
THE EFFECT OF POLYMERIC AND MODEL IMIDAZOLIUM HALIDES ON THE RATE OF HYDROLYSIS OF 4-ACETOXY-3-NITROBENZOIC ACID

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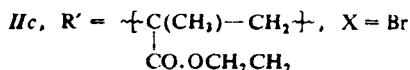
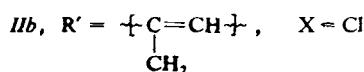
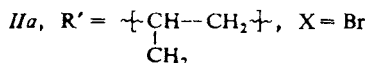
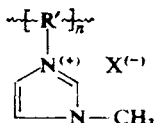
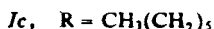
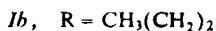
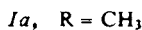
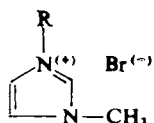
Dedicated to Professor O. Wichterle on the occasion of his 70th birthday.

The course of hydrolysis of an ester, 4-acetoxy-3-nitrobenzoic acid catalyzed with poly(1-methyl-3-allylimidazolium bromide) (*Ila*), poly[1-methyl-3-(2-propinyl)imidazolium chloride] (*Iib*) and poly[1-methyl-3-(2-methacryloyloxyethyl)imidazolium bromide] (*Iic*) in a 28.5% aqueous ethanol was investigated as a function of pH and compared with low-molecular weight models, *viz.*, 1-methyl-3-alkylimidazolium bromides (the alkyl group being methyl, propyl, and hexyl, resp). Polymers *Iib*, *Iic* possessed a higher activity at pH above 9, while the models were more active at a lower pH with a maximum at pH 7.67. The catalytic activity at the higher pH is attributed to an attack by the OH⁻ group, while at the lower pH it is assigned to a direct attack of water on the substrate. The rate of hydrolysis of 4-acetoxy-3-nitrobenzoic acid is proportional to the catalyst concentration [*Iic*] and proceeds as a first-order reaction. The hydrolysis depends on the composition of the solvent and was highest at 28.5% (vol.) of ethanol in water. The hydrolysis of a neutral ester, 4-nitrophenyl acetate, was not accelerated by *Iic*.

Polymers of the imidazole type have been intensively investigated during the last 20 years and were found to possess activity resembling that of esterolytic enzymes¹⁻³. The activity of the enzymes is closely related to the presence of imidazole groups covalently bound on the polymer chains and to their interactions with esters⁴⁻⁶. These interactions may be of two types⁷. In one of them, the electrostatic potential of ionic groups becomes operative. If two ionic compounds carrying a charge of the same sign take part in the reaction and the polymer has an opposite sign, the ions are attracted to the polymer, and the latter behaves as a catalyst. If one or both ionic compounds are repelled from the main chain, the polymer behaves as an inhibitor. In the latter case the ester is directly attacked by the hydrolytically active groups. At a sufficient ester concentration near such groups the rate of hydrolysis may reach high values⁸⁻¹⁰.

Polymeric and model imidazolium salts have permanent electrostatic binding sites, but do not contain any hydrolytically active groups. Such compounds could be catalytically active for esters which carry groups of an opposite sign. This study is concerned with the preparation of polymeric and model imidazolium salts and with their catalytic effect in the hydrolysis of 4-acetoxy-3-nitrobenzoic acid as a function of pH, composition of the solvent, concentration and molecular mass of the catalysts. The compounds prepared were 1,3-dimethyylimidazolium bromide (*Ia*),

1-methyl-3-propylimidazolium bromide (*Ib*), 1-methyl-3-hexylimidazolium bromide (*Ic*), poly(1-methyl-3-allylimidazolium bromide) (*IIa*), poly[1-methyl-3-(2-propinyl)-imidazolium chloride] (*IIb*), and poly[1-methyl-3-(2-methacryloyloxyethyl)imidazolium bromide] (*IIc*).



