

# Copolymers of 1-vinylimidazole and (meth)acrylic acid: Synthesis and polyelectrolyte properties

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## Abstract

New hydrophilic polyampholytes have been synthesized by copolymerization of 1-vinylimidazole with sodium salts of acrylic and methacrylic acids. Copolymerization reactivity ratios of the monomers are equal to:  $0.54 \pm 0.06$  and  $1.3 \pm 0.3$  for 1-vinylimidazole–sodium acrylate,  $0.23 \pm 0.01$  and  $2.6 \pm 0.2$  for 1-vinylimidazole–sodium methacrylate systems, correspondingly. Isoelectric point of the copolymers changes continuously from 2.8 to 6.7 with increasing the 1-vinylimidazole content in contrast to polyampholytes with amino instead of imidazole side groups, whose isoelectric point changes discontinuously with changing composition. Static and dynamic light scattering data point to tendency of polyampholyte macromolecules to aggregation, even at pH values far from isoelectric point.

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## 1. Introduction

Combination of acidic and basic units in a polymer chain imparts the macromolecules highly interesting acid–base and complexing properties [1]. The behavior of such macromolecules is much more pH-dependent than that of the conventional polyelectrolytes, so polyampholytes can be employed in the design of the “intelligent” polymeric systems [2,3]. The use of imidazole moieties in new polyampholytes is very promising because imidazole rings occur in nature, in particular as a part of such important aminoacid as histidine. The basicity of polymeric imidazoles ( $pK_{BH^+} = 5–6$ ) lies be-

tween that of stronger bases such as amines and that of very weakly basic amides and ethers [4]. Unlike amines, imidazole units are not completely protonated at low pH, being very active in hydrogen and donor–acceptor binding [5–7]. Thus, imidazole-containing polyampholytes may exhibit specific properties in the physiological pH range, which is important for the design of biologically active compounds and methods for bioseparation. Esterolytic activity of imidazole-containing copolymers has been found by Overberger et al. [8–10]. Unfortunately, there is little information about copolymers of 1-vinylimidazole (VI) with unsaturated acids, and moreover, the copolymerization of acrylic acid (AA) with vinylimidazoles was reported to be complicated by side reactions [11].

The objective of this study was to synthesize new polyampholytes starting from 1-vinylimidazole (VI), acrylic (AA) and methacrylic (MAA) acids, and to investigate their polyelectrolyte properties.

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## 2. Experimental

### 2.1. Synthesis of copolymers

VI, AA and MAA were purified by vacuum distillation. Sodium salts of AA and MAA (Na-AA and Na-MAA, correspondingly) were obtained by mixing 10% ethanol solutions of the acids with an equimolar amount of NaOH. Precipitates of sodium salts were filtered off, washed with ethanol and dried under vacuum. Copolymers were synthesized by radical copolymerization of VI and Na-AA (Na-MAA) in 10% aqueous solution initiated by 2,2-azobis(isobutyronitrile) (1 wt.% relative to monomers) in sealed ampoules under argon at 60 °C (Table 1) and purified by dialysis through cellophane membrane against water and dried by the freeze-drying procedure. Hydrolysis of Na-AA (Na-MAA) units during the dialysis resulted in formation of AA (MAA) units in the copolymers, so their composition (Table 1) was calculated combining elemental analysis (nitrogen) and potentiometric titration.  $^1\text{H}$  NMR data ( $\delta$ , 0.3–1.0— $\text{CH}_3$ ; 1.0–2.5— $\text{CH}_2$ ; 6.5–8.3—imidazole, 3H) confirmed the proportions of acrylic and azole units.

### 2.2. Potentiometry and viscometry

Potentiometric measurements were performed on a “Multitest” ion meter using a combined pH-electrode in a temperature-controlled cell at  $20 \pm 0.02$  °C under argon with addition of 0.1 mol/l NaCl. 0.1 M NaOH was used for adjusting pH of the solutions up to 11.5, and 0.1 M HCl was employed as a titrant. Concentration of the copolymers was 0.012 M calculating on ionizable units.

