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Synthesis and aqueous solution characterization of novel diblock polyampholytes containing imidazole

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Abstract

A series of diblock copolymers of 2-(1-imidazolyl)ethyl methacrylate and tetrahydropyranyl methacrylate (THPMA) were synthesized by group transfer polymerization using propylene carbonate rather than tetrahydrofuran as the solvent to ensure homogeneous polymerizations. The resulting copolymers were characterized by gel permeation chromatography and proton nuclear magnetic resonance spectroscopy (^{1}H NMR) to determine their molecular weights and compositions, respectively. The THPMA units of the copolymers were subsequently converted to methacrylic acid units by acid hydrolysis. The resulting polyampholytes were characterized in terms of their composition and solubility characteristics using ^{1}H NMR and hydrogen ion titration. Moreover, dynamic light scattering in alkaline water (pH 9.3) indicated the presence of large non-micellar aggregates of the block polyampholytes. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Polyampholytes; 2-(1-imidazolyl)ethyl methacrylate; Methacrylic acid

1. Introduction

Synthetic polyampholytes are synthetic copolymers bearing groups which can acquire both positive and negative charge [1,2]. A common type of polyampholytes is based on weak bases and weak acids. Usually, monomer units based on amines contribute the positive charge, whereas the negative charge frequently comes from carboxylic acid groups. In such cases, the p*K* of the amine is higher than that of the acid. A less frequent, but interesting, case is when the p*K*s of the amine and the acid are equal or very close to each other. An example is vinyl pyridine and methacrylic acid (MAA) [3,4]. Both groups are titrated in the same pH region and the isoelectric points of the corresponding polyampholytes are weakly dependent on acid–base composition [3–5].

In this investigation, such polyampholytes with weak acid and weak base units with approximately the same p*K* values were prepared. The acid unit was MAA whereas the basic unit was 2-(1-imidazolyl)ethyl methacrylate (ImEMA) rather than vinyl pyridine. Imidazole is an interesting group with strong nucleophilic character (when not ionized) [6], encountered in nature as the side-group of amino acid histidine found in the catalytic site of many hydrolytic enzymes [7]. Another novel characteristic of the present polyampholytes is their structure. They are block copolymers of a narrow size distribution rather than statistical copolymers of a broad size distribution. To date, most of the studies on synthetic polyampholytes, even recent ones [8–17], involve statistical polyampholytes [3, 18–22], with only a limited number of recent studies investigating block polyampholytes [23–40].

The synthesis of the copolymers was accomplished by group transfer polymerization (GTP) [41–44], a ‘living’ polymerization technique compatible with methacrylate monomers, which is to secure the narrow size distribution of the polymers and their block structure. To avoid termination of GTP by the labile protons of MAA, the monomer tetrahydropyranyl methacrylate (THPMA) was used, whose repeat units were readily deprotected after the polymerization to yield MAA units. To ensure homogeneous GTP, propylene carbonate, a good solvent for the ImEMA homopolymer, was used as the polymerization solvent rather than the conventionally used tetrahydrofuran (THF), a precipitant of polyImEMA [45–47].

2. Results and discussion

Neither monomer is commercially available. Thus, both

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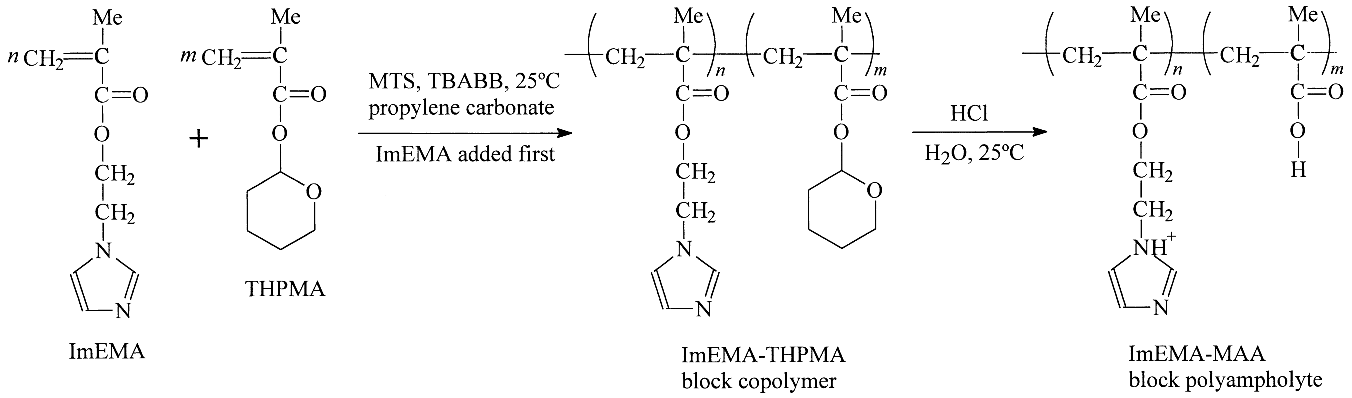

Scheme 1. GTP synthesis and hydrolysis of ImEMA–THPMA diblock copolymers.

