water. These ampoules were stored at *ca.* 5° until all the ampoules had been collected. Because the polarimeter tube held less than 3 ml., each ampoule was charged with only 4 ml. of solution. Usually 12 points were used for a kinetic determination. All optical measurements were made using the technique described in the accompanying paper.[9]

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The Enhanced Esterolytic Catalysis of Poly-4(5)-vinylimidazole and Poly-5(6)-vinylbenzimidazole[1]

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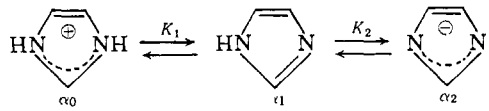
The homopolymers of 4(5)-vinylimidazole and 5(6)-vinylbenzimidazole were found to be better catalysts than imidazole and benzimidazole, respectively, for the solvolysis of p-nitrophenyl acetate at high pH values. The polymeric effect is pH dependent and is a result of enhanced contributions of the anionic fractions of the polymers. With the negatively charged substrate 4-acetoxy-3-nitrobenzoic acid and poly-4(5)-vinylimidazole a bell-shaped pH–rate profile was observed as a result of electrostatic attraction to the protonated sites of the polymer. This effect was not operating with poly-5(6)-vinylbenzimidazole at low pH values. On the other hand, the anionic sites of poly-5(6)-vinylbenzimidazole were found to be very reactive toward the negatively charged substrate at high pH values, which was in contrast to the inertness of the anions of the monomer. The possible mechanisms for the high reactivity of the polymeric anions are discussed.

Introduction

Imidazole has been implicated in the active site of several esterolytic enzymes by chemical and kinetic studies. Imidazole is an ampholyte having two pK_a values. In chymotrypsin imidazole probably participates in the acylation and deacylation steps, either as a



nucleophile or as a general base.[2] In chymotrypsin it reacts as the free base (α_1), though some indications point to contributions of the anionic form (α_2) as well.[3] In acetylcholinesterase[4] and β-galactosidase[5] the basic group may be supplied by the imidazole function. However, in α-amylase imidazole is probably furnishing the general acid part of the active site.[6] Ribonuclease may be utilizing two imidazole functions, one in the acidic (α_0) and one in the free-base form (α_1).[7]

The important role of imidazole in enzymatic reactions has prompted an extensive study of the esterolytic catalysis of monomeric imidazoles by Bruice,[8,9] Jencks,[10] and Bender.[11] No catalytic action of [IMH^+] in the monomers has yet been observed. So far the following contributions were noted.

$$\text{rate} = k_1[\text{IM}][\text{substrate}] + k_2[\text{IM}]^2[\text{substrate}] + k_3[\text{IM}][\text{OH}^-][\text{substrate}]^{10} \quad (1)$$

If the interaction between the imidazole group and the hydroxyl group occurs in a pre-equilibrium step, the contribution of the imidazole anion can be described as

$$k_{\text{anionic}}[\text{IM}^-][\text{substrate}] \quad (2)$$

or the total second-order contribution will be[8]

$$k_1 = k_{\text{neutral}}\alpha_1 + k_{\text{anionic}}\alpha_2 \quad (3)$$

k_3 and k_{anionic} are related by the equation

$$k_3 = k_{\text{anionic}}K_2/K_w \quad (4)$$

Since enzymatic reactions show different imidazole contributions than monomeric imidazoles, we thought that incorporation of imidazole groups on inert polyvinyl chain would provide additional interactions to those available for the monomers, and that cooperative effects may enhance the over-all catalytic rate. Low and high molecular weight polymers and copolymers of histidine employing the polypeptide backbone have been studied.[12-14] While the high molecular weight

(1) For a previous report see C. G. Overberger, T. St. Pierre, N. Vorchheimer, and S. Yaroslavsky, *J. Am. Chem. Soc.*, **85**, 3513 (1963). This paper comprises a portion of a dissertation submitted by T. St. Pierre in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

(2) M. L. Bender, G. E. Clement, F. J. Kézdy, and B. Zerner, *ibid.*, **85**, 348 (1963); M. L. Bender, *Chem. Rev.*, **60**, 105 (1960); M. L. Bender, G. R. Schonbaum, and G. E. Hamilton, *J. Polymer Sci.*, **49**, 94 (1961).

(3) See footnote 29 in ref. 8.

(4) I. B. Wilson and F. Bergmann, *J. Biol. Chem.*, **185**, 683 (1950); F. Bergmann, I. B. Wilson, and D. Nachmanshon, *ibid.*, **186**, 693 (1950).

