The "saturation" or autoinhibitory behavior of R_p with respect to [A] and [T] has been observed by others;[12,13] so has its half-order dependence on [A].[12] These phenomena can be accounted for satisfactorily by a simple catalyst formation scheme involving a competition for active surface sites between a polymerization-inhibiting species and monomeric $AlEt_2Cl$, subsequent to its decomposition from the dimeric form in solution. We postulate that the active sites are exposed titanium atoms having the requisite geometric characteristics and that the inhibitor has its origin in the catalyst perhaps, as previously suggested,[4] owing to the presence of $AlCl_3$.

Such a scheme may be written as

$$A_2 \rightleftarrows 2A \quad K_1'$$
$$S + A \rightleftarrows C_a \quad K_2'$$
$$S + I \rightleftarrows C_i \quad K_3'$$

with the constraint

$$[S]_0 = [S] + [C_i] + [C_a]$$

This leads to

$$\theta_a = \frac{(K_1')^{1/2}K_2'[A_2]^{1/2}}{(K_1')^{1/2}K_2'[A]^{1/2} + K_3'[I] + 1} \quad (17)$$

where A_2 = dimeric aluminum alkyl, $(AlEt_2Cl)_2$; S = initial sites on the catalyst surface which are capable of complexing aluminum-containing compounds; I = inhibiting species which are capable of complexing with S to form inactive sites; C_a = active sites which become polymerization intermediates; C_i = inactive sites which cannot cause polymerization; θ_a = fraction of the catalyst surface covered with active polymerization sites.

If we now assume that most of the original catalyst is present as dimer in solution and that the concentration of the inhibitor is proportional to the concentration of catalyst added, we obtain an expression for [P], with the aid of

$$[P] = \theta_a[T] \quad (18)$$

which is identical with that deduced from eq 5 and 9.

Acknowledgments. The authors wish to express their gratitude to the National Science Foundation and to the Plastics Institute of America for their support of this work. The authors also wish to thank Professors A. A. Volpe and F. T. Jones for their helpful discussions and suggestions.

(13) See Table VI, footnote *d*.

Esterolytic Catalyses by Copolymers Containing Imidazole and Carboxyl Functions

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Received July 30, 1969

ABSTRACT: The electrostatic interactions involved in the imidazole–carboxylic acid copolymer-catalyzed solvolyses of 3-acetoxy-N-trimethylanilinium iodide (ANTI), *p*-nitrophenyl acetate (PNPA), and 3-nitro-4-acetoxybenzoic acid (NABA) were studied and compared with the monomeric analog γ-4(5)-imidazolebutyric acid. The effects of copolymer composition of the 4(5)-vinylimidazole–acrylic acid copolymers on their catalytic activities were investigated in detail. These effects became apparent by inspecting the dependencies of their activities on the monomer sequence distributions, which were found to control the overall catalytic activities of the copolymers for the charged esters. The most catalytically active species toward ANTI is the carboxylate–imidazole–carboxylate triad.

The efficiency and specificity of esterolytic, enzymatic catalyses are, in some cases, caused partly by electrostatic attraction between groups carrying ionic charges of opposite sign, one in a substrate and the other in an active site of an enzyme. Typical examples could be acetylcholine esterase[2] and ribonuclease[3] in their catalytic action toward charged substrates or inhibitors. This type of electrostatic effect has been also observed to enhance the rates of solvolyses of negatively charged substrates catalyzed by partially protonated polymers containing nucleophilic functions.[4-8]

A copolymer of 4(5)-vinylimidazole with acrylic acid was of interest because it had both binding sites (carboxylate anions) and catalytically active groups (neutral

(1) Taken from the dissertation submitted by H. Maki in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the University of Michigan. Mitsui Petrochemical Ind., Ltd., Research Center, Wakimura, Kuga-gun, Yamaguchi, Japan.

(2) I. B. Wilson in the "Enzymes," Vol. IV, P. D. Boyer, H. A. Lardy, and K. Myrback, Ed., Academic Press, New York, N. Y., 1960, pp 501–520; F. Bergmann, *Advan. Catal.*, **10**, 130 (1958); N. Engelhard, K. Prchal, and M. Nenner, *Angew. Chem. Intern. Ed. Engl.*, **6**, 615 (1967).

(3) C. H. Hirs, M. Halmann, and J. H. Kycia in "Biological Structure and Function," Vol. I, Academic Press, New York, N. Y., 1962, p 41.

(4) (a) R. L. Letsinger and T. J. Savereide, *J. Amer. Chem. Soc.*, **84**, 3122 (1962); (b) R. L. Letsinger and I. S. Klaus, *ibid.*, **87**, 3380 (1965).

(5) C. G. Overberger, T. St. Pierre, N. Vorchheimer, J. Lee, and S. Yaroslavsky, *ibid.*, **87**, 296 (1965).

(6) C. G. Overberger, T. St. Pierre, and S. Yaroslavsky, *ibid.*, **87**, 4310 (1965).

(7) H. Ladenheim, E. M. Loebl, and H. Morawetz, *ibid.*, **81**, 20 (1959).

