this type because of observed large primary isotope effects. Diffusion-controlled protonations are expected to have small primary isotope effects; since the equilibrium isotope effect is also normally close to unity, the primary isotope effect for the forward reaction for such cases is likewise small.

The cyclohexylamine reactions are ion-pair reactions. The reverse reaction of protonation of a carbanion is actually a protonation of a lithium aryl with formation of a LiCHA ion pair. The involvement in this reaction of a lithium cation with its solvation demands undoubtedly accounts for the comparative slowness of the reverse protonation. The lithium cation is the moiety undergoing structural reorganization! For such a case the rate of the reverse protonation might well be approximately independent of structure for a related series and would give the effect of a Brønsted correlation for exchange with $\beta = 1$. Note that this type of argument probably does not apply to exchange reactions that involve delocalized carbanions, for here the organic moiety is also undergoing structural reorganization; that is, such different types of C–H bonds cannot be put on the same Brønsted scale.

Finally, we note that the log k_0 derived above, -16.8 at 40°, represents an extrapolated exchange rate of benzene itself. We are currently measuring this quantity directly and defer further comment until the completion of such studies.

Acknowledgment. We are pleased to acknowledge helpful conversations with Professors D. J. Cram and C. D. Ritchie.

Selective Catalytic Effects of Strongly Ionizing Polycations on Ester Solvolysis[1]

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Abstract: The cationic polyion, poly(1-vinyl-3-methylimidazolium iodide) (PVMI), was found to enhance the solvolytic rates of the negatively charged esters 4-acetoxy-3-nitrobenzoic acid and sodium 4-acetoxy-3-nitrobenzenesulfonate in 28.5% ethanol–water solutions. These rates were unaffected by the monomeric analog of the polyion, 1,3-dimethylimidazolium iodide. At high pH values, the enhanced solvolytic rates of the negatively charged esters may be accounted for by the high local concentration of hydroxyl counterions in the vicinity of the polymer chain. At intermediate pH values, the large catalytic effect is attributed to an enhanced susceptibility of the anionic ester to direct water attack in the vicinity of the polycation. The solvolyses of uncharged esters (*p*-nitrophenyl acetate and *p*-nitrophenyl hexanoate) were not accelerated, indicating that hydrophobic forces are insufficient to concentrate the esters in the neighborhood of the polyion. A copolymer of 1-vinyl-3-methylimidazolium iodide (VMI) containing 86 mol % vinyl alcohol residues catalyzed the hydrolysis of anionic esters with an efficiency similar to that of the PVMI homopolymer, if the two were compared at equal stoichiometric concentrations of imidazolium groups. On the other hand, a copolymer of VMI containing 63 mol % *p*-vinylphenol residues was about twice as effective as PVMI. This is due to the fact that the polycation draws the anionic ester into a region with a high local concentration of the phenoxide nucleophile.

Effects of polyions on the rates of reactions of low molecular weight species may be classified into two categories. (1) The large local fluctuations in the electrostatic potential characterizing polyelectrolyte solutions lead to corresponding fluctuations in the local concentration of charged species. If a reaction involves two ionic species with a charge of the same sign, a polyion of opposite sign will tend to concentrate these reagents in its immediate neighborhood and enhance the rate of their collisions with each other. The polyion will then act as a catalyst. Conversely, if the two reagents carry charges of opposite sign, the polyion will attract one and repel the other, and it will act as an inhibitor. The quantitative analysis of this effect may be used to characterize the distribution of the electrostatic potential in polyelectrolyte solutions.[3] As typical examples of these phenomena we may cite the powerful catalysis of the benzidine rearrangement (involving an attack of a hydrogen ion on the conjugate acid of hydrazobenzene) by a polysulfonic acid[4] and the inhibition of the hydroxide ion catalyzed hydrolysis of a cationic ester in the presence of polymeric acids.[3b] (2) A second effect will be observed if the polyion carries catalytically active substituents. In this case, a reactive counterion may be attracted to the polyion where it finds itself in a region of high local concentration of the catalytic groups. Such a sit-

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(2) (a) The University of Michigan, Ann Arbor, Mich. (b) Deceased, July 1967.

(3) (a) H. Morawetz, *J. Polymer Sci.*, 42, 125 (1960); (b) H. Morawetz and J. A. Shafer, *J. Phys. Chem.*, 67, 1293 (1963).