EXPERIMENTAL

Low-Molecular Weight Salts (*I*)

1-Methyl-3-alkylimidazolium bromides *Ia* and *Ic* were prepared by reacting the corresponding 1-alkylimidazoles with methyl bromide. *Ib* was obtained by a reaction between 1-methylimidazole and propyl bromide. The reactions were carried out in anhydrous ether at the boiling point of the solvent for one hour. The reaction mixture was left to stand overnight at room temperature, and the product was isolated. *Ia* (m.p. 384–386 K) crystallized as a white compound. *Ib* and *Ic* were light brown viscous liquids. The results of the reactions and of elemental analysis have been described elsewhere¹¹.

Polymeric Imidazolium Halides (*II*) Poly(1-methyl-3-allylimidazolium) Bromide (*IIa*)

Allyl bromide (11.7 g, 0.098 mol), was dissolved in 18 ml of anhydrous benzene and 7.7 g (0.094 mol) of 1-methylimidazole in 18 ml of anhydrous benzene was added. The reaction mixture was left to stand at room temperature for 24 h. The solvent was evaporated *in vacuo*, and 1-methyl-3-allylimidazolium bromide was obtained as yellowish oil in a yield of 17.5 g. Oil (10.7 g) and 0.5 g of diisopropyl percarbonate were dissolved in 60 ml of 50% aqueous ethanol, oxygen was removed by bubbling with nitrogen (40 min), and polymerized in an ampoule at 323 K for 48 h. The solvent was eventually evaporated *in vacuo*, the residue was stirred with a mixture of ethanol and benzene, and the mixture was evaporated. Polymer *IIa* was isolated as brown viscous oil. The relative molar mass was 2 600. For C₇H₁₁N₂Br (203.1), calculated: 41.39% C, 5.46% H, 39.35% Br, 13.79% N; found: 40.03% C, 5.79% H, 39.23% Br, 13.56% N.

Poly[1-methyl-3-(2-propinyl)imidazolium Chloride] (*Ib*)

1-Methylimidazole (1.64 g, 0.02 mol) and 1.6 g (0.021 mol) of 2-propinyl chloride were dissolved in 12 ml of anhydrous benzene and heated under reflux for 5 h. On cooling, a light-yellow crystalline precipitate of 1-methyl-3-(2-propinyl)-imidazolium chloride was formed in the solution; m.p. 331–338 K. For $C_7H_9N_2Cl$ (156.6), calculated: 53.68% C, 5.79% H, 17.88% N; found: 53.29% C, 5.85% H, 18.03% N.

The monomer prepared as described above (6 g) and 0.2 g of 2,2'-azobis(isobutyronitrile) were dissolved in 35 ml of methanol, and the solution was polymerized in an ampoule at 323 K for 48 h in the usual way. The solvent was eventually evaporated *in vacuo*, the residue was dissolved in ethanol and refiltered with carboraffin. The filtrate was concentrated, and the polymer was isolated by precipitation into benzene. Ether was used as precipitant in the second operation. The raw product was dissolved in the ethanol-benzene mixture several times, evaporated *in vacuo* and dried *in vacuo* over P_2O_5 . Polymer *Ib* was brown powder. The relative molar mass was 160 000. For $C_7H_9N_2Cl$ (156.6), calculated: 53.68% C, 5.78% H, 17.88% N; found: 53.74% C, 6.41% H, 16.76% N.

Poly[1-methyl-3-(2-methacryloxyethyl)imidazolium Bromide] (*Ic*)

1-Methyl-3-(2-hydroxyethyl)imidazolium bromide was prepared by a reaction between 5.75 g (0.07 mol) of 1-methylimidazole and 10 g (0.08 mol) of 2-bromoethanol in 20 ml of benzene which were heated in an autoclave to 353–373 K for 4 h. Ethanol was added to the reaction mixture consisting of two layers. The crystals that precipitated were recrystallized from ethanol, white needle-like crystals. m.p. 370–371 K. For $C_6H_{11}N_2OBr$, calculated (207.12): 34.80% C; 5.35% H, 38.59% Br, 13.53% N; found: 34.87% C, 5.41% H, 37.87% Br, 13.58% N.