(8) C. G. Overberger, J. C. Salamone, and S. Yaroslavsky, *ibid.*, **89**, 6231 (1967).

imidazoles), a situation similar to that observed for acetylcholinesterase. The high selectivity of this copolymer toward a positively charged ester, 3-acetoxy-N-trimethylanilinium iodide (ANTI), compared with those toward a neutral and a negatively charged ester, *p*-nitrophenyl acetate (PNPA) and 3-nitro-4-acetoxybenzoic acid (NABA), respectively, has been previously reported.[9] Copolymers containing two different functional groups have an advantage over the homopolymers in that the concentration and, at the same time, the sequences of each functional group along the polymer chain can be varied by changing the polymerization conditions. By utilizing different compositions of copolymers as catalysts, the specific characteristics of an interaction among two different functional groups and a substrate in solvolytic reactions could become apparent.

In the present work, the detailed characteristics of electrostatic interaction between the substrates (ANTI, PNPA, and NABA) and the imidazole–carboxylic acid copolymers or their monomeric analog, γ-4(5)-imidazolylbutyric acid will be discussed.

Experimental Section

The Syntheses of the Substrates. *p*-Nitrophenyl acetate (PNPA), 3-nitro-4-acetoxybenzoic acid (NABA), and 3-acetoxy-N-trimethylanilinium iodide (ANTI) were previously reported.[5,9]

Copolymers of 4(5)-Vinylimidazole with Acrylic Acid. Various molar ratios of 4(5)-vinylimidazole[10] and freshly distilled acrylic acid were dissolved with azobisisobutyronitrile (AIBN, 0.1%) in 20 ml of absolute methanol in polymerization tubes. After flushing with nitrogen, the tubes were sealed and placed in a constant-temperature bath at 70° for proper periods. The polymerization mixtures were continuously stirred by shaking. The formed copolymers precipitated from solution during polymerizations. The obtained suspensions were poured into a larger excess of acetone and the precipitated polymers were collected by filtration. The polymers were dissolved in 3% aqueous ammonium hydroxide and purified further by extensive dialyses. The copolymer compositions were calculated from their nitrogen contents. The results are summarized in Table I. The monomer reactivity ratios were determined to be $r_1 = 0.06 \pm 0.01$; $r_2 = 0.11 \pm 0.04$ (Figure 1), where suffix 1 is for acrylic acid, suffix 2 is for 4(5)-vinylimidazole.

Copolymer of 4(5)-Vinylimidazole with Maleic Acid. 4(5)-Vinylimidazole (0.50 g, 0.0053 mol), freshly distilled diethyl maleate (9.16 g, 0.053 mol), and AIBN (0.02 g) were dissolved in 18 ml of thiophene-free benzene in a polymerization tube. The tube was degassed three times by repeated freezing and melting under vacuum, sealed, and then placed in a constant-temperature bath at 70° for 20 hr with shaking. The polymer obtained was reprecipitated three times from methanol in a large excess of dry ether. After drying at room temperature under vacuum, 0.51 g (5.3% conversion) of the white polymer was obtained.

Anal. Found: N, 11.33, 11.46 (diethyl maleate–4(5)-vinylimidazole 1/1.13).

The above copolymer (0.136 g) was hydrolyzed by refluxing in 50 ml of deionized water. After 48 hr the solution became clear and transparent. The copolymer was recovered by freeze-drying. An infrared spectrum (KBr pellet) of this polymer indicated the complete disappearance of ester absorption bands and the appearance of acid absorption bands.

Anal. Found: N, 12.34 (maleic acid–4(5)-vinylimidazole 1/0.986).

Poly-4(5)-vinylimidazole. 4(5)-Vinylimidazole was polymerized as previously described.[5] The obtained polymer was purified by an extensive dialysis in 28.5% ethanol–water. Although the crude polymer exhibited two absorption maxima at 250 and 214 mμ[5] in 28.5% ethanol–water, no absorption maxima was found at 250 mμ for the dialyzed polymer. Since 4(5)-vinylimidazole has a strong absorption at 250 mμ, the previous result could be due to contamination with monomer.

4-(2-Chloroethyl)imidazole Hydrochloride. Essentially the same procedure for preparation of α-chloro-β-(4-imidazolyl)-propionic acid from histidine[11] was used. Diazotization of histamine dihydrochloride (15 g, 0.0815 mol) with aqueous sodium nitrite (0.435 mol in 35 ml) in concentrated hydrochloric acid yielded a hygroscopic crude product (8.6 g, 42%), which was used without further purification.

γ-4(5)-Imidazolylbutyric Acid Monohydrate. Condensation of 4-(2-chloroethyl)imidazole hydrochloride with diethyl

TABLE I[a]
RESULTS OF COPOLYMERIZATION OF 4(5)-VINYLIMIDAZOLE WITH ACRYLIC ACID

Polymerization conditions		Results	
Feed composn, VIM mol %	Time, hr	Conversion, Wt %	Copolymer composn,[c] VIM mol %
2.1	0.25	6.5	26.1
5.1	0.5	13.9	31.9
11.5	0.5	5.6	39.7
37.2[b]	1.0	23.6	35.2
49.7	0.5	9.9	46.3
65.0[b]	0.15	28.8	45.8
85.4	2.0	15.6	58.8
86.5[b]	12.0	29.0	56.3
94.6	14.0	17.2	79.4

[a] AIBN as an initiator, in methanol, at 70°, with shaking during polymerization except footnote *b*. [b] Without shaking during polymerization. [c] Calculated from nitrogen content.