(4) C. L. Arcus, T. L. Howard, and D. S. South, *Chem. Ind.* (London), 1756 (1964).

uation arises when partially ionized polyvinylpyridine[5] or poly(4(5)-vinylimidazole)[6] are added to solutions of anionic esters or if a copolymer of 4(5)-vinylimidazole and acrylic acid is used to catalyze the hydrolysis of a cationic ester.[7] Another interesting case of this type involves the oxidation of ascorbic acid or hydroquinone by atmospheric oxygen which is powerfully catalyzed in solutions containing the Cu(II) complex of poly-L-histidine.[8] Catalytic and inhibition effects somewhat similar to those observed in polyelectrolyte solutions have been reported by a number of investigators who studied organic reactions in solutions containing cationic or anionic micelles.[9] However, there is a characteristic difference in the behavior of the two types of systems. In solutions of the flexible chain polyelectrolytes, past evidence suggested that Coulombic long-range electrostatic forces are mainly responsible for the interaction of the polyions with reactive molecules, so that the polyions did not affect the reaction rate of uncharged species.[3b] By contrast, charged detergent micelles may bind very efficiently uncharged species and phenomena such as the powerful catalysis of the reaction of methyl bromide with cyanide ion in the presence of cationic micelles[9b] are characteristic consequences of this effect. In fact, the powerful hydrophobic forces responsible for micelle formation may even draw into the micelle reagent molecules carrying a charge of the same sign. Thus, the cationic triphenylmethane dyes are solubilized in cationic micelles, where their exposure to hydroxyl ion attack is enhanced, with a consequent sharp increase of the dye fading rate.[9c] In principle, one might expect such hydrophobic interactions to make some contribution also to the binding of small molecules to flexible chain polyions. The existence of such an effect was demonstrated in a study of ester hydrolysis in the presence of cation exchange resins neutralized with aromatic quaternary ammonium bases, where the catalytic efficiency of the resin increased markedly with the length of the hydrophobic residue in the ester.[10] Here the selectivity is favored by the high polymer concentration in the resin phase and a much smaller selectivity due to hydrophobic forces would be expected with linear polyions in solution. However, even in such cases dialysis equilibrium data demonstrate that hydrophobic interactions may affect appreciably the binding of counterions to a polyion.[11]

In the present study we were interested in examining the effect of a positively charged polyion, poly(1-vinyl-3-methylimidazolium iodide) (PVMI), on the solvolytic rates of neutral and anionic esters, and in determining if hydrophobic forces are involved in such solvolytic reactions. This investigation was extended to include copolymers of 1-vinyl-3-methylimidazolium iodide with vinyl alcohol and with *p*-vinylphenol in order to ascertain if the covalently bound hydroxyl and phenolic functions were involved in the catalytic processes. Possible effects of charge on the nucleophilicity of adjacent, pendent hydroxyl and phenol groups were also considered, in view of a previous observation that such effects exist in trimethylammonium derivatives of phenols and catechols and that they enhance the nucleophilicity of the phenolate ions to a larger extent than predicted by the Brønsted relationship.[12]

Experimental Section

Poly(1-vinylimidazole) was prepared as previously described.[7]

Poly(1-vinyl-3-methylimidazolium iodide) was prepared by the method of Gregor and Gold.[13] To a solution of 0.9 g of poly(1-vinylimidazole) dissolved in 4 ml of methanol was added 2.1 g of methyl iodide. The solution was refluxed for 2 hr and 4 ml of methanol was added to maintain homogeneity. The resulting solution was stirred at reflux overnight. After cooling, the heterogeneous solution was precipitated into a tenfold excess of ethyl acetate giving 1.6 g (70% yield) of an off-white polymer.

Anal. Calcd for $C_6H_9N_2I$: C, 30.5; H, 3.8; N, 11.9; I, 53.8. Found: C, 30.4: H, 4.7; N, 11.6: I, 53.2.

Copolymerization of 1-Vinylimidazole and *p*-Vinylphenol. In a polymerization tube was placed 0.570 g (0.006 mol) of 1-vinylimidazole, 0.545 g (0.0045 mol) of *p*-vinylphenol, 0.011 g of azobisisobutyronitrile, and 11 ml of benzene. The tube was cooled to −78°, flushed with nitrogen, degassed, and sealed under reduced pressure. After heating for 24 hr in a refluxing hexane bath, the precipitated off-white solid was filtered and washed with benzene giving 0.60 g (54% conversion) of polymer. The copolymer was purified by twice reprecipitating from dimethylformamide into ethyl acetate.

Anal. Found: C, 73.6; H, 6.9; N, 9.2 (0.33 mol of imidazole and 0.58 mol of phenol per 100 g of polymer).

Quaternization of Copolymer of 1-Vinylimidazole and *p*-Vinylphenol. In a 25-ml, round-bottomed flask was placed 0.2 g of the above copolymer, 2.1 g of methyl iodide, and 5 ml of dimethylformamide. The solution was stirred at room temperature for 2 hr and then heated for 20 hr at 100°. Water (1 ml) was added during the course of the reaction to maintain a homogeneous solution. After cooling, the solution was precipitated into ethyl acetate. The light yellow solid obtained was twice reprecipitated from a dimethylformamide–water mixture into ethyl acetate giving an off-white polymer. Infrared spectrum (potassium bromide pellet) showed the presence of imidazolium groups and phenol groups.

Anal. Found: C, 52.1; H, 5.6; N, 6.3; I, 29.1 (0.23 mol of imidazolium groups and 0.39 mol of phenol groups per 100 g of polymer).