Viscosities of the polymer solutions were measured with an Ubbelohde viscometer at  $20 \pm 0.02$  °C. Intrinsic

viscosity (Table 1) was determined in 0.1 M NaOH with addition of 1 mol/l KBr.

### 2.3. Light scattering experiments

Aqueous solutions were prepared from dry polymer samples in de-ionized bi-distilled water. Dry polymers studied were first dissolved in pure water. After complete dissolution of the polymers, respective amounts of 0.2 M NaCl were added dropwise to reach the ionic strength of 0.1 M. The solutions were kept at room temperature for 24 h to reach the equilibrium state. After that, pH of the solutions was adjusted to the desired value by titration with 0.1 M NaOH or 0.1 M HCl solutions, and the final concentration of the polymer was recalculated. Solutions of various polymer concentrations were made by dilution of the stock solutions.

Static (SLS) and dynamic (DLS) light scattering experiments were performed using a Brookhaven Instrument BIC-200 SM goniometer and a BIC-9000 AT digital correlator. An argon laser (LEXEL 85, 1 W) operating at 30 mW power with  $\lambda = 514.5$  nm wavelength was the light source. In SLS experiments, scattered light was collected between 30° and 150° scattering angles. The solutions were investigated in the range of polymer concentration from 0.11 to 1.00 mg/ml. Calibration for SLS measurements was done according to the standard procedure using toluene as a calibration standard. Intensities of scattered light were analyzed using Zimm’s double extrapolation method. A WYATT/OPTILAB 903 interferometer was employed to measure the  $\text{dn}/\text{dc}$  at 514.5 nm wavelength. In DLS experiments, correlation functions were collected with the shortest sample time of 0.4  $\mu\text{s}$  and the last delay was 10 ms. Correlation functions were analyzed with an inverse Laplace transform program CONTIN. 3–4 correlation

Table 1  
Copolymerization of VI with AA and MAA

Run	VI in initial mixture, mol%	Time, h	Yield, %	Copolymer composition, mol%			[η], dl/g	IEP, 0.1 M NaCl	Turbidity interval, pH
				VI	Na–(M)AA	(M)AA			
VI–AA									
1	80.8	15	47	77.3	11.0	11.7	0.52	6.7	–
2	71.0	15	45	53.5	37.7	8.8	1.30	5.0	5.1–5.9
3	51.7	8	24	41.6	45.3	13.1	2.28	4.8	3.4–5.5
4	31.5	8	16	20.1	65.0	14.9	3.40	3.2	1.9–4.8
5	21.9	8	6.4	17.5	66.1	16.4	6.16	3.0	1.9–4.11
VI–MAA									
6	89.4	3	29	66.6	33.4	20.3	0.55	5.8	–
7	73.1	3	26	54.9	34.0	11.1	0.98	5.7	4.1–6.5
8	61.0	3	14	38.4	30.1	31.5	1.21	4.4	3.1–6.4
9	51.1	3	11	30.4	36.7	32.9	1.19	3.8	2.3–5.8
10	40.9	3	12	17.1	70.4	12.5	1.45	3.1	2.1–4.7
11	10.5	3	6.2	4.0	94.9	1.1	1.67	2.8	–

curves were collected for each sample to check the reliability of the mathematical solution by the CONTIN program. DLS measurements at pH 10.5 were done at concentrations of 0.95 mg/ml for copolymers no. 1, 3, 6, 9 and 10 and at 0.33 mg/ml for no. 5 (Tables 1 and 3). At pH < 2.0, solutions with polymer concentration of 1.6 mg/ml (for copolymer no. 1) and 2.1 mg/ml (for no. 10) were used. All polymer solutions were purified from dust using filter units with 0.45  $\mu\text{m}$  pore size (Millex, HV). The experiments were performed at  $20 \pm 0.1$  °C.