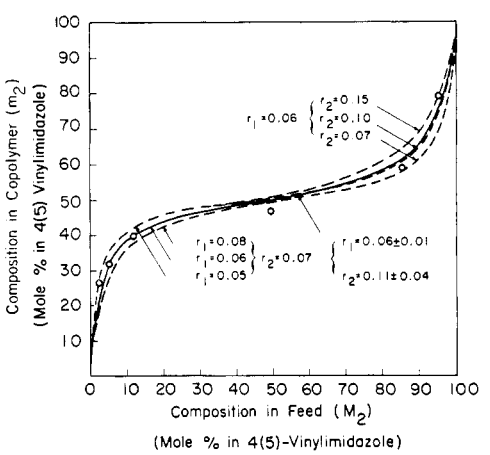


Figure 1. Feed and copolymer composition relationship in the copolymerization of 4((5)-vinylimidazole with acrylic acid; conditions, see Table I.

(9) C. G. Overberger, R. Sitaramaiah, T. St. Pierre, and S. Yaroslavsky, *J. Amer. Chem. Soc.*, **87**, 3270 (1965).

(10) C. G. Overberger and N. Vorcheimer, *J. Amer. Chem. Soc.*, **85**, 95 (1963).

(11) S. Edlbacher and H. von Bidder, *Z. Physiol. Chem.*, **276**, 126 (1942).

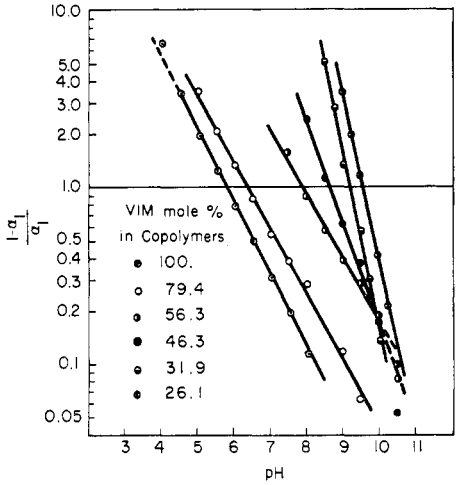


Figure 2. Plots of $(1 - \alpha_1)/\alpha_1$ *vs.* pH for the imidazole–acrylic acid copolymers.

malonate was carried out by following the procedure of Bruice and Sturtevant.[12] After the hydrolysis of the product in concentrated hydrochloric acid, the solvent was evaporated to dryness. The residue was dissolved in water and neutralized with aqueous ammonium hydroxide, and the solvent was evaporated to dryness again. The solid residue was dissolved in a minimum amount of hot water, and, on cooling, the crude solid product was obtained. Recrystallization from water–ethanol yielded colorless needles, mp 103–104°.

Anal. Calcd for $C_7H_{16}N_2O_2 \cdot H_2O$: C, 44.99; H, 7.55; N, 17.49. Found: C, 44.93; H, 7.72; N, 17.45.

Titration. In 10 ml of 28.5% ethanol–water was dissolved *ca.* 10 mg of a sample. The ionic strength was adjusted by hydrochloric acid or sodium hydroxide to give $\mu = 0.02$ at the end point of titration. By using a microburet and a Beckman Expandomatic pH meter, the solutions were titrated with 1 *N* aqueous NaOH or HCl at room temperature under nitrogen atmosphere with stirring. The blank titration curves were obtained by titrating 10 ml of 10^{-2} *N* HCl in 28.5% ethanol–water with 1 *N* aqueous NaOH. Differential titration curves were derived graphically,[13,14] from which the degree of dissociations were evaluated.

The copolymers precipitated in the course of titration around the isoelectric points. The inflection points between the dissociation of the imidazolium ions and the carboxyl groups on the polymer chain were, consequently, not always clearly observed. The titration ranges of imidazolium and carboxyl groups were, therefore, estimated by dividing the total range of dissociable, pendent groups into two ranges, each of which had a width proportional to the copolymer composition. Although the estimated ranges might contain some overlapping regions of dissociation of both imidazolium and carboxyl groups, these values are apparently not far from reaility, since an inflection point was normally observed near the estimated point of alteration of the dissociating group. By taking a higher pH range of dissociation of pendent imidazolium ions, pH–α_1 relationship was found to follow the modified Henderson equation (eq 1),[14–16] where α_1 is the fraction of neutral imidazole groups. The pK_a values were evaluated graphically (Figure 2, Table II).

(12) T. C. Bruice and J. M. Sturtevant, *J. Amer. Chem. Soc.*, **81**, 2360 (1959).
(13) T. V. Parke and W. W. Davis, *Anal. Chem.*, **26**, 642 (1954).
(14) T. Alfrey and H. S. Pinner, *J. Polym. Sci.*, **13**, 533 (1954).
(15) A. Katchalsky and I. R. Miller, *ibid.*, **13**, 57 (1954).
(16) H. L. Wagner and F. A. Long, *J. Phys. Colloid Chem.*, **55**, 1912 (1951).