Copolymerization of 1-Vinylimidazole and Vinyl Acetate. In a polymerization tube was placed 1.1 g (0.012 mol) of 1-vinylimidazole, 17.8 g (0.207 mol) of vinyl acetate, and 26 mg of azobisisobutyronitrile. The tube was cooled to −70°, flushed with nitrogen, degassed, sealed *in vacuo*, and heated at 69° for 60 hr. The resulting viscous solution was added to a 20-fold excess of cyclohexane, precipitating an off-white solid. The polymer was dissolved in acetone and reprecipitated twice into ether giving 4.5 g of polymer (71% conversion).

Anal. Found: C, 56.4; H, 7.0; N, 5.6 (0.20 mol of imidazole and 0.94 mol of acetate per 100 g of polymer).

Hydrolysis of Copolymer of 1-Vinylimidazole and Vinyl Acetate. A suspension of 3 g of the above copolymer in 100 ml of water was refluxed for 2 weeks, during which time the mixture turned into a clear light yellow solution. The solution was filtered and lyophilized giving 1.96 g of an off-white powder. The polymer was redissolved in water and precipitated into a large excess of ethyl

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(5) R. L. Letsinger and T. J. Savereide, *J. Amer. Chem. Soc.*, 84, 3122 (1962).

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

(7) C. G. Overberger, R. Sitaramaiah, T. St. Pierre, and S. Yaroslavsky, *ibid.*, 87, 3270 (1965).

(8) I. Pecht, A. Levitzki, and M. Anbar, *ibid.*, 89, 1587 (1967).

(9) (a) J. Steinhardt, *J. Biol. Chem.*, 141, 995 (1949); (b) I. M. Kolthoff and W. F. Johnson, *J. Amer. Chem. Soc.*, 73, 4563 (1951); (c) E. F. J. Duynstee and E. Grunwald, *ibid.*, 81, 4540, 4542 (1959); (d) M. B. Lowe and J. N. Phillips, *Nature*, 190, 262 (1961); (e) J. L. Kurz, *J. Phys. Chem.*, 66, 2239 (1962); (f) M. T. A. Behme and E. H. Cordes, *J. Amer. Chem. Soc.*, 87, 260 (1965); (g) M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, 87, 266 (1965); (h) L. J. Winters and E. Grunwald, *ibid.*, 87, 4608 (1965).

(10) P. Riesz and L. P. Hammett, *ibid.*, 76, 992 (1954).

(11) H. Morawetz and A. Y. Kandanian, *J. Phys. Chem.*, 70, 2995 (1966).

(12) J. E. Epstein, R. E. Plapinger, H. O. Michel, J. R. Cable, R. A. Stephani, R. J. Hester, C. Billington, Jr., and G. R. List, *J. Amer. Chem. Soc.*, 86, 3075 (1964); J. Epstein, H. O. Michel, D. H. Rosenblatt, R. E. Plapinger, R. A. Stephani, and E. Cook, *ibid.*, 86, 4959 (1964).

(13) H. P. Gregor and D. H. Gold, *J. Phys. Chem.*, 61, 1347 (1957).

acetate. The polymer tenaciously held a substantial amount of water.

Anal. Found: C, 56.0; H, 7.3; N, 6.1 (0.22 mol of imidazole per 100 g of polymer).

Quaternization of Copolymer of 1-Vinylimidazole and Vinyl Alcohol. The procedure utilized was the same as that for the quaternization of poly(1-vinylimidazole). Nitrogen and iodine analyses reveal almost complete quaternization of the imidazole groups. The polymer still held some water tenaciously.

Anal. Found: C, 45.3; H, 6.2; N, 4.7; I, 20.9 (0.17 mol of imidazolium groups per 100 g of polymer).

***p*-Nitrophenyl acetate, 4-acetoxy-3-nitrobenzoic acid, sodium 4-acetoxy-3-nitrobenzenesulfonate, and 3-acetoxy-N-nitromethylanilinium iodide** were prepared as previously described.[14]

Spectrophotometric Titration. Determination of the state of ionization of the phenol groups in the 1:1.72 copolymer of 1-vinyl-3-methylimidazolium iodide and *p*-vinylphenol was performed in 80% methanol-water solutions at concentrations of approximately 10^{-4} M in phenol. The copolymer was insoluble in solvents containing lower percentages of alcohol. The details of measurements and calculations were previously reported.[6] The plot of the fraction of phenolate ions (α_{PhO^-}) *vs.* pH appears in Figure 1. The apparent pK_a of the phenol groups in the copolymer in 80% methanol-water, as determined from Figure 1, is 10.2 at the point where $\alpha_{\text{PhO}^-} = 0.5$.

Kinetic Measurements. In the case of poly(1-vinyl-3-methylimidazolium iodide) and 1,3-dimethylimidazolium iodide, catalyst solutions of 5×10^{-4} M in imidazolium groups were prepared in 28.5% ethanol-water with sufficient potassium chloride added in each case to adjust the ionic strength to 0.02. The following solutions were utilized to obtain the desired pH values: (a) for pH values 1.7 and 3.0, hydrochloric acid was used; (b) for pH values 4.1 and 6.0, solutions were buffered with 0.02 M acetic acid-sodium acetate; (c) for pH values 7.1-9.0, solutions were buffered with 0.02 M tris(hydroxymethyl)aminomethane (Tris) and hydrochloric acid; (d) for pH 10.5, a 0.02 M buffer of triethylamine-hydrochloric acid was employed.