THPMA and ImEMA were in house synthesized. For the preparation of THPMA, MAA was catalytically esterified with 100% excess 3,4-dihydro-2*H*-pyran (DHP) at 55 °C [48] using a modification of the procedure reported by Hertler [49]. Thus, sulfuric acid, rather than cross-linked poly(4-vinyl pyridine hydrochloride), was used as the acid catalyst. Excess DHP was removed by vacuum evaporation, and the product was recovered by distillation. A second distillation was performed after the addition of a free radical inhibitor, 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH), to the product. Subsequently, the product was passed twice through basic alumina columns to neutralize the unreacted MAA. Finally, the resulting THPMA was stirred over calcium hydride and DPPH, and it was distilled just before the polymerization. The overall recovery yield of THPMA was between 20 and 50%. For the synthesis of ImEMA, imidazole reacted with an excess of ethylene carbonate in the absence of solvent to give 2-(imidazolyl)ethanol at ca. 50% yield [45–47,50–52], which then reacted with an excess of methacryloyl chloride in chloroform in the presence of triethylamine at room temperature to give ImEMA in nearly quantitative yield (ca. 90%) [45–47]. ImEMA was purified by vacuum distillation over calcium hydride in the presence of DPPH.

A series of ImEMA–THPMA diblock copolymers and one equimolar statistical copolymer were prepared using GTP [41–44] at room temperature. 1-Methoxy-1-trimethylsiloxy-2-methyl prop-1-ene and tetrabutylammonium bibenzoate [41–44] were used as the polymerization initiator and catalyst, respectively. Due to the insolubility of the ImEMA homopolymer [45–47] in the most usual GTP solvent, THF, a more polar solvent, propylene carbonate, was used. Scheme 1 shows the sequential GTP of the two monomers, ImEMA and THPMA, and the deprotection reaction of the THPMA units.

Near-quantitative yields were obtained in all polymerizations. The completion of the polymerization of the first block was confirmed by ^{1}H NMR, which showed the absence of olefinic protons. The polymers were recovered from their polymerization solutions by precipitation, effected by the addition of *n*-hexane (a precipitant of most polymethacrylates), which produced a two-phase system with propylene carbonate, followed by acetone which compatibilized the system [45–47]. The polymers were dried in a vacuum oven at room temperature to avoid thermolysis of the THPMA units, which, in addition to the acid, leads to the formation of the water-insoluble anhydride [33–35]. The structures of the prepared copolymers appear in Table 1. This table also shows the molecular weights (MWs) and polydispersities of the copolymers determined by gel permeation chromatography (GPC) in THF (PMMA standards, RI detector, Polymer Laboratories PL Mixed 'E' column). The ImEMA-rich diblock, ImEMA$_{10}$-*b*-THPMA$_5$, and the statistical copolymer did not give any polymer chromatographic peaks, suggesting their retention within the column. The three eluting copolymers exhibited narrow molecular weight distributions (MW/M_n < 1.2) and their number average MWs, M_ns, increased in the same order as the theoretical ones. However, the values of the M_ns were higher than the theoretical MWs due to partial initiator deactivation.

Fig. 1 shows the ^{1}H NMR spectrum of one of the diblock copolymers, ImEMA$_{10}$-*b*-THPMA$_{20}$ (a), as well as the spectrum of its hydrolyzed form, ImEMA$_{10}$-*b*-MAA$_{20}$ (b), both in d$_6$-DMSO. The compositions of all protected copolymers were determined from the ratio of the areas of the characteristic peaks of ImEMA and THPMA, peaks e and h, respectively, and are also presented in Table 1. These compositions agree well with the theoretical compositions, calculated from the comonomer feeds.

Samples of the ImEMA–THPMA copolymers were hydrolyzed using HCl in water at pH 2 to give ImEMA–MAA polyampholytes. The resulting polyampholytes were recovered by adjusting the pH to the isoelectric region, around 5.5, which led to quantitative polymer precipitation. The polyampholytes were collected and vacuum dried at room temperature. Analysis by ^{1}H NMR in d$_6$-DMSO showed complete removal of the ester acetal proton h of THPMA (Fig. 1(b)) for all samples, suggesting quantitative hydrolysis to MAA.