TABLE II[a]
RESULTS OF POTENTIOMETRIC TITRATIONS OF PENDENT IMIDAZOLIUM IONS IN THE COPOLYMERS OF 4(5)-VINYLIMIDAZOLE WITH ACRYLIC ACID

Copolymer composn, VIM mol %	pK_1	n	Pptn range[b]
100[c]	5.78	2.42	*Ca.* 8.5∼
79.4	6.35	2.69	7.0 ∼ 8.9
56.3	7.85	2.77	3.2 ∼ 7.9
46.3	8.60	1.80	2.8 ∼ 7.8
31.9	9.20	1.00	2.4 ∼ 6.1
26.1	9.55	1.05	∼5.2

[a] In 28.5% ethanol–water, at room temperature, ionic strength 0.015∼0.02, under nitrogen. [b] The range of pH where precipitation was observed. [c] Poly-4(5)-vinylimidazole.

$$pH = pK_1 - n \log \frac{1 - \alpha_1}{\alpha_1} \quad (1)$$

γ-4(5)-Imidazolylbutyric acid and imidazole were titrated in the same manner. The obtained pK_a values are 4.51 and 7.55 for the carboxyl and the imidazolium group, respectively, in γ-4(5)-imidazolylbutyric acid and 6.34 for imidazole in 28.5% ethanol–water and at an ionic strength of 0.02. These values are in good accordance with the reported values.[12,17]

Kinetic measurements were performed as previously described.[5] The solvent, 28.5% ethanol–water, was used for every kinetic run. The solutions were buffered with sodium acetate–acetic acid (0.02 *M*) at pH 6 and below, with tris(hydroxymethyl)aminomethane (Tris) (0.02 *M*)–hydrochloric acid at pH 7–9 and with 3-(N,N-dimethylamino)-propanol (0.02 *M*)–hydrochloric acid at pH above 9. The ionic strength was adjusted by addition of potassium chloride. The rates of the solvolyses were determined by following the increase in the absorbance of the released phenols at the following wavelengths: PNPA, 400 mμ (pH 6–10), 320 mμ at pH 5; ANTI, 293 mμ at pH 9 and above, 277 mμ at pH below 9; NABA, 416 mμ.

All the obtained data followed first-order kinetics. The pseudo-first-order rate constants k_{measd} (with catalyst) and k_{blank} (without catalyst), were treated by the expressions $k_{obsd} = k_{measd} - k_{blank}$ and $k_{cat} = k_{obsd}/[catalyst]$ where [catalyst] is the molar concentration of imidazole functions.

Results and Discussion

In order to substantiate the previously reported electrostatic effects on the catalytic activity of the copolymer of 4(5)-vinylimidazole with acrylic acid,[9] the catalytic activities of the 4(5)-vinylimidazole with maleic acid and of γ-4(5)-imidazolylbutyric acid were examined. In Figure 3, the second-order catalytic rate constants of the imidazole–acrylic acid copolymer (46.3 mol % in imidazole), the imidazole–maleic acid copolymer, and the monomeric analogs, γ-4(5)-imidazolylbutyric acid and imidazole, were plotted against α_1 values. For the solvolysis of ANTI, the catalytic activities are in the order imidazole < γ-4(5)-imidazolylbutyric acid < imidazole–acrylic acid copolymer < imidazole–maleic acid copolymer. For the solvolysis of NABA, however, the order of catalytic activities is reversed. At

(17) K. Hofmann, "The Chemistry of Heterocyclic Compounds: Imidazole and Its Derivatives," Part 1, Interscience Publishers, New York, N. Y., 1953, p 15.

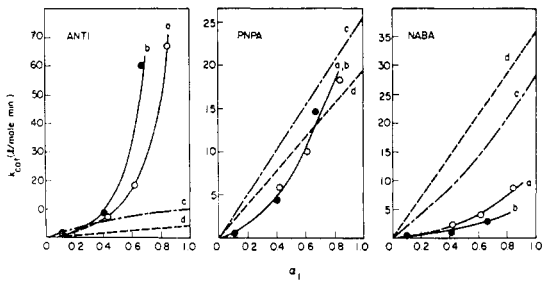


Figure 3. Comparison of catalytic activities of the imidazole–acrylic acid copolymer (46.3 mol%) (a), the imidazole–maleic acid copolymer (b), γ-4(5)-imidazolylbutyric acid (c), and imidazole (d) in the solvolyses of ANTI, PNPA, and NABA; solvent 28.5% ethanol–water, μ = 0.02, at 26°.

high α_1 values, the much larger acceleration and deceleration of the rates were observed for these copolymer-catalyzed solvolyses of ANTI and NABA, respectively, compared with those by γ-4(5)-imidazolylbutyric acid. On the other hand, in the solvolyses of PNPA, no significant difference was noted between these copolymers. The difference observed in the solvolysis of PNPA catalyzed by imidazole and by γ-4(5)-imidazolylbutyric acid appears to be due to the structural difference of the imidazole ring system. The rate constant for the 4(5)-methylimidazole catalyzed solvolysis of PNPA, obtained under similar conditions (at 30° in 28.5% ethanol–water),[18] is in good agreement with that of γ-4(5)-imidazolylbutyric acid.