Similar experimental conditions were employed for the copolymer of 1-vinyl-3-methylimidazolium iodide and vinyl alcohol.

In the case of the 1:1.72 copolymer of 1-vinyl-3-methylimidazolium iodide and *p*-vinylphenol, catalyst solutions of 2.5×10^{-4} M in imidazolium groups were prepared in 80% methanol-water buffered with 0.02 M Tris and hydrochloric acid. Sufficient potassium chloride was added to adjust the ionic strength to 0.02. For comparison, 2.6×10^{-4} M solutions of poly(1-vinyl-3-methylimidazolium iodide) were employed under the same experimental conditions.

The performance of kinetic measurements and the methods of calculation of the first-order rate constants were as previously described.[6] In each instance the temperature employed was 26°.

Results and Discussion

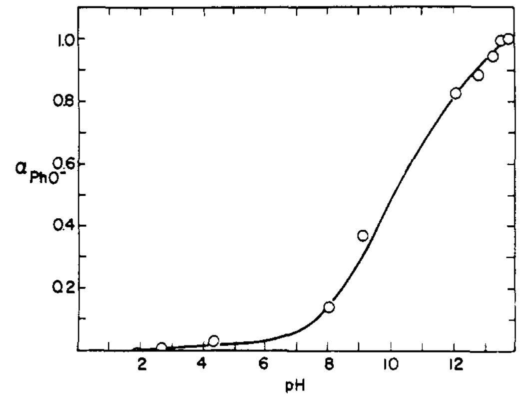
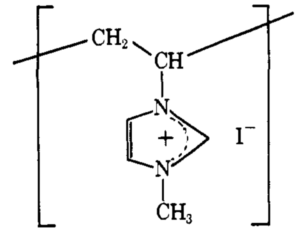


Figure 1. Spectrophotometric titration. Plot of α_{PhO^-} *vs.* pH for the phenol groups in the 1:1.72 copolymer of 1-vinyl-3-methylimidazolium iodide and *p*-vinylphenol in 80% methanol-water at an ionic strength of 0.02.

Syntheses. The quaternization of poly(1-vinylimidazole) with methyl iodide has been shown to proceed in a quantitative manner by Gregor and Gold.[13] Since the structure of the quaternized imidazole ring in the resulting polycation was not indicated, it was necessary to ascertain if methylation occurred on the pyrrole-like single-bonded nitrogen (1 position) or on the pyridine-like double-bonded nitrogen (3 position). This was determined by an nmr spectrum of the simplest dialkylimidazolium salt, *viz.*, dimethylimidazolium iodide, prepared by quaternization of 1-methylimidazole with methyl iodide.[15] The nmr spectrum demonstrated the symmetry of the molecule. The fact that the pyridine-like double-bonded nitrogen is the more basic can be anticipated by considerations of aromaticity. Analogous observations were made by Staab, *et al.*[16] The structure of the quaternized polymer can therefore be represented as I.



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Copolymerization of 1-vinylimidazole with *p*-vinylphenol and with vinyl acetate proceeded by free-radical initiation. It was found that hydrolyis of the acetyl functions in the copolymer of 1-vinylimidazole and vinyl acetate could be affected in boiling water, though a longer period of time was required than for the corresponding copolymer with 4(5)-vinylimidazole.[14] This effect can be correlated to a neighboring group participation of the imidazole groups. It was found that under the specified conditions, quaternization of the imidazole functions in the copolymers of 1-vinylimidazole with *p*-vinylphenol and with vinyl alcohol was nearly quantitative. Infrared spectra indicated that neither the phenol nor the hydroxyl functions were affected.

Kinetics. The first-order rate constants for the solvolyses of sodium 4-acetoxy-3-nitrobenzenesulfonate (NABS) in the presence (k) and absence (k_0) of 5×10^{-4} M poly(1-vinyl-3-methylimidazolium iodide) (PVMI) over a broad range of pH are presented in Table I. The ratio k/k_0 is also given. Logarithmic

Table I. First-Order Rate Constants for the Solvolyses of NABS in the Presence and Absence of PVMI, Ionic Strength 0.02[a]

pH	$k_0 \times 10^4$, min^{-1}	$k \times 10^4$, min^{-1}	k/k_0
1.7	1.6	1.7	1.1
3.0	0.5	4.4	9
4.1	0.5	8.5	17
6.0	0.4	25.3	63
7.1	2.3	22.4	10
8.0	13.4	35.2	2.6
9.0	68.9	104.0	1.5
10.5	1360.0	1750.0	1.3

[a] In 28.5% ethanol-water.

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(14) C. G. Overberger, J. C. Salamone, and S. Yaroslavsky, *J. Amer. Chem. Soc.*, **89**, 6231 (1967).