### 3. Results and discussion

Copolymerization of AA with VI was described previously [12], but we have found that this reaction results in AA–VI copolymers contaminated with monomeric VI (Fig. 1). Apparently, this is associated with acid–base interactions between carboxylic groups in the polymeric chain and imidazole cycle in VI. The-

oretically, the copolymerization is to be complicated by deviation from the classical mechanism because a part of monomer molecules is coordinated with polymeric chains, which reduce the effective concentration of the monomers and may stimulate competing reactions, for example, template polymerization [13]. Thus, taking into account these circumstances, we have obtained copolymers of VI with acrylic and methacrylic acids by copolymerization of VI with sodium salts of the corresponding acids. The resulting products contain no monomer admixtures and their  $^1\text{H}$  NMR spectra (Fig. 1) are in good accordance with their structure:

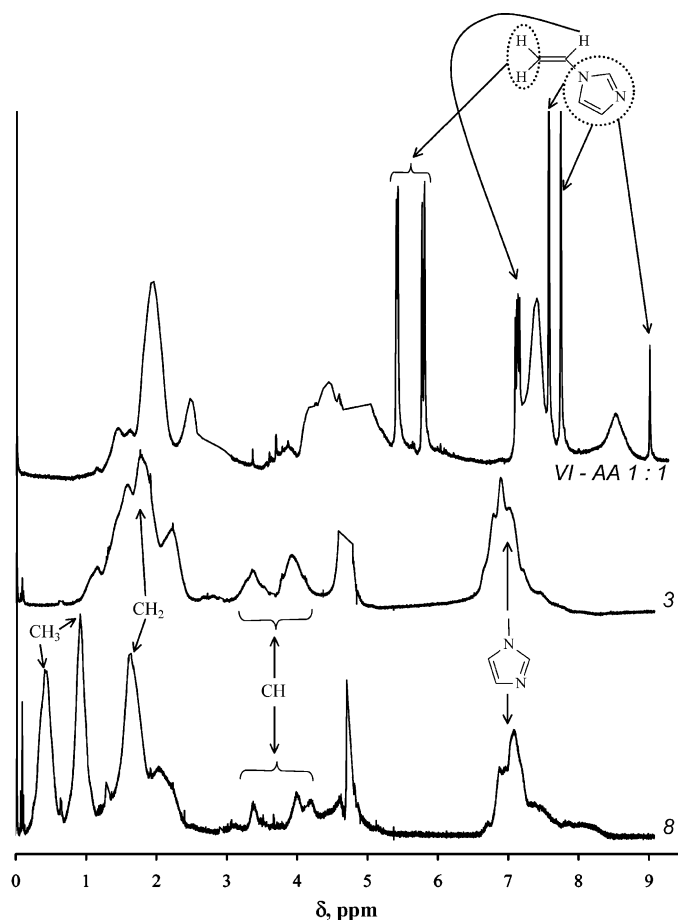
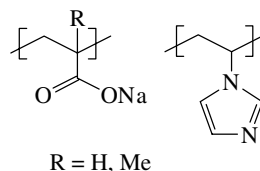


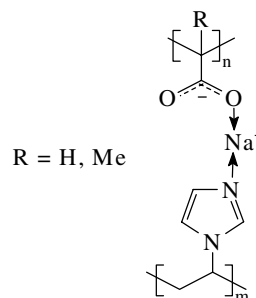
Fig. 1.  $^1\text{H}$  NMR spectra of 1:1 VI–AA mixture copolymerization product and copolymers of VI with Na–AA and Na–MAA (numbers correspond to Table 1).

FTIR spectra of the copolymers also confirm this structure: 1500, 1406, 1286, and 1228  $\text{cm}^{-1}$  (vibrations of imidazole cycles), 1110 and 1082  $\text{cm}^{-1}$  (bands of azole C–H), 917, 827 and 744  $\text{cm}^{-1}$  (deformational vibrations of the heterocycle), 1582  $\text{cm}^{-1}$  ( $\sim\text{COO}^-$ ). The bands of the vinyl group (1650, 1008, 961, 881  $\text{cm}^{-1}$ ) are absent in the spectra.

The copolymers obtained are poor in VI units in comparison with the monomer mixture (Table 1) and their yields decrease with increasing the content of acrylic monomer in the mixture. Copolymerization reactivity ratios of the monomers (Table 2) point to a higher activity of Na–MAA than Na–AA ( $1/r_1$  values), which might be associated with higher stability of the resulting Na–MAA radical due to conjugation with the methyl group.