These results clearly indicate that the localized negative charge around the polymer chains are the primary cause of the high selectivity of these polymers toward ANTI.[9]

In order to gain more insight into an electrostatic interaction between negative charges on a catalytically active polymer and a charged substrate, the effects of copolymer compositions of 4(5)-vinylimidazole with acrylic acid were investigated. The rates of solvolyses of ANTI, NABA, and PNPA catalyzed by the imidazole–acrylic acid copolymers as a function of the concentration of the copolymers are shown in Figure 4. Regardless of the type of substrate and of the compositions of the copolymers, the rates were first order with respect to both the substrates and the polymers.

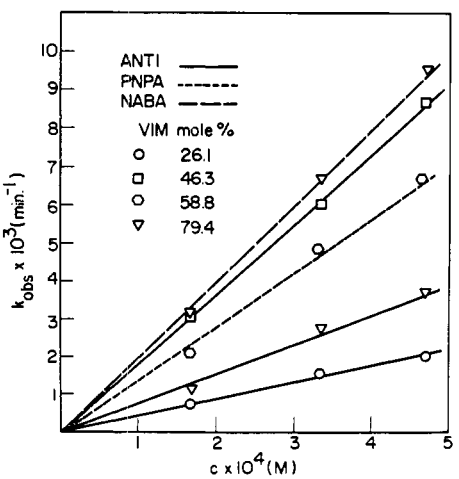


Figure 4. Plots of k_{obsd} *vs.* concentration of the imidazole–acrylic acid copolymers; solvent 28.5% ethanol–water, pH 9.0, μ = 0.02, at 26°.

(18) T. C. Bruice and G. L. Schmir, *J. Amer. Chem. Soc.*, **80**, 148 (1958).

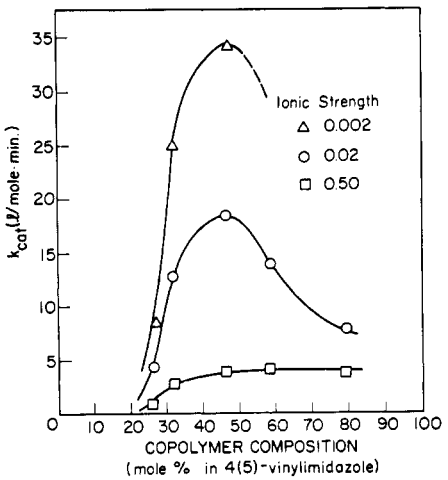


Figure 5. Effects of copolymer composition and ionic strength on k_{cat} for the imidazole–acrylic acid copolymer catalyzed solvolyses of ANTI; solvent 28.5% ethanol–water, pH 9.0, at 26°.

The second-order catalytic rate constants of the imidazole–acrylic acid copolymer catalyzed solvolysis of the positively charged substrate ANTI are plotted against copolymer compositions in Figures 5 and 6. These results clearly indicate that the catalytic activities of the copolymers are dependent upon the compositions of copolymers as well as upon the ionic strength and the pH of the reaction system. The strong dependence of the catalytic activities of the copolymers upon the ionic strength (Figure 5) reveals that the primary cause of the existence of optimum composition is the electrostatic interaction between the copolymers and ANTI.

The effects of copolymer composition could become more apparent by inspecting the monomer sequence distributions along the copolymer. The enhanced

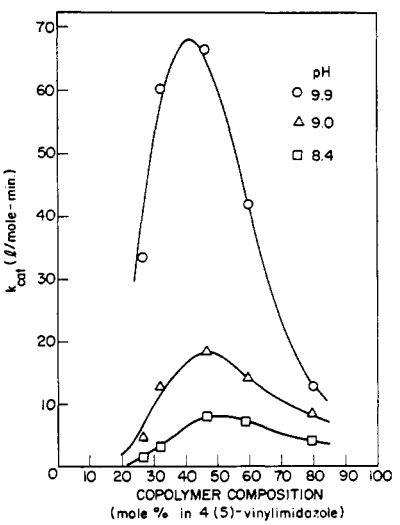


Figure 6. Effects of copolymer composition and pH on k_{cat} for the imidazole–acrylic acid copolymer catalyzed solvolyses of ANTI; solvent 28.5% ethanol–water, μ = 0.02, at 26°.

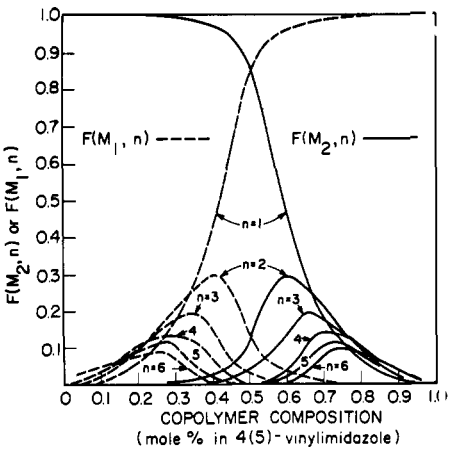
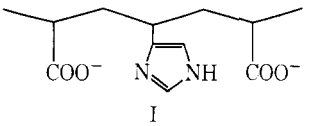


Figure 7. Estimated monomer sequence distribution in the imidazole–acrylic acid copolymers.

catalytic activities of the copolymers in the range of their composition of 42–50 mol % in imidazole are most likely due to the interaction between carboxylate anions in the copolymers and a cationic site of imidazole. A catalytically significant group on the copolymer chain seems to be a pendent imidazole group in the copolymer chain, because polyacrylic acid alone showed inhibitory effects instead of catalytic effects toward ANTI, an observation similar to that reported by Morawetz and Shafer.[19] Consequently, the arrangement of these functional groups along the copolymer chain would control the overall catalytic activities of the copolymer.