(15) C. G. Overberger, J. C. Salamone, and S. Yaroslavsky, *J. Org. Chem.*, **30**, 3580 (1965).

(16) H. A. Staab and A. Mannschreck, *Tetrahedron Letters*, 913 (1962); A. Mannschreck, W. Seitz, and H. A. Staab, *Ber. Bunsenges. Physik. Chem.*, **67**, 470 (1963).

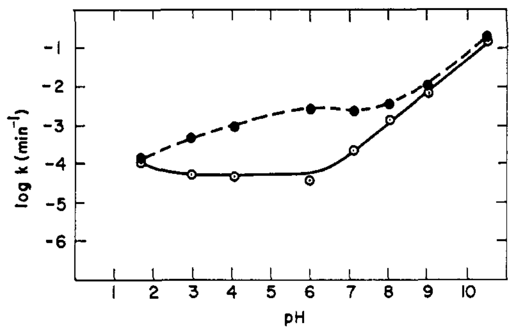

Figure 2. pH dependence of the first-order rate constants k and k_0 (min^{-1}) for the solvolysis of NABS in the presence (●) and absence (○) of PVMI: 28.5% ethanol–water, ionic strength 0.02. The solid line represents calculated values for the rate in the absence of polyelectrolyte using the uncatalyzed rate constant $k_{\mathrm{H_2O}} = 4.8 \times 10^{-5}$ min^{-1} and the catalytic coefficients $k_{\mathrm{H}^+} = 5.2 \times 10^{-3}$ l. mol^{-1} min^{-1}, $k_{\mathrm{OH}^-} = 5.0$ l. mol^{-1} min^{-1}, and $k_{\mathrm{Tris}} = 0.1$ l. mol^{-1} min^{-1}.

plots of k_0 and k against pH are shown in Figure 2. In the absence of PVMI, NABS is solvolyzed in 28.5% ethanol-water by three different mechanisms. At a pH below 2 the hydrogen ion catalyzed reaction is dominant, and above pH 7 hydroxyl ion catalysis makes the largest contribution with a smaller effect due to catalysis by the basic form of the Tris buffer employed.[17] In the intermediate region (pH 4–6) the rate is almost independent of pH so that direct water attack on the ester seems to be rate determining.

The addition of PVMI was expected to enhance hydroxide ion catalyzed hydrolysis of anionic esters, since both the hydroxide ion and the negatively charged ester are attracted to the polycation, so that the rate of their mutual collisions is increased. For any given polyelectrolyte concentration, the factor by which the rate is increased should be independent of pH and the effect should, therefore, appear on a plot of log k against pH as a parallel upward displacement from the log k_0 line. Figure 2 shows that this is the behavior observed above pH 9, where hydroxide ion catalysis makes the dominant contribution to the reaction rate both in the presence and absence of PVMI. According to the theoretical analysis of the catalytic effect of a polyion expected in the case where two singly charged counterions are the reactive species[3a]

$$k/k_0 = 1 + (\sigma_x/\bar{x})^2$$

where $x = \exp(-q\psi/\mathrm{k}T)$, q is the charge of the counterion, ψ the electrostatic potential, k the Boltzmann constant, and T the absolute temperature, while $\bar{x}$ is the mean value of x and σ_x is the standard deviation of x in the system. In the presence of some simple electrolyte, x would be expected to deviate appreciably from unity only in the immediate vicinity of the polyion, and $(k/k_0) - 1$ should then be linear in polyelectrolyte concentration as long as this concentration is so low that the mutual interpenetration of the polyions can be neglected. This was, in fact, found to be the case for both anionic esters NABS and NABA as shown in Figure 3. Taking the average of the data for pH 9 and 10.5 in Table I, we find $(k/k_0) - 1 = 0.4$ for a PVMI concentration $c_\mathrm{p} = 5 \times 10^{-4}$ *M*, *i.e.*, $(k - k_0)/k_0c_\mathrm{p} = 800$ in 28.5% ethanol and at an ionic strength of 0.02. The only data with which this result can be compared were obtained in a study of the benzidine rearrangement in a solution of a polysulfonic acid,[4] which involves also the interaction of two singly charged counterions in the presence of a polyion. In this case, the normality of the polyion was 100 times as high as in the present study and $(k/k_0) - 1$ was 117. This yields $(k - k_0)/k_0c_\mathrm{p} = 2340$, of nearly the same order of magnitude as in the present investigation, although a different solvent medium (96% ethanol) was used and the system contained no simple electrolytes. Clearly, it would be desirable to carry out studies of the polyelectrolyte effect on a variety of reactions under more nearly comparable conditions.