(5) K. Wallenfels and O. P. Malhotra, "The Enzymes," Vol. IV, P. D. Boyer, H. A. Lardy, and K. Myrbäck, Ed., Academic Press Inc., New York, N. Y., 1960, pp. 409–430.

(6) E. H. Fisher and E. A. Stein in ref. 5, pp. 313–343.

(7) D. G. Herries, *Biochem. Biophys. Res. Commun.*, **3**, 666 (1960).

(8) T. C. Bruice and G. E. Schmir, *J. Am. Chem. Soc.*, **80**, 148 (1958).

(9) T. C. Bruice and S. J. Benkovic, *ibid.*, **86**, 418 (1964).

(10) I. F. Kirsch and W. P. Jencks, *ibid.*, **86**, 833, 837 (1964).

(11) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1652, 1656 (1957).

(12) E. Katchalski, G. D. Fasman, E. Simons, E. R. Blout, F. R. N. Gund, and W. L. Koltun, *Arch. Biochem. Biophys.*, **88**, 361 (1960).

polymers usually demonstrate rates comparable to that of imidazole itself,[12] some oligomers have rates faster than that of the monomers.[13,14]

Experimental

Poly-4(5)-vinylimidazole was prepared as previously described.[15] The polymer did not melt below 300°: $[\eta]$ = 0.34; $\bar{\nu}_{max}^{KBr}$ 628, 735, 770, 820, 940, 980, 1085, 1110, 1150, 1230, 1250, 1300, 1350, 1450, 1480, 1575, 1630, and 2600–3400 (broad) cm.$^{-1}$.

Poly-5(6)-vinylbenzimidazole was prepared directly by the dehydrochlorination of 5(6)-(β-chloroethyl)-benzimidazole.[16] The conversion may be accomplished by a strong base or simply heating in a vacuum oven. 5(6)-(β-Chloroethyl)benzimidazole (4.14 g.) was heated for 16 hr. at 80° in a vacuum oven (100 mm.) to yield a clear brown film of a polymer. The solid was crushed and extracted with acetone for 2 days, dissolved in dilute hydrochloric acid, and then precipitated with sodium bicarbonate solution. The polymer was redissolved in ethanol and precipitated in ether. This procedure was repeated to yield 1.5 g. (47%) of polymer as a pale yellow powder, m.p. 260–270° dec.; $[\eta]$ = 0.03. The infrared absorption in KBr pellets indicated a broad band at 2800–3500 cm.$^{-1}$ for N–H···N bond,[17] and sharp bands at 1500, 1600, and 1620 cm.$^{-1}$ for C=C and C=N bonds with no substitution in the heterocyclic ring.

Anal. Calcd. for $(C_9H_8N_2 \cdot H_2O)_x$: C, 66.6; H, 6.2; N, 17.2. Found: C, 66.1; H, 6.5; N, 17.1.

Poly-N-vinylimidazole was prepared by free-radical polymerization of N-vinylimidazole.[18] In a polymerization tube was placed a solution of 1.0 g. of freshly distilled N-vinylimidazole and 20 mg. of azobisisobutyronitrile in 10 ml. of anhydrous benzene. The tube was cooled to −70° and the mixture was degassed *in vacuo* by successive flushing with nitrogen and evacuation. The tube was sealed under vacuum and heated at 70° for 48 hr. The solid obtained was collected by filtration, dissolved in 20 ml. of methanol, and precipitated in acetone two times, yielding 0.67 g. (67%). The compound did not melt below 280°; $\bar{\nu}_{max}^{KBr}$ 632, 660, 735, 815, 909, 1080, 1110, 1225, 1283, 1360, 1415, 1500, 1630, 1710, 2950, and 3105 cm.$^{-1}$.

Anal. Calcd. for $(C_5H_6N_2 \cdot {}^1/_3H_2O)_x$: C, 60.0; H, 6.7; N, 28.0; H_2O, 6.0. Found: C, 60.5; H, 6.9; N, 27.1; H_2O, 6.4.

Poly-2-methyl-N-vinylimidazole was prepared from 2-methyl-N-vinylimidazole[19a] in a similar fashion to that of the former polymer. The compound dissolved in methanol and was reprecipitated in methyl ethyl ketone twice; conversion 65%. The compound did not melt below 280°; $\bar{\nu}_{max}^{KBr}$ 675, 735, 985, 1110, 1130, 1155, 1280, 1420, 1490, 1530, 1630, 2930, and 3110 cm.$^{-1}$.