To a solution of 2.07 g (0.01 mol) of 1-methyl-3-(2-hydroxyethyl)imidazolium bromide in 20 ml of DMF, a solution of 1.05 g (0.01 mol) of methacryloyl chloride in 20 ml of DGF was added. After the addition of 1 g triethyl amine, the mixture was kept at 263–273 K for five hours and then left to stand overnight at room temperature. The salt that precipitated was removed by filtration, and the remaining oil was shaken with ether several times. The residue was dissolved in methanol, 0.1 g of 2,2'-azobis(isobutyronitrile) was added, nitrogen was bubbled through the mixture and the mixture was polymerized in an ampoule at 333 K for 48 h. Methanol was cooled, evaporated *in vacuo*, the residue was dissolved in distilled water and filtered with carboraffin. The filtrate was treated by ultrafiltration, and eventually lyophilized. Polymer *Ic* was obtained in a yield of 0.6 g as colourless powder. For $C_{10}H_{15}N_2O_2Br$ (275.16), calculated: 43.65% C, 5.49% H, 10.18% N; found: 43.78% C, 5.97% H, 9.69% N.

Substrates and Other Materials

p-Nitrophenyl acetate (E_a) was prepared as reported¹⁰, by reacting *p*-nitrophenol and acethanhydride in benzene. 4-Acetoxy-3-nitrobenzoic acid (E_n) was obtained¹⁰ by a reaction between 4-hydroxy-3-nitrobenzoic acid and acethanhydride in an alkaline solution. Potassium chloride, commercial (Lachema, Brno), was dried before use. Distilled water was redistilled in a quartz apparatus in the presence of $KMnO_4$ and NaOH, boiled and bubbled with nitrogen. Buffer, KH_2PO_4 and $Na_2B_4O_7 \cdot 10 H_2O$, was a commercial product and was used without further purification.

Kinetic Measurements

In all cases, $c. 5 \cdot 10^{-4} M$ stock solutions of catalysts *I* and *II* in 28.5% (vol.) aqueous ethanol

were prepared, and their pH in the range 6–10 was adjusted by using the buffer KH_2PO_4 and $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10 \text{H}_2\text{O}$. The ionic strength of the solutions was adjusted to 0.02 by adding a calculated amount of KCl. Acetates were dissolved in spectrally pure ethanol, and their concentration was adjusted to $c. 10^{-3} \text{M}$.

The rate of hydrolysis of the esters was measured with a UV spectrophotometer Cary 14 (USA) in a 1 cm quartz cell on mixing 2.8 ml of the stock solution of catalyst with 0.2 ml of the ester solution; absorption, A_t , was recorded as a function of time (for E_a at 400 nm, for E_n at 415 nm). Within a time about ten times that needed for reaching a 50% conversion of hydrolysis, absorption A_t was read off, which represents a 100% course of hydrolysis. The rate of esterolysis of the substrate caused only by the buffer solution (blank test) was recorded in the same way.

The recorded data were evaluated using a first-order equation (with respect to the catalyst), and the rate constant was calculated as the slope from the relation $\log A_\infty / (A_\infty - A_t)$ vs t , where A_∞ is absorbance at 100% conversion, and A_t is absorbance of the mixture at a time t . The dependences were represented by straight lines up to 80% conversion and more. The slope was the rate constant of hydrolysis, $K_{\text{measd}} \cdot K_{\text{obsd}}$ is calculated from the equation $K_{\text{obsd}} = K_{\text{measd}} - K_{\text{blank}}$. Constant K_{blank} is the rate constant of noncatalyzed hydrolysis. $K_{\text{cat}} = K_{\text{obsd}} / [\text{catalyst}]$.

RESULTS AND DISCUSSION

Synthesis

Low-molecular weight imidazolium salts *I* and the corresponding monomers were prepared by reacting 1-methylimidazolium with alkyl halides in anhydrous ether of benzene at elevated temperature (in the case of *Ia* and *Ic*, 1-alkylimidazole was reacted with methyl bromide). Compounds *I* and the monomers were viscous brownish liquids with the exception of *Ia* and 1-methyl-3-(2-propinyl)imidazolium chloride which was crystalline. During the isolation of oily products, the respective solvent was always evaporated *in vacuo*; the temperature of the heating bath was maintained below 323 K in order to prevent decomposition of the quaternary salt. Polymer *Iia* was obtained by the radical polymerization of 1-methyl-3-allylimidazolium bromide in aqueous ethanol with diisopropyl percarbonate as initiator. *Iib* and *Iic* were prepared in methanol from the respective monomers with 2,2'-azobis(isobutyronitrile) as initiator, and their relative molar mass was above 100 000. 1-Methyl-3-allylimidazolium bromide was very reluctant to polymerize even within a comparatively long reaction time, the yield of the polymer was low, and the relative molar mass was small (2 600). Imidazolium salts *I* and *II* are strongly hygroscopic compounds, and had to be stored in a dry place.