Viscometry (Table 1) and light scattering data (Table 3) revealed decreasing molar mass of the copolymers studied upon increasing VI content in the initial monomer mixture. DLS studies showed rather broad distributions of hydrodynamic size for the copolymers studied. At pH 10.5, size distributions obtained for the samples nos. 2, 4 and 6 are obviously monomodal. The difference between mean (i.e. weight average) and peak values of  $R_h$  is due to asymmetry of the distributions (see Table 3). Distributions of hydrodynamic size of the samples nos. 1, 8 and 10 are bimodal at pH 10.5 owing to the presence of intermolecular aggregates. No significant effect of polymer concentration on the hydrodynamic size was observed: the differences lied within

the experimental error range. A possible mechanism of aggregation at pH 10.5 and 0.1 M NaCl may be the interaction of imidazole and carboxylate moieties via  $\text{Na}^+$  bridging similar to the interpolymer complex formation between poly(acrylic acid) and poly(1-vinylimidazole) [7]:



Copolymers nos. 1, 8 and 10 form aggregates also in solutions with  $\text{pH} < 2.0$ . Although aggregates of the samples nos. 1 and 10 decompose upon filtration, they form again within an hour thereafter. Fig. 2 represents an example of hydrodynamic size distributions obtained for the sample no. 1 before and after filtration. One may see that the relative contribution of the aggregates to the intensity distribution of hydrodynamic size is minor. No aggregates were observed at lower polymer concentrations. These results suggest that the molar masses for the samples nos. 1 and 10 are true masses because they are obtained by extrapolation to infinite dilution. Copolymer no. 8 forms stable aggregates which do not disintegrate on filtration and dilution.

Copolymers of VI and acrylic acids show polyampholyte properties; their titration curves have an inflection point at pH 4–6 (Fig. 3) which is accompanied by opalescence and turbidity of the solutions. IEP of the copolymers were determined from potentiometry data using the following assumptions:

Table 2

Copolymerization reactivity ratios of VI ( $M_1$ ) and sodium salts of AA and MAA

$M_2$	$r_1$	$r_2$	$1/r_1$
Na–AA	$0.54 \pm 0.06$	$1.3 \pm 0.3$	1.9
Na–MAA	$0.23 \pm 0.01$	$2.6 \pm 0.2$	4.3

Table 3

Light scattering data for VI-acrylic acid copolymers

Polymer no. (from Table 1)	VI, mol%		pH	SLS data		DLS data		
	In monomer mixture	In copolymer		$M_w$	$R_g$ , nm	Mean $R_h$ , nm	Peak I $R_h$ , nm	Peak II $R_h$ , nm
<i>VI–Na–AA copolymers</i>								
1	80.8	77.3	10.5	276,000	59.3	100	21	259
1	80.8	77.3	1.6	232,000	30.2	145	12	550
2	71.0	53.5	10.5	1,060,000	89.5	51	43	–
4	31.5	20.1	10.5	2,520,000	141.0	98	50	–
<i>VI–Na–MAA copolymers</i>								
6	89.4	66.6	10.5	102,000	21.3	18	11	–
8	61.0	38.4	10.5	425,000	56.9	90	33	204
10	40.9	17.1	10.5	890,000	88.5	153	26	247
10	40.9	17.1	1.7	298,000	32.6	115	14	416