Anal. Calcd. for $(C_6H_8N_2 \cdot {}^1/_3H_2O)_x$: C, 63.1; H, 7.7; N, 24.6. Found: C, 63.5; H, 8.0; N, 23.8.

p-Nitrophenyl acetate was prepared from *p*-nitrophenol and acetic anhydride in the conventional fashion; m.p. 81° (lit.[19b] 81–82°) from aqueous ethanol.

4-Acetoxy-3-nitrobenzoic Acid. A solution of 18.3 g. (0.1 mole) of 4-hydroxy-3-nitrobenzoic acid[20] was prepared in 168 ml. of 5% sodium hydroxide (0.21 mole). The solution was cooled in ice and a large excess of acetic anhydride was added dropwise with stirring until the solution was definitely acidic. The solid obtained in 80–90% yield was collected and recrystallized from benzene, m.p. 152°.

Anal. Calcd. for $C_9H_7NO_6$: C, 48.0; H, 3.1; N, 6.2. Found: C, 48.5; H, 3.4; N, 6.1.

Ultraviolet Titrations. In order to determine the state of ionization of poly-4(5)-vinylimidazole at different pH values, 10^{-4} *M* solutions were prepared in 28.5% ethanol–water with KCl added to adjust the ionic strength to 0.1. These solutions were titrated with concentrated hydrochloric acid or sodium hydroxide. After each addition the pH of the solution was measured by a Beckman pH meter and the ultraviolet spectra were determined for aliquots with a Cary recording spectrophotometer in cells thermostated at 26.0°. Poly-4(5)-vinylimidazole gave two absorptions maxima, 214 and 250 mμ, with an isosbestic point at 235 mμ. With decreasing pH the absorbancy at 214 mμ increased to a constant value of 0.440 (A_+) at pH ≤2.4. The absorption of the neutral species was determined as 0.354 (A_N) at pH 9.6.

In a similar manner 10^{-4} *M* solutions of poly-5(6)-vinylbenzimidazole were prepared in 30% *n*-propyl alcohol–water which was 0.01 *N* in hydrochloric acid. This solution was titrated with 1.0 *N* sodium hydroxide thereby maintaining constant ionic strength of 0.01 up to the neutralization point. Poly-5(6)-vinylbenzimidazole gave two absorption maxima at 272 and 278 mμ with an isosbestic point at 245 mμ. The absorbancy at 272 mμ increased with increasing pH to a constant value of 0.691 (A_+) at pH ≤2.4. The absorption of the neutral species was determined as 0.538 (A_N) at pH 10.6.

The extent of dissociation of the protonated polymer was calculated according to the equation[21]

$$\frac{1 - \alpha_1}{\alpha_1} = \frac{A - A_N}{A_+ - A}$$

where A is the absorbancy of the equilibrium mixture of both protonated (α_0) and unprotonated species (α_1), assuming that the contribution of α_2 in this region is negligible.

The plots of α_1 *vs.* pH for the two polymers are described in Figure 1. The apparent pK_1 for the polymers can be obtained from the value of pH for which α_1 = 0.5. In accordance with the modified Henderson equation[22]

$$pH = pK_a - a \log \frac{1 - \alpha_1}{\alpha_1}$$

(13) J. Noguchi and T. Saito, "Polyamino Acids, Polypeptides and Proteins," M. A. Stahmann, Ed., The University of Wisconsin Press, Madison, Wis., 1962, pp. 313–327.
(14) P. Cruickshank and J. C. Sheehan, *J. Am. Chem. Soc.*, **86**, 2070 (1964).
(15) C. G. Overberger and N. Vorchheimer, *ibid.*, **85**, 951 (1963).
(16) To be published.
(17) D. J. Rabiger and M. M. Joullié, *J. Org. Chem.*, **29**, 476 (1964).
(18) Obtained from BASF, Germany.
(19) (a) Obtained from Houdry Process Corporation, Paulsboro, N. J.; (b) I. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1953.
(20) Obtained from K and K Laboratories, Inc., Jamaica, N. Y.
(21) W. Stenstrom and N. Goldsmith, *J. Phys. Chem.*, **30**, 1683 (1926).
(22) A. Katchalsky and P. Spitnik, *J. Polymer Sci.*, **2**, 432 (1957); A. Katchalsky, N. Shavit, and H. Eisenberg, *ibid.*, **13**, 69 (1954); I. Kagawa and H. P. Gregor, *ibid.*, **23**, 477 (1957).