Hydrolysis of 4-Acetoxy-3-nitrobenzoic Acid

The rate constants of hydrolysis of the ester in a 28.5% aqueous ethanol catalyzed with imidazolium salts *I* and *II* at various pH are summarized in Table I. The de-

pendence of the rate constant K_{cat} on pH (Fig. 1a) shows that polymers *Ib* and *Ic* are relatively effective hydrolytic catalysts at pH higher than 9. At lower pH values their efficiency is small. *Ila* and low-molecular weight models *I* (Fig. 1b) are only little active within the whole range of pH used. The curves representing the rate of hydrolysis catalyzed with *I* and *Ila* have the same character, with a maximum at pH *c.* 7.67. With increasing volume of the alkyl group of compounds *I* their catalytic activity increases. The behaviour of the hexyl derivative *Ic* is somewhat

TABLE I

Rate constants K_{obsd} ($\text{min}^{-1} \cdot 10^{-4}$) and K_{cat} ($\text{M}^{-1} \text{min}^{-1}$) of esterolysis of 4-acetoxy-3-nitrobenzoic acid ($6.66 \cdot 10^{-5} \text{M}$) catalyzed with low-molecular weight and polymeric imidazolium salts *I* and *II* (in M; $297 \pm 1 \text{K}$, $\eta 0.02$, 28.5% vol. of ethanol in water)

Catalyst (C)		pH 6.70		pH 7.67		pH 8.95		pH 9.68	
C	[C] · 10 ⁴	K_{obsd}	K_{cat}	K_{obsd}	K_{cat}	K_{obsd}	K_{cat}	K_{obsd}	K_{cat}
<i>Ia</i>	4.518	0	0	0.33	0.07	0	0	0	0
<i>Ib</i>	4.514	0.007	0.0015	2.10	0.47	0	0	0	0
<i>Ic</i>	4.514	4.51	1.00	14.20	3.15	14.20	3.17	19.30	4.28
<i>Ila</i>	4.707	0.29	0.15	4.91	1.04	0	0	0	0
<i>Ilb</i>	4.823	—	—	7.69	1.59	10.24	2.12	86.10	17.85
<i>Ilc</i>	4.724	0	0	1.54	0.33	17.19	3.79	178.0	37.68

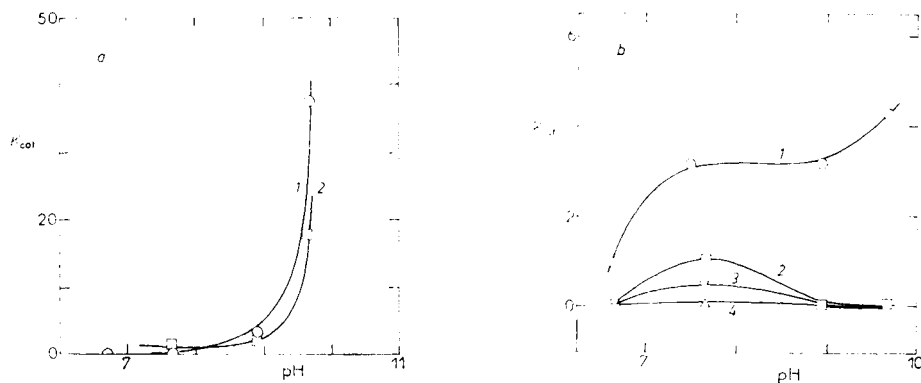


FIG. 1

Rate constant K_{cat} ($\text{M}^{-1} \text{min}^{-1}$) of hydrolysis of 4-acetoxy-3-nitrobenzoic acid ($6.66 \cdot 10^{-5} \text{M}$; 28.5% vol. ethanol in water, $\eta 0.02$, $297 \pm 1 \text{K}$) as a function of pH. Catalysts: (a) \square *Ib*; \circ *Ic*; (b) \triangle *Ia*, ∇ *Ib*, \circ *Ic*, \square *Ila*

different. On reaching a certain plateau at pH 7.67–8.75 the rate of esterolysis slightly increases once again. *Ia* is virtually ineffective within the whole range of pH used, and oligomeric *Ila* at a pH below 6.70 behaves as an inhibitor of hydrolysis ($K_{\text{cat}} = -0.15\text{M}^{-1}\text{min}^{-1}$).

