 9. pH–rate profiles for the solvolysis of NABS catalyzed by 1 : 1·95 imidazole–phenol copolymer (△), by poly-4(5)-vinylimidazole (□), and by imidazole (○).

Figure 10. pH–rate profiles for the solvolysis of ANTI catalyzed by 1 : 1·95 imidazole–phenol copolymer (△), and by imidazole (○).

This situation is analogous to that observed in the poly-5(6)-vinylbenz-imidazole catalyzed solvolyses of NABA and NABS at high pH where neutral and anionic benzimidazole were believed to be involved in a ter-functional reaction of substrate and neutral and anionic benzimidazole[4].

A further indication of the cooperative intramolecular interaction between imidazole and phenol groups on a polymer chain is evident in the imidazole–phenol copolymer catalyzed solvolysis of the positively charged ester ANTI. It was believed that the imidazole–phenol copolymer would be more reactive towards ANTI than towards PNPA, NABA, or NABS, since ANTI should be electrostatically attracted to the anionic phenoxide groups on the polymer chain. This greater reactivity was indeed observed. In *Table 8* the observed rate constants for the solvolyses of ANTI catalyzed by the imidazole–phenol copolymer and by imidazole are listed. Neither poly-4(5)-vinyl-imidazole, phenol nor poly-*p*-vinylphenol affected the solvolytic rate of ANTI in the pH range investigated.

The plot of pH *vs.* k_{obs} for the solvolysis of ANTI catalyzed by the imida-zole–phenol copolymer and by imidazole appears in *Figure 10*. It is apparent that the copolymer exhibits marked selectivity towards ANTI. While the copolymer of 4(5)-vinylimidazole and acrylic acid was approximately four times more reactive than imidazole in solvolyzing ANTI at pH 9·5[5], the

Table 8. First-order observed rate constants for 1:1·95 imidazole–phenol copolymer and imidazole catalyzed solvolyses of ANTI

pH	$k_{obs} \times 10^3$ (min^{-1})	
	Im–ϕOH	Imidazole
7·38	0·09	0·06
8·22	2·12	0·20
9·12	37·66	0·57

imidazole–phenol copolymer had an observed rate constant approximately 66 times larger than imidazole at pH 9·1.

Presumably, the enhanced activity of the imidazole–phenol copolymer towards ANTI can in part be explained by an argument analogous to that utilized for the imidazole–acrylic acid copolymer, i.e. by the electrostatic attraction of ANTI to the anionic sites on the polymer chain. However, while the carboxylate groups in the imidazole–acrylic acid copolymer served only as binding sites for ANTI, the nucleophilic phenoxide groups, besides functioning as binding sites, may cooperate with imidazole in the catalytic process. The latter argument appears to be realized in this investigation because neither phenol, poly-p-vinylphenol nor poly-4(5)-vinylimidazole were found to catalyze separately the solvolysis of ANTI to a detectable extent.

Based on the results obtained in this study, a mechanicam is given below which illustrates the cooperative catalytic interaction of imidazole and phenol groups; imidazole acts as a nucleophile on the substrate, and anionic phenol acts as a general base on the intermediate.
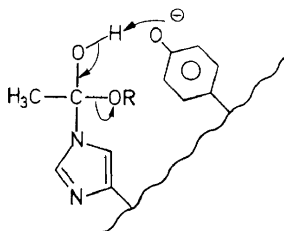
Although the catalytic efficiencies of polymeric imidazoles have yet to approach those of enzymes, we have demonstrated that reactions catalyzed by such polymers behave in a manner characteristic of enzyme catalyzed reactions.

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