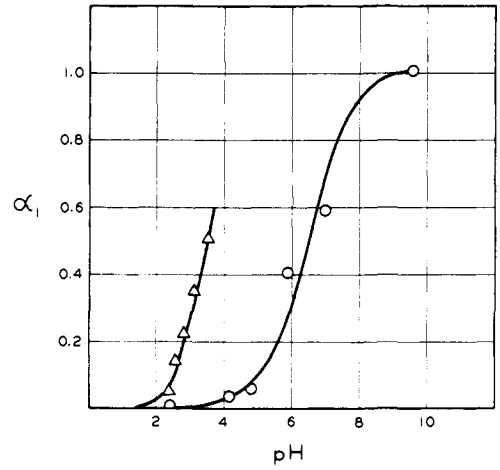


Figure 1. Ultraviolet titrations. Plots of α_1 *vs.* pH for poly-4-(5)-vinylimidazole (O, μ = 0.1) and poly-5(6)-vinylbenzimidazole (△, μ = 0.01). Solid lines represent calculated curves.

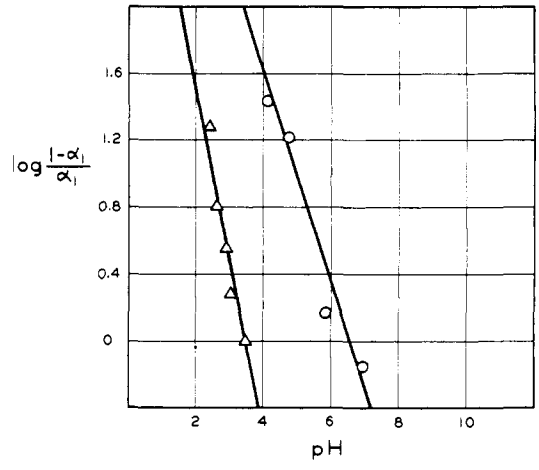


Figure 2. Plots of $\log (1 - \alpha_1)/\alpha_1$ *vs.* pH for poly-4(5)-vinylimidazole (O) and poly-5(6)-vinylbenzimidazole (△).

the plot of $\log (1 - \alpha_1)/\alpha_1$ *vs.* pH affords pK_1 as the intercept and a as the slope. In this manner (Figure 2) the following relationships were found. $pK_1 = 6.6 = pH + 1.6 \log (1 - \alpha_1)/\alpha_1$ (for poly-4(5)-vinylimidazole) and $pK_1 = 3.5 = pH + 1.01 \log (1 - \alpha_1)/\alpha_1$ (for poly-5(6)-vinylbenzimidazole).

Potentiometric Titrations. For poly-N-vinylimidazole and poly-2-methyl-N-vinylimidazole the first dissociation constants were determined in 28.5% ethanol–water and ionic strength 0.02 by the method of half-neutralization, and the pK_a values were found to be 4.4 and 4.8, respectively. If we denote by β the equivalents of acid added to protonate the polybase, the following relationships were found to hold. For poly-N-vinylimidazole $pK_a = 4.4 = pH + 2.7 \log \beta/(1 - \beta)$ (between pH 3.0 and 6.5) and for poly-2-methyl-N-vinylimidazole $pK_a = 4.8 = pH + 2.1 \log \beta/(1 - \beta)$ (between pH 3.0 and 6.5). In a similar manner the corresponding values for poly-4(5)-vinylimidazole at ionic strength 0.1 were $pK_1 = 6.6 = pH + 1.7 \log \beta/(1 - \beta)$ (between pH 5.0 and 8.0) and at ionic strength 0.02 were $pK_1 = 6.2 = pH + 1.85 \log \beta/(1 - \beta)$ (between pH 4.5 and 8.0). In 30% propanol–water and ionic strength 0.01 the values for poly-5(6)-vinylbenzimidazole were $pK_1 = 3.5 = pH + 1.0 \log \beta/(1 - \beta)$ (between pH 3.4 and 4.7).

Kinetic Measurements. In the case of imidazole, poly-4(5)-vinylimidazole, poly-N-vinylimidazole, and poly-2-methyl-N-vinylimidazole 5×10^{-4} *M* catalyst solutions were prepared in 28.5% ethanol–water buffered with 0.02 *M* tris(hydroxymethyl)aminomethane (Tris) and hydrochloric acid with sufficient KCl to adjust the ionic strength to 0.02. Below pH 6.5 sodium acetate–acetic acid was employed as the buffer.

In the case of benzimidazole and poly-5(6)-vinylbenzimidazole 5×10^{-4} *M* catalyst solutions were prepared in 30% *n*-propyl alcohol–water buffered with 0.01 *M* Tris and hydrochloric acid and sufficient KCl to adjust the ionic strength to 0.01. Above pH 9 2-amino-2-methyl-1,3-propanediol–hydrochloric acid was employed as buffer while below 6.5 sodium acetate–acetic acid was used. The substrates, *p*-nitrophenyl acetate and 4-acetoxy-3-nitrobenzoic acid, were dissolved in the appropriate solvents at 10^{-3} *M*.