Hydrolysis of the ionogenic ester at pH 6–10 may proceed *via* two mechanisms. At pH 6–8, the decisive step is a direct attack of water on the ester. At a higher pH, the main role is played by the hydroxyl ion OH^- which is present as a basic part of the buffer used. The results of the measurements indicate that low-molecular weight halides *I* and oligomer *Ila* prefer the attack of water on the ester, while polymers *Iib*, *Iic* prefer the hydroxyl ions. In the case of the hexyl derivative *Id* both mechanisms seem to take part in the hydrolysis. The hydrolytic efficiency of polymers *Iib*, *Iic* at a higher pH may be explained on the basis of their polyionic structure. Due to electrostatic forces, positively charged imidazolium groups attract oppositely charged ions of the hydroxyl group and substrate to their vicinity, thus raising the probability of their interaction and at the same time the reaction rate.

Morawetz and coworkers^{12,13} investigated the hydrolysis of E_n catalyzed with poly-(1-methyl-3-vinylimidazolium iodide) under comparable conditions and obtained results that were somewhat different. The esterolytic activity of the polymeric catalyst appeared mainly at a lower pH and was highest at pH 6. Compared with our results, this difference may be explained through the validity of other factors, such as electronegativity of the halide anion, distance between the imidazolium ring and the main chain, and the like.

The lower efficiency of model compounds *I* compared with polymeric salts *Iib* and *Iic* is directly related to their molecular mass¹². It has been shown, for instance, that formation of a single binding site on the polymer¹⁴ requires at least 10 ± 3 monomer units with the respective groups. During the hydrolysis of sodium 4-acetoxy-3-nitrobenzenesulfonate catalyzed with oligomeric imidazoles, the reaction rate increased with the increase of their molar mass¹⁵.

Fig. 2 shows the dependence of the rate constant of hydrolysis of ester, K_{obsd} , on the concentration of catalyst *Iic* at pH 9.68. The rate of hydrolysis is directly proportional to the catalyst concentration within the whole range. The dependence shows that the hydrolysis is not accompanied by saturation effects, such as those occurring in enzymatic reactions. Hence, the hydrolysis does not obey the Michaelis-Menten mechanism¹⁶, passing through formation of an activated complex between the substrate and catalyst, but proceeds by the first-order mechanism with respect to the catalyst^{10,17}.

The effect of composition of the solvent on the rate of hydrolysis of esters was also investigated. Table II gives results of the hydrolysis of ester catalyzed with polymer *Iic* at pH 8.95 at various ethanol contents in water. The reaction rate of hydrolysis, K_{cat} , depends on the composition of the solvent and reaches its maximum at c. 28% vol. of ethanol in water (Fig. 3). At both a lower and higher content of ethanol

the rate of hydrolysis decreases. Quite obviously, in a mixture of solvents, where the rate of hydrolysis is highest, the steric order of the polymer is optimal for an electrostatic attraction of the ester to the polymer surface. This fact may be closely

TABLE II

Rate constants of esterolysis of 4-acetoxy-3-nitrobenzoic acid ($6.66 \cdot 10^{-5} \text{ M}$) catalyzed with *Ic* ($4.724 \cdot 10^{-4} \text{ M}$) at various compositions of the solvents (pH 8.95, η 0.02, $297 \pm 1 \text{ K}$)