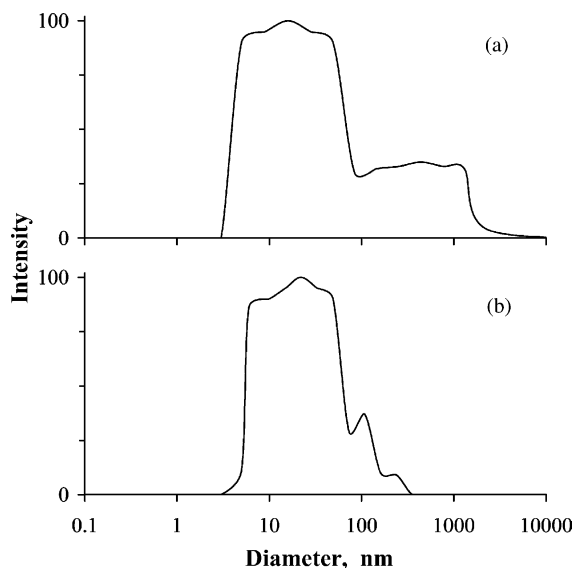


Fig. 2. Hydrodynamic size distributions obtained for the sample no. 1 before (a) and after (b) filtration in solution with pH of 1.6, 0.1 M NaCl and 1.6 mg/ml polymer concentration. Data obtained at 90° scattering angle.

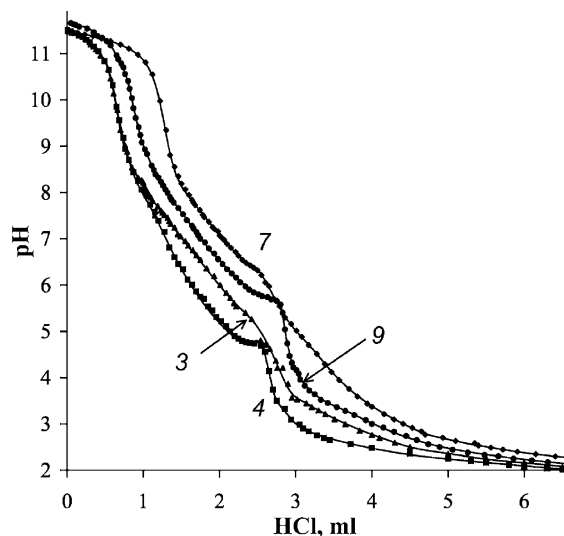


Fig. 3. Potentiometric titration curves for copolymers of VI with Na-AA and Na-MAA (numbers correspond to Table 1).

Polyampholyte was considered a polymeric acid bearing two types of acidic groups: HA—carboxylic and BH—protonated imidazole units. The titration was started from the alkaline region (pH=11.5), and the point corresponding to the full neutralization of the acid ( $V_1$ ) was found from the inflection point at the titration curve. Ionization degree of the copolymer ( $\alpha$ ) was calculated using the equation [14]:

$$\alpha = ([\text{NaOH}] + [\text{H}^+] - [\text{OH}^-]) / C_{\text{total}},$$

where  $[\text{NaOH}]$  is the concentration of the alkali added,  $C_{\text{total}}$  is the total concentration of acidic units. In the case of the reverse titration of polyampholytes this equation changes into:

$$\alpha = \{ (V_1 - V) \cdot C_{\text{HCl}} + ([\text{H}^+] - [\text{OH}^-]) \cdot (V_0 + V) \} / (C_0 \cdot V_0),$$

where  $V$  is the titrant volume (HCl),  $C_{\text{HCl}}$ —HCl concentration,  $V_0$ —initial volume of the solution,  $C_0$ —initial concentration of the ionizable groups calculated from mass and composition of the copolymer.

In the case of polyampholytes,  $\alpha$  values reflect total ionization degree of the acidic units and of conjugated acid of basic units. A more important value is the average charge of the polymeric unit ( $q$ , calculated for one ionizable unit). We can write:

$$q = hb - a$$

$$\alpha = b + a$$

where  $a$ ,  $hb$  and  $b$  are the molar fractions of acidic anions, protonated and unprotonated basic units, correspondingly. Combination of these equations gives the following:

$$\alpha + q = b + hb$$

From the other hand,  $b + hb$  is equal to molar fraction of basic units in the copolymer. So, we have:

$$q = (\text{molar fraction of VI}) - \alpha$$

Thus, from potentiometry data we can calculate  $q$  depending on pH and determine IEP values for  $q = 0$ . IEP of the imidazole-acrylic polyampholytes shifts to lower pH upon decreasing the VI content (Table 1). In the case of completely water-soluble samples, it was possible to find the IEP by viscometry (Fig. 4) and the values thus obtained correlate with potentiometry data.