The catalyst solution (2.8 ml.) and the substrate solution (200 μl.) were mixed in a quartz cell and the rates were studied in a Beckman (Model DU) spectrophotometer thermostated at 26.0°, by measuring the absorption (A_t) of the *p*-nitrophenol (400 mμ) as a function of time (t). After at least 10 half-lives the absorption was measured for complete reaction (A_∞). Catalysis by buffer only (blank) was measured in the same fashion.

The measured data were treated as first-order kinetics by plotting $A_\infty - A_t$ on a log scale *vs.* t on a linear scale. The plots were straight lines for 70% conversion or more. The slope after correcting for natural logarithms was taken as k_{measd}. The measured rate constant was also determined by applying the method of least square (on an IBM 7040 computer) or by the method of Guggenheim[23] where A_∞ is not required.

The solvolysis of the substrate, k_{measd}, is the composite of the catalyzed (k_{obsd}) and the uncatalyzed reaction (k_{blank}). k_{obsd} is therefore obtained by subtraction, *i.e.*, $k_{obsd} = k_{measd} - k_{blank}$.

Results

At pH 7.4 about 25% of poly-4(5)-vinylimidazole exists as the protonated form (α_0). The plot of k_{obsd} *vs.* concentration at this pH reveals first-order reaction in catalyst (Figure 3). A similar observation was made at pH 8.0 where *ca.* 90% of the polymer exists as the free-base form (α_1). At pH 8.8 poly-5(6)-vinylbenzimidazole completely exists in the free-base form. Its k_{obsd} also shows linear dependency with concentration.

The pseudo-second-order catalytic rate constants for the reaction of poly-4(5)-vinylimidazole and *p*-nitrophenyl acetate (PNPA) at different pH values are summarized in Table I and plotted against α_1 in Figure 4. Above pH 8.0 there is a strong enhancement of the catalytic rate of the polymer over the monomer. Inspection of Figure 4 reveals that at $\alpha_1 = 0.8$ the catalytic rates of the polymer and the monomer are the same. The higher rates of the polymer at high pH values therefore cannot be rationalized on the basis of α_1. The pH dependency of this enhancement indicates relation to the *anionic* (α_2) forms of the polymer.

(23) E. A. Guggenheim, *Phil. Mag.*, 2, 538 (1926).

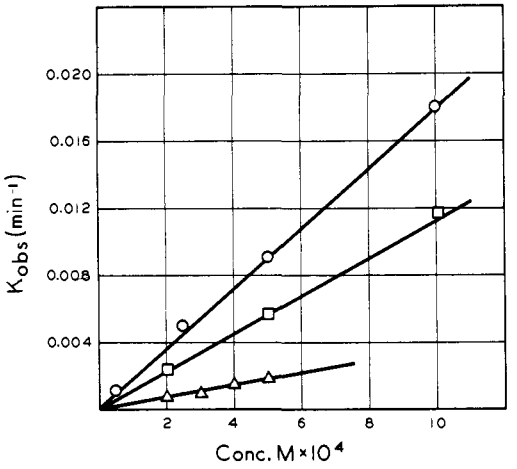


Figure 3. The observed rates of disappearance of PNPA as a function of the concentration of poly-4(5)-vinylimidazole (□, pH 7.4; ○, pH 8.0), and poly-5(6)-vinylbenzimidazole (△, pH 8.8).

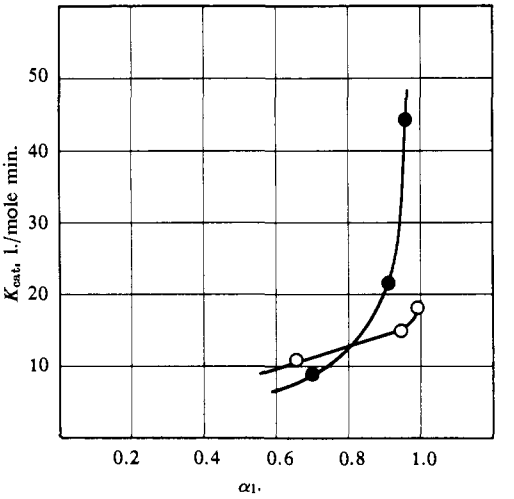


Figure 4. Solvolysis of PNPA catalyzed by poly-4(5)-vinylimidazole (●) and imidazole (○).