The distributions of monomer sequences along the copolymer chains were estimated statistically based on the determined monomer reactivity ratios by using the equations derived by Bovey.[20] The results are shown in Figure 7. In the copolymer composition range of 42–50 mol % in imidazole, the most predominant sequence of the imidazole component is the isolated imidazole sequence. Since it is unlikely that imidazolium ions play a catalytic role in ester hydrolyses,[18] the neutral, pendent imidazole groups would be the catalytically active species under the conditions employed. The fraction of the isolated, neutral imidazole sequence (I) was estimated as the product of the isolated imidazole fraction, $F(M_2, 1)$, and the determined degree of dissociation of pendent imidazolium ions, α_1 (Figure 8). $F(M_2, n) = np_{22}^{n-1}(1 - p_{22})^2$, $p_{22} = r_2/(r_2 + F)$ for



I

4(5)-vinylimidazole; $F(M_1, n) = np_{11}^{n-1}(1 - p_{11})^2$, $p_{11} = r_1F/(1 + r_1F)$ for acrylic acid, where $F(M_2, n)$ is the fraction of 4(5)-vinylimidazole and acrylic acid, respectively, that belongs to an n consecutive monomer sequence in a copolymer; p_{22} and p_{11} are the probabilities of occurrence of M_2–M_2 and M_1–M_1 sequences, respectively; F is the molar ratio of the monomers in feed, $F = [M_1]/[M_2]$.

Upon comparing Figure 6 with Figure 8, similar trends in bell-shaped curves and in the compositions of maximum catalytic activity are observed between the determined rate constants and the estimated isolated, neutral imidazole fraction. These accordances suggest that the catalytic activities of the copolymers toward ANTI are controlled primarily by the isolated, neutral imidazole sequence (I). The large pH dependence of the catalytic activities of the copolymers appears to be partly due to the increase of bulk negative charge density along the copolymer chains, which controls the localized distribution of the charged substrate around the catalytic sites, and also to the specific nature of the polymeric catalysts, which has been observed in the solvolyses of neutral substrates catalyzed by poly-4-vinylpyridine[4] and poly-4(5)-vinylimidazole.[5]

When the negatively charged ester NABA was employed as a substrate, another type of effect of copolymer composition was observed. For this substrate, the carboxylate anions in the copolymer chain act as repulsive sites toward the substrate. The composition dependence of catalytic activities of the copolymers toward NABA at different pH values is summarized in Figure 9. The second-order catalytic rate constants increase, in general, with increasing imidazole content.

In Figure 10 are shown the dependencies of the catalytic activities of the copolymers on α_1 values. The copolymers containing less than 60 mol % imidazole exhibit increasing activities with an increase of α_1, while the copolymer of 79.4 mol % imidazole exhibits a decreasing activity toward NABA. This difference in the behavior of the copolymers can be accounted for by the difference in the monomer sequence distributions in each copolymer (Figure 7). The former copolymers, composed mainly of the imidazole sequences containing isolated units and two consecutive units, are incapable of binding the substrate, since the positive charges of the imidazolium groups would be neutralized by the negative charges of the carboxylate groups. On the other hand, the latter copolymer, composed mainly of the longer imidazole sequences, has imidazolium groups which can function as binding sites.

The solvolyses of the neutral substrate PNPA were also of interest. For this substrate no electrostatic interaction was expected and therefore the observation of other characteristics of the imidazole–acrylic acid

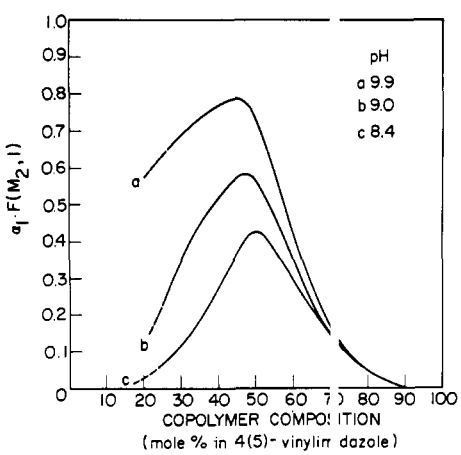


Figure 8. Estimated fractions of isolated, neutral imidazole sequence in the imidazole–acrylic acid copolymers.

(19) H. Morawetz and J. J. Shafer, *J. Phys. Chem.*, 67, 1293 (1963).
(20) F. A. Bovey, *J. Polym. Sci.*, 62, 197 (1962).