1% (w/w) aqueous solutions of the polyampholytes were titrated in the pH range of 2–12, using a standard 0.5 M

Table 1
Molecular weights, polydispersities and compositions of the ImEMA–THPMA copolymers, and isoelectric points of the corresponding ImEMA–MAA polyampholytes

Polymer formula	Theor.MW[a]	GPC in THF[b]		mol% ImEMA		pH range of precip.	Isoelectric point		Hydrodynamic diameters[c] (nm)	Max diam of sph micelle[d] (nm)
		M_n	MW/M_n	Theor.	^{1}H NMR		Theor.[e]	Exper.[f]		
$(ImEMA)_5$-*b*-$(THPMA)_5$	1850	3170	1.06	50.0	52.0	–	5.2	–	4.9, 15.5	5.1
$(ImEMA)_{10}$-*b*-$(THPMA)_5$	2750	–	–	66.7	69.5	4.8–8.2	5.5	6.5	20.4, 78.3	7.6
$(ImEMA)_{10}$-*b*-$(THPMA)_{10}$	3600	9520	1.14	50.0	53.6	5.0–6.6	5.2	5.8	50.1	10.2
$(ImEMA)_{10}$-*b*-$(THPMA)_{20}$	5300	18,100	1.05	33.3	32.7	4.2–6.0	5.0	5.1	44.5	15.2
$(ImEMA)_{10}$-*co*-$(THPMA)_{10}$	3600	–	–	50.0	56.7	–	5.2	–	4.9, 10.7, 20.7	–

[a] Initiator fragment (100 g mol^{-1}) included.
[b] PMMA standards, PL mixed 'E' column, RI detector.
[c] Calculated from MSD analysis.
[d] Calculated by doubling the theoretical contour length, which is equal to the degree of polymerization times 0.254 nm, the contribution of one monomer repeat unit to the contour length.
[e] Assumed p*K* = 5.4 [53] and 5.0 [45–47] for MAA and ImEMA, respectively.
[f] Taken as the midpoint of the pH precipitation region.

NaOH solution. The hydrogen ion titration allowed the estimation of the effective p*K*s of the ImEMA and MAA units and of the isoelectric points of the polyampholytes. The ImEMA and MAA units were titrated in same pH range, presenting a common p*K* around 5.2, which is in agreement with those of the ImEMA and MAA homopolymers of 5.0 [45–47] and 5.4 [53], respectively.

During titration, the block copolymers were precipitated from solution, leading to milky dispersions (prevented from precipitation by stirring). The ranges of precipitation, shown in Table 1, moved to lower pH as the MAA content increased. Polyampholyte precipitation takes place around the isoelectric point (p*I*), the pH of zero net charge, and is driven by the interparticle attractive hydrophobic, Van der Waals and electrostatic forces [25–32,54,55]. The p*I*s were estimated as the midpoints of the precipitation ranges and are listed in Table 1, along with the theoretical p*I*s, calculated [5] from the polyampholyte composition and using the literature values of 5.0 [45–47] and 5.4 [53] for the p*K*s of ImEMA and MAA, respectively. The agreement between experimental and theoretical p*I*s is fair and acceptable provided the uncertainties in the values of the p*K*s used. Note that perfect agreement between the experimental and the theoretical p*I*s would have been obtained if values of 6.5 and 5.1 had been used for the p*K*s of ImEMA and MAA, respectively. The decrease in the p*I*s with the decrease in the ImEMA/MAA molar ratio is much smaller than that observed with more conventional polyampholyte systems in which the p*K* of the basic units is typically three pH units higher than that of the acidic [25–32,56]. It is noteworthy that, the statistical polyampholyte did not precipitate during titration, a result of the combination of the absence of strong interblock electrostatic attractive interactions, because of the random distribution of the positively and negatively charged units along the polymer chain, and of the relatively low MW [25–32].

In order to characterize the aggregation behavior of these materials, dynamic light scattering was performed on aqueous solutions of the polyampholytes at pH 9.3 using a Brookhaven 90Plus spectrometer (BI9000 correlator, 30 mW red diode laser operating at 673 nm, observation angle of 90 °, room temperature). The hydrodynamic diameters, calculated from multimodal size distribution (MSD) analysis based on non-negatively constrained least squares (NNLS), are presented in Table 1. In only two cases were the distributions unimodal, and in all cases the hydrodynamic sizes were rather large compared to the expected diameters of well-defined spherical micelles. The latter, also listed in Table 1, was estimated as twice the maximum chain length (contour length), which is equal to the degree of polymerization times 0.254 nm, the contribution of one monomer repeat unit to the contour length. This implies that these aggregates are not micellar, and do not have compact hydrophobic cores, probably due to the moderate hydrophobicity of ImEMA [45–47]. This has also been