It could be predicted that a polymer with a lower pK_2 value than that of poly-4(5)-vinylimidazole would be a better catalyst than its monomer even at lower pH values. This was confirmed in the case of poly-5(6)-vinylbenzimidazole which is a better catalyst than benzimidazole even at pH 7.0. The results are summarized in Table II. Because of the low pK_2 of this polymer (3.5) α_1 = 1.0, and the pH dependency of the catalytic enhancement can be only explained on the basis of α_2. Indeed a plot of log k_{cat} *vs.* pH (Figure 5) demonstrates almost a linear dependency with pH at pH values higher than 9 with the slope approaching one (see Discussion).

Table I. Catalytic Rate Constants of Imidazole and Poly-4(5)-vinylimidazole with PNPA

pH	k_{cat}, l./mole min. Poly-4(5)-vinylimidazole	k_{cat}, l./mole min. Imidazole
7.2	9.1	11.4
8.2	21.4	15.0
9.0	44.2	17.8

Table II. Catalytic Rate Constants of Benzimidazole and Poly-5(6)-vinylbenzimidazole with PNPA

pH	k_{cat}, l./mole min. Poly-5(6)-vinylbenzimidazole	k_{cat}, l./mole min. Benzimidazole
7.8	1.2	0.4
8.6	3.2	0.7
9.7	17.0	2.7

Further confirmation for the involvement of the anionic sites in the polymeric effect was obtained through the study of the esterolytic catalysis of poly-N-vinylimidazole and poly-2-methyl-N-vinylimidazole in which no anionic sites exist. The pH–rate profiles for both show hardly any change with pH above pH 7 (Table III).

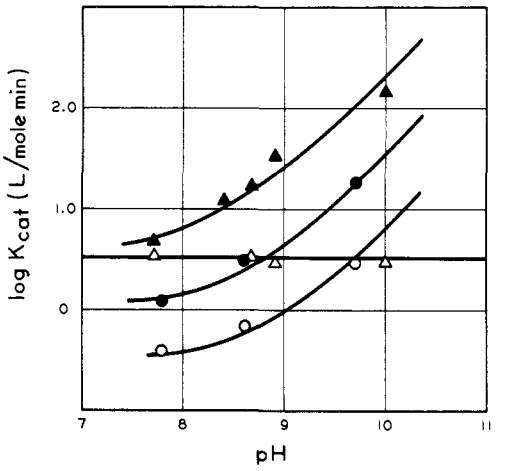


Figure 5. Plots of log k_{cat} *vs.* pH for the solvolysis of PNPA catalyzed by poly-5(6)-vinylbenzimidazole (●), and benzimidazole (○), and for the solvolysis of NABA with poly-5(6)-vinylbenzimidazole (▲) and benzimidazole (△).

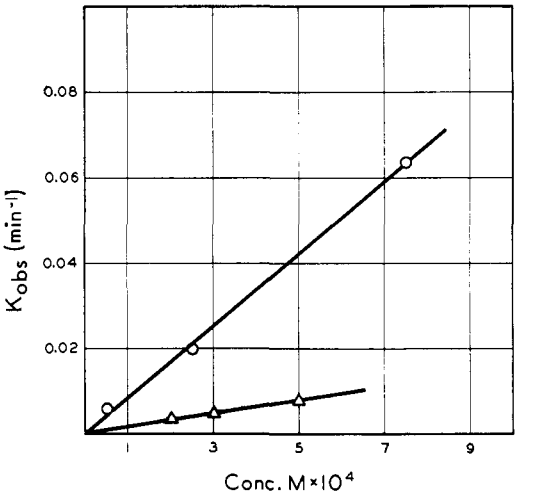


Figure 6. The observed rates of disappearance of NABA as a function of the concentration of poly-4(5)-vinylimidazole (○, pH 8.3) and poly-5(6)-vinylbenzimidazole (△, pH 8.7).

For the negatively charged substrate, 4-acetoxy-3-nitrobenzoic acid (NABA), rates were first order in

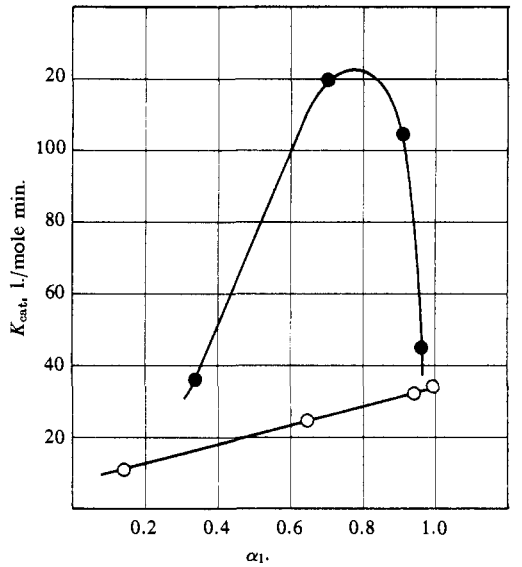


Figure 7. Solvolysis of NABA catalyzed by poly-4(5)-vinylimidazole (●) and imidazole (○).