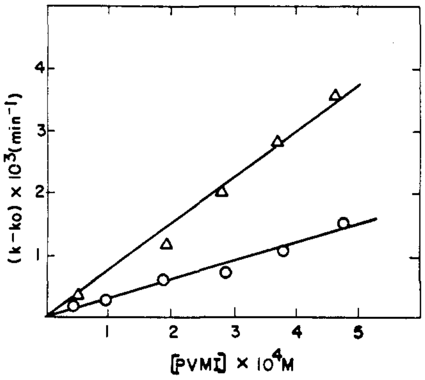

Figure 3. The observed rates of solvolysis of NABS (△) and of NABA (○) as a function of the concentration of PVMI at pH 9.0 in 28.5% ethanol-water at ionic strength 0.02.

Further inspection of Table I and Figure 2 reveals the completely unexpected fact that the polycation increases the hydrolysis rate of NABS by the largest factor in the pH range in which the direct water attack on the ester makes the dominant contribution to the reaction rate. This factor reaches a value of 63 at pH 6.0. It must be concluded that the accumulation of the substrate in the vicinty of the polymer, where the local concentration of the cationic groups is very high, leads to an increased efficiency of the water attack on the ester. Characteristically, in systems containing the same stoichiometric concentration of a low molecular weight analog of the polymer repeat unit (*i.e.*, 5×10^{-4} *M* 1,3-dimethylimidazolium iodide), no catalytic effect of NABS solvolysis was observed. This is not surprising, since the "effective local concentrations" of groups attached to every residue of a vinyl polymer are found to attain, in the neighborhood of the polymer chain, values of the order of 1 *M*.[18] However, the cause of the increased susceptibility of the esters to water attack in the neighborhood of the cationic groups is at present completely obscure.

The effect of increased salt concentration on the solvolytic rates of NABS in the presence and absence of 5×10^{-4} *M* PVMI was investigated by determining the first-order rate constants over the pH range 6–9 at the ionic strength of 0.10. The first-order rate constants for the solvolyses of NABS in the presence and

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[17] T. C. Bruice and J. L. York, *J. Amer. Chem. Soc.*, **83**, 1382 (1961); S. A. Bernhard and H. Gutfreund, *Proc. Intern. Symp. Enzymes Chem. Tokyo, Kyoto*, 127 (1958); W. Jencks and J. Carriuolo, *J. Amer. Chem. Soc.*, **82**, 1778 (1960).

[18] H. Morawetz, "Macromolecules in Solution," Interscience Division of John Wiley and Sons, Inc., New York, N. Y., 1965, pp 432–434.

absence of PVMI are reported in Table II. Comparison with Table I shows clearly that the increase of the ionic strength from 0.02 to 0.10 reduces sharply the ratio k/k_0 both in the region where direct water attack on the ester and where hydroxide ion catalysis make the largest contribution to the reaction rate. In both cases $(k/k_0) - 1$ is decreased by an order of magnitude.

Table II. First-Order Rate Constants for the Solvolyses of NABS in the Presence and Absence of PVMI at an Ionic Strength of 0.10[a]

pH	$k_0 \times 10^4$, min^{-1}	$k \times 10^4$, min^{-1}	k/k_0
6.1	0.9	4.6	5
7.2	3.5	8.8	2.5
8.2	18.2	24.3	1.3
9.2	92.1	96.4	1.05

[a] In 28.5% ethanol–water solutions buffered with 0.02 *M* Tris–hydrochloric acid above pH 7 and 0.02 *M* acetic acid–sodium acetate at lower pH.

In order to test whether hydrophobic forces participate in the attraction of the substrate to the polyion, the effect of PVMI on the solvolytic rates of the neutral esters *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyl hexanoate (PNPH) was investigated. It was observed that PVMI had no effect on either of these substrates. This is in contrast to the behavior of detergent micelles[9g] which catalyze the hydrolysis of the hexanoate, carrying a longer paraffinic chain more efficiently than that of acetate.

It was of interest to study the catalytic behavior of 1-vinyl-3-methylimidazolium iodide copolymers carrying hydroxyl or phenol groups covalently bound to the macromolecule. Cooperative catalytic effects have previously been observed in copolymers of 4(5)-vinylimidazole with vinyl alcohol and with *p*-vinylphenol.[14] Employing a 1:4.7 copolymer of 1-vinyl-3-methylimidazolium iodide and vinyl alcohol in 28.5% ethanol–water, no enhanced catalytic effects were found for either PNPA or the positively charged ester 3-acetoxy-N-trimethyanilinium iodide (ANTI). The results with the negatively charged substrates NABA and NABS at pH 9.1, at equal concentration of imidazolium groups, were similar to those when PVMI was employed. Therefore, the pendent hydroxyl groups appear to possess no catalytic activity.