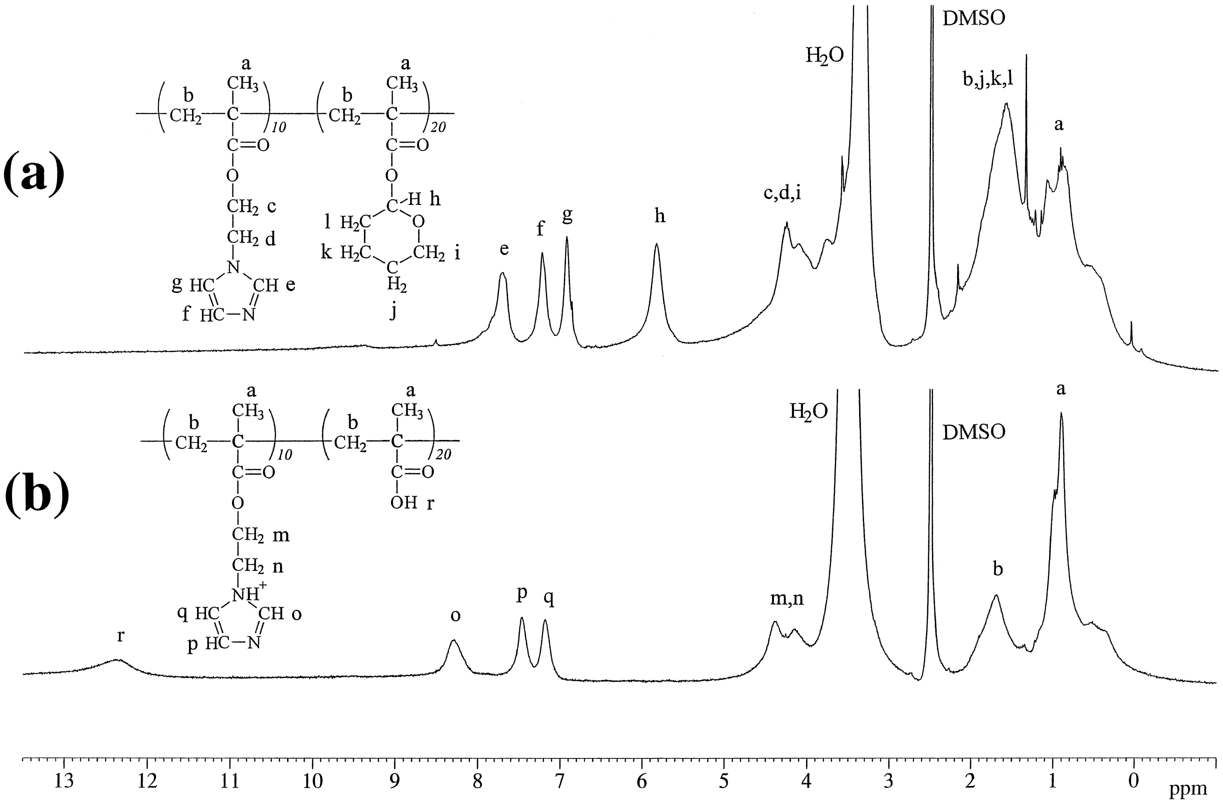

Fig. 1. Proton NMR spectra in d_6-DMSO of the protected and hydrolyzed forms of the copolymers. (a) $(ImEMA)_{10}$-*b*-$(THPMA)_{20}$; (b) $(ImEMA)_{10}$-*b*-$(MAA)_{20}$. Note the complete absence of h protons and the appearance of carboxylic acid protons r in (b). The shifts of the m, n, o, p and q protons in (b) relative to the c, d, e, f and g protons in (a) are due to the protonation of the imidazole ring in (b).

reported for polyampholytes based on MAA and 2-(dimethylamino)ethyl methacryate [33–38,57], for which, vesicular aggregates were observed by cryo-TEM [57]. Well-defined block polyampholyte micelles have been observed when a third, neutral, hydrophobic block was also present (ABC triblocks) [25–32], or when the acidic and basic monomer repeat units were of sufficient hydrophobicity (diblocks) [58].

3. Conclusions

Novel diblock polyampholytes, bearing imidazole and carboxylic acid groups, were prepared using GTP. Both monomers required preparation in the laboratory due to their commercial unavailability. The success in polymer synthesis was confirmed by GPC and proton nuclear magnetic resonance spectroscopy analyses. A unique feature of these polyampholytes is the proximity in the p*K* values of the basic and acidic units, which led to the weak dependence of the isoelectric point on copolymer composition. The moderate hydrophobicity of the imidazole-containing monomer repeat unit leads to the formation of block copolymer aggregates, which are large and non-micellar, most likely with diffuse cores.

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