TABLE IV[a]
SECOND-ORDER CATALYTIC RATE CONSTANTS FOR 4(5)-VINYLIMIDAZOLE–ACRYLIC ACID COPOLYMER CATALYZED SOLVOLYSES OF PNPA

Copolymer composn, VIM mol %	K_{cat}, l./mol min[b] pH 8.0	pH 8.4	pH 9.0	pH 9.9
26.1	0.28	0.64	3.0	11.6
31.9	0.78	1.4	6.1	15.5 (2)
46.3		5.9	9.9	18.3 (2)
58.8		9.5	14.4 (3)	26.2 (2)
79.4		18.7	22.2	32.1 (2)

[a] At 26°, in 28.5% ethanol–water, ionic strength 0.02. [b] Average value based on the number of determinations shown in parentheses.

copolymers, previously overshadowed by electrostatic effects, was anticipated. In Table IV is summarized the composition dependence of the second-order catalytic rate constants in the solvolysis of PNPA at different pH values. The activities of the copolymers increase with increases of both pH and copolymer composition.

In Figure 11, the second-order catalytic rate constants of the copolymers and of the homopolymer in the solvolyses of PNPA are plotted against α_1 values. Among the copolymers, effects of monomer sequence distributions are not observed to a significant extent within the conditions investigated. On the other hand, the copolymers containing 26–59 mol % imidazole are significantly more active than the homopolymer below an α_1 value of 0.7. Considering that these copolymers consist mainly of the isolated imidazole sequence or of the consecutive two imidazole sequence (Figure 7), this difference in the catalytic activity between the copolymers and the homopolymer could be caused by the existence of carboxylate anions in the vicinity of pendent neutral imidazole groups, and by the cooperative participation of the carboxylate group in the catalytic action of a pendent imidazole group. This was actually found and will be discussed in the following paper.[21]

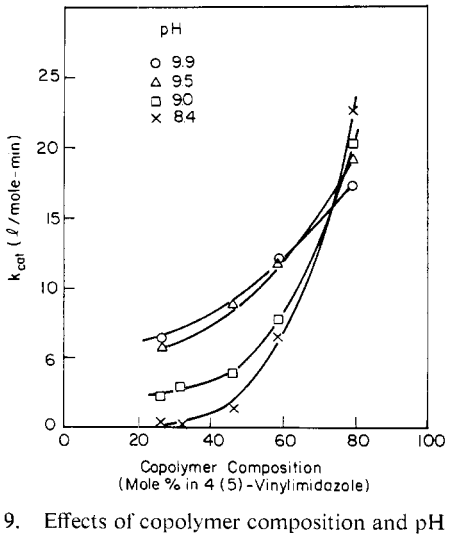


Figure 9. Effects of copolymer composition and pH on k_{cat} for the imidazole–acrylic acid copolymer catalyzed solvolyses of NABA; solvent 28.5% ethanol–water, μ = 0.02, at 26°.

(21) C. G. Overberger and H. Maki, *Macromolecules*, 3, 220 (1970).

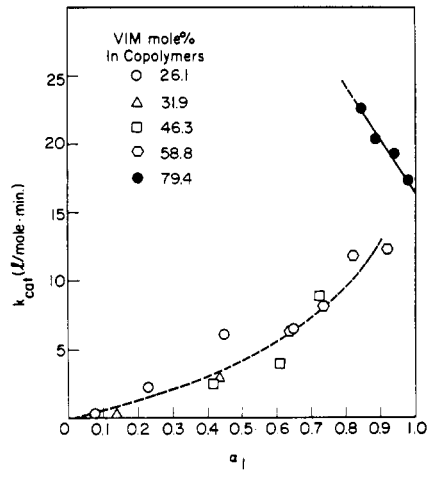


Figure 10. Plots of k_{cat} *vs.* α_1 for the imidazole–acrylic acid copolymer catalyzed solvolyses of NABA; solvent 28.5% ethanol–water, μ = 0.02, 26°.

An electrostatic interaction between a polymeric catalyst and a charged substrate can modify their reaction rate resulting in either an acceleration or a deceleration of the reaction rate.[4–9] Counterions in aqueous solution can interact with polyions in several ways: (1) through covalent bond formation, (2) through ion-pair formation, and (3) through long-range forces owing to the electrostatic potential of the polyions.[22] A reaction between a polyelectrolyte and a charged species is consequently involved in the same types of interaction. The last one controls the actual concentration of a reactant around a polymer chain; the second controls the specific interaction of a reactant with a polymeric reagent, and the first is the reaction itself.

The present study indicates that all of these effects were observed in the imidazole–carboxyl copolymer catalyzed solvolyses of ANTI and NABA. The effects of monomer sequence distributions observed for the

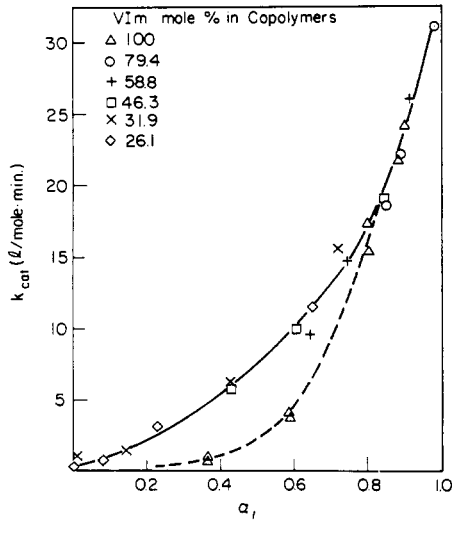


Figure 11. Plots of k_{cat} *vs.* α_1 for the solvolyses of PNPA catalyzed by the imidazole–acrylic acid copolymers and by poly-4(5)-vinylimidazole; solvent 28.5% ethanol–water, μ = 0.02, at 26°.