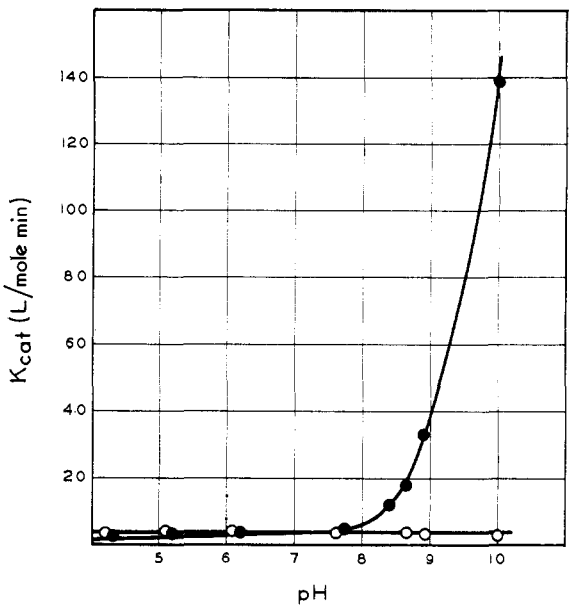


Figure 8. pH–rate profiles for the solvolysis of NABA catalyzed by poly-5(6)-vinylbenzimidazole (●) and benzimidazole (○).

catalysts (Figure 6). With poly-4(5)-vinylimidazole and NABA the results (Table IV) were similar to those previously observed by Letsinger and Savereide[24] for analogous systems. The protonated sites (α_0) which do not catalyze the hydrolysis of PNPA serve as binding sites for NABA. As a result a bell-shaped pH–rate profile was observed (Figure 7) with a strong maximum near pH 7.5. At this point the catalytic rate constant of poly-4(5)-vinylimidazole is five times larger than that of imidazole with NABA, and *ca.* 12 times the latter's rate with PNPA. Following Letsinger's approximations, the contribution to the catalytic rate constant due to the electrostatic attraction (k_{el}[24]), can be estimated as *ca.* 130 l./mole min. as compared to $k_{neutral}$ for the monomer which is *ca.* 35 l./mole min.

Table III. Catalytic Rate Constants of Poly-N-vinylimidazole and Poly-2-vinyl-N-methylimidazole with PNPA

pH	k_{cat}, l./mole min. Poly-N-vinylimidazole	Poly-2-methyl-N-vinylimidazole
7.2	3.0	0.5
8.0	3.5	0.5
9.2	3.5	0.5

Table IV. Catalytic Rate Constants of Imidazole and Poly-4(5)-vinylimidazole with NABA

pH	k_{cat}, l./mole min. Poly-4(5)-vinylimidazole	Imidazole
6.1	35.8	11.3
7.2	120.2	24.4
8.2	104.4	31.9
9.0	55.5	34.5

With poly-5(6)-vinylbenzimidazole and NABA no bell-shaped profile has been observed (Table V, Figure 8), probably as a result of the low pK_1 of the polymer and the relatively high pK_a of the substrate used. The possibility of strong steric interference to the internal interaction of the bulky benzimidazole groups is now being studied with a substrate having a lower pK_a. On the other hand while at pH 8.0 the catalytic activity of poly-5(6)-vinylbenzimidazole was found comparable to that of benzimidazole, at pH 10.0 the polymer was found to be 50-fold faster than the monomer. Since at these pH values α_0 for this polymer is zero, this enhancement can be only due to the anionic sites of the polymer (α_2). In contrast to the polymer, benzimidazole anions seem unable to interact with the negatively charged substrate, as almost no change in rate is observed with advancement of pH (Figures 5 and 8).