Owing to the low solubility of the 1:1.72 copolymer of 1-vinyl-3-methylimidazolium iodide and *p*-vinylphenol in 28.5% ethanol–water, solvolytic rate measurements were performed in 80% methanol–water solutions. For comparison, solvolytic rates utilizing PVMI were repeated in this solvent system. The quaternized imidazole–phenol copolymer accelerated the solvolyses of the negatively charged substrates, while no catalytic effects were noted for PNPA or the positively charged ester ANTI. In contrast to the behavior of the quaternized imidazole–alcohol copolymer, the quaternized imidazole–phenol copolymer was found to be more effective than PVMI for the solvolyses of NABA and NABS (Table III). This enhanced effect must be attributed to catalysis owing to the covalently bound phenolate nucleophiles, and it is formally analogous to the high efficiency with which partially ionized polyvinylpyridine quaternizes α-bromoacetate[19] and catalyzes the hydrolysis of anionic esters[5] or the catalytic action of an acrylic acid copolymer with 4(5)-vinylimidazole in the solvolysis of cationic esters.[7] In all these cases, the low molecular weight reagent is brought into the domain of the polyion by long-range electrostatic forces and finds itself in a region of high local concentration of a nucleophile.[20] In the present case, the catalysis might have been expected to be further increased by the enhanced ionization of the phenol residues when they are attached to a polymer chain with a high density of cationic charges. However, the spectrophotometric titration data shown in Figure 1 correspond to a pK = 10.2 at half-neutralization, which is identical with the pK of *p*-cresol, a low molecular weight analog of the *p*-vinylphenol residues of the copolymer, derived from the titration of the dilute *p*-cresol solutions in water. It may be concluded that attachment of the phenol residues to the cationic chain, which favors increased ionization, is compensated by the reduction in the ionization resulting from the use of a solvent medium with a lower dielectric constant (*i.e.*, 80% methanol–water).

Table III. First-Order Rate Constants for the Solvolyses of NABA and NABS in the Presence of 1:1.72 Copolymer of 1-Vinyl-3-methylimidazolium Iodide and *p*-Vinylphenol, PVMI, and the Blank[a]

pH	$k_0 \times$ 10^4, min^{-1}	k(PVMI) $\times$ 10^4, min^{-1}	k(copolymer) $\times$ 10^4, min^{-1}
		NABA	
7.4	0.8	2.2	3.7
8.2	9.9	10.2	19.4
9.1	77.3	84.7	122.0
		NABS	
7.4	3.2	6.1	11.9
8.2	19.7	26.3	53.6
9.1	162.0	187.0	405.0

[a] In 80% methanol–water buffered with 0.02 *M* Tris–hydrochloric acid at an ionic strength of 0.02. Concentration of imidazolium groups 2.6×10^{-4} *M* for PVMI and 2.5×10^{-4} *M* for the copolymer.

In a very limited sense, the catalytic action of the copolymer described above may be likened to the action of the enzyme acetylcholineesterase. This enzyme is known to have an active site in which the cationic end of acetylcholine faces a negative charge of the enzyme while the ester function is being attacked by a nucleophile.[21] In addition to the fact that the catalytic effects described in the present study are minute compared to the efficiency of enzymatic catalysis, the following differences should be noted. (1) The contact between enzyme and substrate is a very intimate one, so that only molecules with a closely defined spacing between the two interacting groups will be strongly bound.[22] In

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(19) H. Ladenheim, E. M. Loebl, and H. Morawetz, *J. Amer. Chem. Soc.*, **81**, 20 (1959).

(20) The *p*-vinylphenol homopolymer with the same stoichiometric concentration of *p*-vinylphenol residues as in the experiments with the copolymer was without any catalytic effect on the solvolysis of the anionic esters. This is not surprising since in this case no electrostatic forces operate to concentrate the ester in the region with a high concentration of the nucleophile.

(21) I. B. Wilson and F. Bergmann, *J. Biol. Chem.*, **185**, 479; **186**, 683 (1950). For a review of acetylcholine esterase studies see I. B. Wilson in "The Enzymes," Vol. 4, 2nd ed, P. D. Boyer, H. Lardy, and K. Myrbäck, Ed., Academic Press Inc., New York, N. Y., 1960, Chapter 30.

(22) I. B. Wilson and C. Quan, *Arch. Biochim. Biophys.*, **73**, 131 (1958).

the case of the synthetic polymer catalyst, the absence of the conformational rigidity characteristic of proteins precludes a similar degree of specificity. (2) The intimate association of enzyme and substrates increases the effectiveness of hydrophobic forces. Thus, the uncharged analog of acetylcholine, 3,3-dimethyl-*n*-butyl acetate, in which a carbon is substituted for the quaternary nitrogen atom, is attacked by the enzyme only 23% more slowly than the cationic substrate.[23] Another example of the importance of hydrophobic interactions with the enzyme is provided in a comparison of its rate of attack on acetylcholine and on dimethylammoniumethyl acetate.[24] Although the two substrates have their cationic and ester groups at the same spacing, the acetylcholine, with an additional methyl group on the nitrogen, is attacked more than twice as fast. This is in sharp contrast with the lack of any indication of hydrophobic interactions in the present study with synthetic flexible chain polyions. (3) Although long-range electrostatic forces make some contribution to the substrate binding to acetylcholineesterase, this contribution is relatively small. For instance, an increase in the ionic strength from 0.025 to 0.185 produces, at low substrate concentration, a decrease of enzymatic activity by only 45%.[25] The action of synthetic polyions on oppositely charged substrates is much more sensitive to the ionic strength of the medium.