Solvent, % vol.		$K_{\text{obsd}} \cdot 10^4$ min^{-1}	K_{cat} $\text{M}^{-1} \text{min}^{-1}$	$K_{\text{meas.}} \cdot 10^3$ min^{-1}
water	ethanol			
100	0	5.63	1.19	4.09
90	10	6.14	1.30	4.86
80	20	8.19	1.73	6.04
75	25	10.20	2.16	5.83
71.5	28.5	17.90	3.79	6.39
70	30	12.30	2.60	6.24
65	35	6.14	1.30	5.94
60	40	3.84	0.81	6.24
50	50	2.56	0.54	6.65

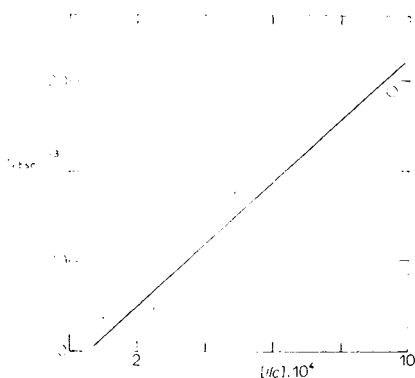


FIG. 2

Rate constant K_{obsd} (min^{-1}) of hydrolysis of 4-acetoxy-3-nitrobenzoic acid ($6.66 \cdot 10^{-5} \text{ M}$) as a function of the molar concentration of catalyst *Ic* (28.5% vol. ethanol in water, pH 9.68, η 0.02, $297 \pm 1 \text{ K}$)

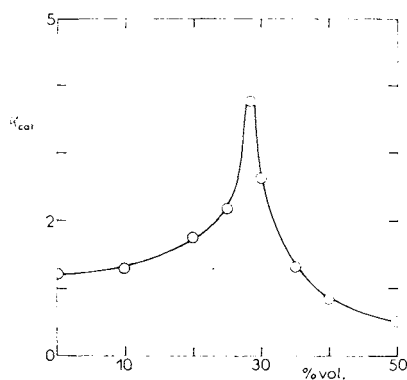


FIG. 3

Rate constant K_{cat} ($\text{M}^{-1} \text{min}^{-1}$) of hydrolysis of 4-acetoxy-3-nitrobenzoic acid ($6.66 \cdot 10^{-5} \text{ M}$) as a function of the composition of solvent (% vol. ethanol in water); pH 8.95, η 0.02, $297 \pm 1 \text{ K}$, catalyst *Ic* ($4.724 \cdot 10^{-4} \text{ mol l}^{-1}$)

related to the internal order of the mixture of solvents. As has been reported¹⁸, an addition of ethanol to water affects its internal structure which attains its maximum at c. 27 vol.%. Further addition of ethanol reduces the order of water; at 54% and 297 K the mixture of solvents becomes a binary system.

To verify if apolar forces participate in the interaction of polymers *II* with the substrate, we examined the course of hydrolysis of the nonionogenic ester, 4-nitrophenyl acetate (E_a), catalyzed with *IIC*. The hydrolysis took place at pH 7.2 and 9.2 in 28.5% aqueous ethanol at 297 ± 1 K and at the ionic force 0.02. At no pH value given above did polymer *IIC* cause any increase in the rate of hydrolysis of the neutral ester ($K_{measd} = K_{blank} = 5.18 \cdot 10^{-4} \text{ min}^{-1}$ for pH 7.2 and $6.1 \cdot 10^{-3} \text{ min}^{-1}$ for pH 9.2). The experiment shows that apolar forces are not operative or that they are too weak to be able to concentrate this ester to the polymer surface in an amount which would affect the course of the hydrolysis. A similar conclusion has been reached by Overberger and coworkers¹² in the hydrolysis of 4-nitrophenyl acetate catalyzed with other polymeric imidazolium salts.

The polymeric imidazolium salts of type *II* having a high molecular mass prepared in this study are effective catalysts in the hydrolysis of 4-acetoxy-3-nitrobenzoic acid at pH above 9. The reaction obeys the pseudo first-order mechanism and proceeds *via* an attack of the hydroxyl anion on the ester; predominant interactions between the polymer and ester consist in electrostatic attractive forces of oppositely charged ionic groups. The low-molecular weight models are less active, with the highest effectiveness at pH 7.67. The internal structure of the mixture of solvents (ethanol-water) has some influence on the reaction rate of esterolysis.

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