It was found [15] that pH in IEP (pI) could be calculated from ionization constants of the acidic and basic groups:

$$\text{pI} = \text{pK}_b + \log \left\{ \frac{(1/2)[(1-R)/R + ((1-R)/R)^2 + (4/R)10^{\text{pK}_a - \text{pK}_b}]^{1/2}}{1} \right\}$$

where  $\text{pK}_a$  and  $\text{pK}_b$  correspond to ionization of acidic groups and that of conjugated acid of basic units,  $R$  is the basic/acidic unit ratio. Effective  $\text{pK}$  values have been calculated by nonlinear regression from the data of Table 1:  $\text{pK}_a = 3.9 \pm 0.3$  and  $\text{pK}_b = 6.2 \pm 0.3$ . These results are in good accordance with  $\text{pK}$  of poly(acrylic acid) and poly(1-vinylimidazole) [4,16]. Theoretical dependence between pI and composition of copolymer (Fig. 5, line IEP) is also in good agreement with experimental data.

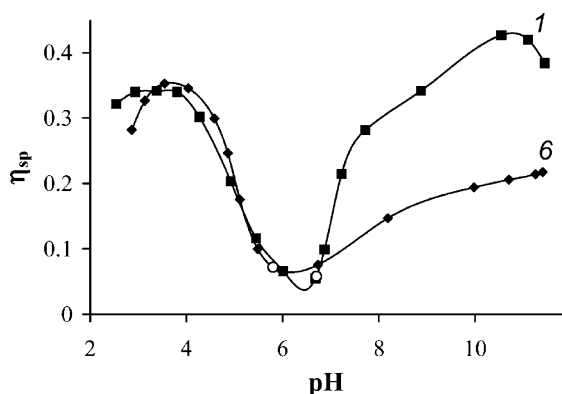


Fig. 4. Dependence of viscosity on pH for polyampholyte copolymers, numbers correspond to Table 1.

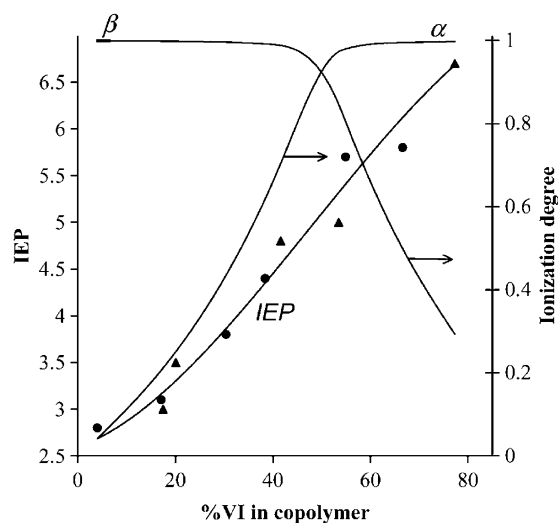


Fig. 5. Dependence of pI, acidic and basic group ionization degrees ( $\alpha$  and  $\beta$ , correspondingly) on the copolymer composition. Triangular and round points correspond to Na-AA and Na-MAA copolymers, respectively. Theoretical line,  $\alpha$  and  $\beta$  values were calculated using  $pK_a = 3.9$  and  $pK_b = 6.2$ .

Points for AA and MAA lie on the same curve, so hydrophobic interactions between methyl groups do not play any important role in the behavior of these copolymers near the IEP. This fact can be explained by high degree of ionization of acidic or basic units at the IEP (Fig. 5, lines  $\alpha$  and  $\beta$ ), which prevents the hydrophobic interactions. It should be mentioned that pI values change continuously from 2.8 to 6.7 with increasing the VI content in contrast to polyampholytes with amino moieties, whose pI changes drastically from 4.5 to 7.5 [11,17].

Thus, new polyampholytes have been obtained by copolymerization of 1-vinylimidazole with sodium salts of acrylic and methacrylic acids. The distinct property of imidazole-containing copolymers is the possibility of adjusting their IEP precisely near pH 7, which is highly important for design of new polymeric systems for biotechnology and medicine.

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