(22) See the review by S. A. Rice and M. Nagasawa, "Polyelectrolyte Solutions," Academic Press, New York, N. Y., 1961.

solvolyses of ANTI and NABA catalyzed by the imidazole–acrylic acid copolymer are most likely the result of ion pair formation between a substrate and a binding site in specific sequences. The enlarged selectivity of the imidazole–maleic acid copolymer, compared to the imidazole–acrylic acid copolymer, would be due to the increased electrostatic field potential around the polymer in solution.

The results obtained in this investigation suggest that this is the first example of synthetic, polymeric catalysts which presumably involve both long and short-range electrostatic interactions in their solvolytic reactions.

Acknowledgments. The authors are grateful to Dr. J. C. Salamone and Dr. I. Cho for their helpful discussions. They also wish to acknowledge financial support from the Research Laboratory, U. S. Army, Edgewood Arsenal, under Contract DAAA-15-67-C-0567, and the National Institutes of Health under Grant No. 2 RO1 GM 15256-02.

Cooperative Effects Involved in Esterolytic Reactions Catalyzed by Imidazole–Carboxylic Acid Copolymers

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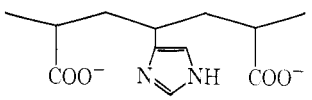
Received July 30, 1969

ABSTRACT: Studies of the esterolytic activities of copolymers of 4(5)-vinylimidazole and vinylsulfonic acid, in comparison with those of 4(5)-vinylimidazole and acrylic acid, were undertaken in order to elucidate the involvement of pendent carboxylate groups in the latter copolymers. It was found that the copolymers which were rich in vinylsulfonic acid were catalytically inactive. These results support the cooperative interaction of pendent imidazole and carboxylate functions in the imidazole–acrylic acid copolymer catalyzed reactions.

In the previous paper[2] it was reported that copolymers of 4(5)-vinylimidazole with acrylic acid had high selectivity toward the positively charged substrate, 3-acetoxy-N-trimethylanilinium iodide (ANTI), and that this high selectivity could be attributed to that of a specific monomeric sequence along the copolymer chain, *i.e.*, the sequence of carboxylate-neutral imidazole carboxylate (I).



I

It was previously reported from our group that basic pendent groups, such as neutral or anionic imidazole groups[3] and phenoxide groups,[4] could participate in the solvolytic reaction by interacting cooperatively with neutral, pendent imidazole groups in the solvolyses of esters. Since carboxylate anion has been known to catalyze hydrolyses of esters both intramolecularly[5,6] and intermolecularly,[5,6] it was anticipated that the pendent carboxylate groups in the imidazole–acrylic acid copolymers (such as in sequence I) might also participate in the catalytic action together with pendent imidazole groups. This possibility was previously suggested[2] in connection with the differences in the catalytic activities between the imidazole–acrylic acid copolymers and the imidazole homopolymer in the solvolysis of the neutral ester *p*-nitrophenyl acetate (PNPA). The former polymers, rich in the distribution of sequence I, were found to be significantly more active than the latter at the same degree of dissociation of the pendent imidazolium groups.

In order to elucidate the above possibility, copolymers of 4(5)-vinylimidazole with vinylsulfonic acid were prepared and their catalytic activities were compared with those of the imidazole–acrylic acid copolymers. The large difference in basicity and/or nucleophilicity between pendent carboxylate and pendent sulfonate groups in these copolymers were expected to reflect on the reactivity of the respective copolymers, if a pendent carboxylate group participates cooperatively with a pendent imidazole group in the solvolyses of esters.

Experimental Section

***n*-Butyl vinylsulfonate** was prepared by the procedure of Whitmore and Landan.[7]

Copolymerization of 4(5)-Vinylimidazole with *n*-Butyl Vinylsulfonate. 4(5)-Vinylimidazole, freshly distilled *n*-butyl vinylsulfonate (total amount of these monomers, 1.0 g) and azobisisobutyronitrile (0.02 g), was dissolved in 20 ml of reagent grade *n*-butyl alcohol in polymerization tubes. After removing oxygen by flushing with dry nitrogen, the

(1) Taken from the dissertation submitted by H. Maki in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of The University of Michigan.

(2) C. G. Overberger and H. Maki, *Macromolecules*, **3**, 214 (1970).

(3) (a) C. G. Overberger, T. St. Pierre, N. Vorchheimer, J. Lee, and S. Yaroslavsky, *J. Amer. Chem. Soc.*, **87**, 296 (1965); (b) C. G. Overberger, T. St. Pierre, and S. Yaroslavsky, *ibid.*, **87**, 4310 (1965); (c) C. G. Overberger, T. St. Pierre, C. Yaroslavsky, and S. Yaroslavsky, *ibid.*, **88**, 1184 (1966).

(4) C. G. Overberger, J. C. Salamone, and S. Yaroslavsky, *ibid.*, **89**, 6231 (1967).

(5) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1966, pp 173–186.

(6) E. Gaetjens and H. Morawetz, *J. Amer. Chem. Soc.*, **82**, 5323 (1960).

(7) W. F. Whitmore and E. F. Landan, *ibid.*, **68**, 1797 (1946).