Table V. Catalytic Rate Constants of Benzimidazole and Poly-5(6)-vinylbenzimidazole with NABA

pH	k_{cat}, l./mole min. Poly-5(6)-vinylbenzimidazole	Benzimidazole
3.2	1.1	0.4
4.3	2.6	2.9
5.2	3.3	4.0
6.2	3.6	4.3
6.8	4.3	...
7.7	4.3	3.6
8.4	11.7	...
8.7	16.7	3.6
8.9	32.9	2.8
10.0	139.0	2.8

Discussion

The enhanced rates of the polymers with PNPA could be a result of reduced pK_2 of the polymers or a change of $k_{anionic}$ or both. Imidazoles are known to create hydrogen-bonded aggregates.[25] Internal hy-

(24) R. L. Letsinger and T. J. Savereide, *J. Am. Chem. Soc.*, 84, 114, 3122 (1962); and also *cf.* H. Ladenheim, E. M. Loebl, and H. Morawetz, *ibid.*, 81, 20 (1959).

drogen bonding could have reduced the pK_2 of the polymers,[26] though polymeric acids usually have higher pK_a values than the corresponding monomers. Poly-4(5)-vinylimidazole and poly-5(6)-vinylbenzimidazole show strong N···H–N interactions[17] in the infrared in the region 2600–3400 cm.$^{-1}$. These interactions are absent in the N-alkylated polymers but appear strongly in imidazole and benzimidazole. The extent of internal interaction on the polymers has not been resolved. So far our attempts to determine the pK_2 of the polymers by potentiometric titrations were unsuccessful due to the low solubility of the polymers at high pH values.

The second-order catalytic rate constant is a composite of the neutral and anionic contributions. At high pH values $k_{neutral}\alpha_1 << k_{anionic}\alpha_2$. Since, at $pH << pK_2$, $\alpha_2 = K_2/(H^+)$, we can write

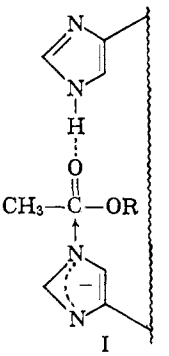
$$\log k_{cat} = \log k_{anionic} - pK_2 + pH \qquad (5)$$

The plot of log k_{cat} *vs.* pH should have a slope of 1 when $k_{neutral}\alpha_1$ becomes negligible, which is observed in Figure 5. Extrapolation to zero pH affords $k_{anionic}$ if pK_2 is known. If it is considered to be the same for the monomer[27] and polymer, $k_{anionic}$ for the reaction of poly-5(6)-vinylbenzimidazole with PNPA is found to be *ca.* 9500 l./mole min., while for the reaction of benzimidazole with this substrate it is *ca.* 1500 l./mole min. In a similar fashion $k_{anionic}$ for the reaction between this polymer with NABA becomes *ca.* 60,000 l./mole min. These values can be also obtained by numerical calculations employing eq. 3.

The high rate in the last case, coupled with the fact that monomeric benzimidazole anions apparently do not interact with the negatively charged substrate, may suggest an additional mechanism for the polymer catalysis which does not operate in the case of the monomer. Such could be the interaction between the neutral imidazoles and imidazole anions.[28] The close proximity of the imidazole groups on the polymers makes this interaction more favorable than in the monomeric case. Since the polymer may behave as a single entity,[29] the rate will be still first order in catalyst and the total anionic contribution will become[30]

$$k'_{anionic}\alpha_2 + k''_{anionic}\alpha_1\alpha_2 \qquad (6)$$

While the neutral imidazoles could assist the attack of the anions behaving as a weak acid (I), the other possibility, *i.e.*, a nucleophilic attack of the neutral imidazoles catalyzed by the anions as a general base (II), looks reasonable in the light of the inertness of the monomer anions toward NABA. If $k''_{anionic} >> k'_{anionic}$ a bell-shaped pH–rate profile should be observed with a maximum close to $pH = pK_2$. This maximum will be hardly noticed if the contribution of $k''_{anionic}$ is very small.



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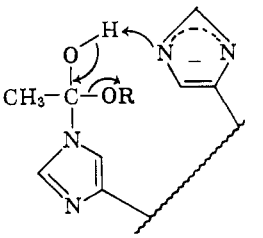

II

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(25) K. Hofmann, "The Chemistry of Heterocyclic Compounds," Part I, Interscience Publishers, Inc., New York, N. Y., 1953.

(26) *Cf.* H. C. Brown, D. H. McDaniel, and O. Hafliger, "The Determination of Organic Structures by Physical Methods," Braude and Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, pp. 567–662.

(27) The pK_2 for benzimidazole was found as 12.5 in our system.

(28) This kind of interaction was suggested to us by Professor H. Morawetz of the Polytechnic Institute of Brooklyn.

(29) *Cf.* C. G. Swain and J. F. Brown, *J. Am. Chem. Soc.*, 74, 2534, 2538 (1952).

(30) Our data do not rule out a similar complex contribution for the neutral species, *i.e.*, $k'_{neutral}\alpha_1 + k''_{neutral}\alpha_1^2$.