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[23] D. H. Adams and V. P. Whittaker, *Biochim. Biophys. Acta*, 4, 543 (1950).

[24] I. B. Wilson, *J. Biol. Chem.*, 197, 215 (1952).

[25] B. Mendel and H. Rudney, *Science*, 102, 616 (1945).

Substituent Effects and Aryl Participation in β-(*syn*-9-Benzonorbornenyl)ethyl *p*-Bromobenzenesulfonate Solvolyses[1,2]

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Abstract: A series of 6-substituted β-(*syn*-9-benzonorbornenyl)ethyl brosylates (Ia–e-OBs), the unsubstituted *anti* isomer (IIa-OBs), and the *syn*-propyl homolog (IX-OBs) were synthesized. The acetolysis of unsubstituted Ia-OBs proceeds 20 times as fast at 100° as that of IIa-OBs and yields mainly a mixture of several benzhydrindanyl derivatives formed with rearrangements. The effects of the 6 substituents on the over-all rates, $k_{\mathrm{OCH_3}}/k_{\mathrm{NO_2}}$, amount to a factor of 146, and those on the anchimerically assisted rates, k_Δ, are well correlated by the modified Hammett relationship, $\log (k_\Delta/k_\Delta{}^0) = {}^1/_2\rho(\sigma_p{}^+ + \sigma_m{}^+)$, with $\rho = -2.88$. These are discussed as evidence for remote aryl participation under a constant steric factor. In contrast, the acetolyses of IIa-OBs and IX-OBs showed neither rate enhancement nor rearrangement.

Studies of substituent effects such as carried out by us in the solvolysis of benzonorbornenyl brosylates[3] have been evaluated as a decisive test for π-participation effects.[4] As a continuation of studies of this kind, this paper deals with the acetolysis of 6-substituted β-(*syn*- and *anti*-9-benzonorbornenyl)ethyl brosylates (Ia–e-OBs and IIa-OBs). The results provide one of the best pieces of evidence for the existence of remote aryl participation (Winstein)[5,6] and are, from a theoretical point of view, instructive for the high solvolytic reactivity of β-(*syn*-7-norbornenyl)ethyl brosylate recently found by Bly, *et al.*,[7] and for the solvolytic ring closure of ω-(Δ^3-cyclopentenyl)alkyl arenesulfonates studied by Lawton[8] and Bartlett and his coworkers.[9]

Results

Preparations. The syntheses of 6-substituted β-(*syn*-9-benzonorbornenyl)ethyl alcohols (Ia–d-OH) and the unsubstituted *anti* alcohol IIa-OH were carried out as outlined in Chart I.

9-Benzonorbornenones (IIIa–d)[10] were condensed with carbethoxymethylenetriphenylphosphorane according to the procedure of Wittig[11] to produce ethyl 9-benzonorbornenylideneacetates (IVa–d) in satisfac-

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[1] Presented, in part, at the 17th Organic Reaction Mechanism Symposium of the Chemical Society of Japan in Tokyo, Oct 1966.

[2] The numbering used in this paper is shown in the charts.

[3] (a) H. Tanida, *J. Amer. Chem. Soc.*, 85, 1703 (1963); (b) H. Tanida, T. Tsuji, and H. Ishitobi, *ibid.*, 86, 4904 (1964); (c) H. Tanida and H. Ishitobi, *ibid.*, 88, 3663 (1966); (d) H. Tanida, Y. Hata, S. Ikegami, and H. Ishitobi, *ibid.*, 89, 2928 (1967).

[4] H. C. Brown and K. Takeuchi, *ibid.*, 88, 5336 (1966).

[5] For recent reviews, see (a) P. D. Bartlett, "Nonclassical Ions," W. A. Benjamin, Inc., New York, N. Y., 1965; (b) B. Capon, *Quart. Rev.* (London), 18, 45 (1964).

[6] R. Baird and S. Winstein, *J. Amer. Chem. Soc.*, 84, 788 (1962), and references cited therein.

[7] R. S. Bly, R. K. Bly, A. O. Bedenbaugh, and O. R. Vail, *ibid.*, 89, 880 (1967).

[8] R. G. Lawton, *ibid.*, 83, 2399 (1961).

[9] (a) P. D. Bartlett, S. Bank, R. J. Crawford, and G. H. Schmid, *ibid.*, 87, 1288 (1965); (b) P. D. Bartlett and G. D. Sargent, *ibid.*, 87, 1297 (1965); (c) P. D. Bartlett, W. S. Trahanovsky, D. A. Bolon, and G. H. Schmid, *ibid.*, 87, 1314 (1965).

[10] (a) H. Tanida, H. Miyazaki, and H. Ishitobi, *Can. J. Chem.*, 44, 98 (1966); (b) R. Muneyuki and H. Tanida, *J. Org. Chem.*, 31, 1988 (1966).

[11] Refer to A. Maercker in "Organic Reactions," Vol. 14, A. C. Cope, Ed., John Wiley and Sons, Inc., New York, N. Y., 1965, p 270.