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Model Random Polyampholytes from Nonpolar Methacrylic Esters

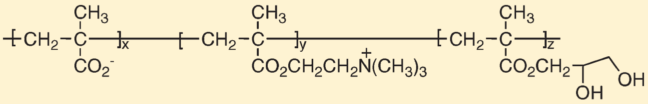
Baljinder Kaur,[†] Larissa D'Souza,[†] Lisa A. Slater,[‡] Thomas H. Mourey,[‡] Siwei Liang,[§] Ralph H. Colby,[§] and Warren T. Ford*[,†]

[†]Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078, United States

[‡]Eastman Kodak Company, Corporate Research and Engineering, 1999 Lake Avenue, Rochester, New York 14650-2136, United States

[§]Department of Materials Science and Engineering, Pennsylvania State University, University Park, Pennsylvania 16802, United States

S *Supporting Information*



ABSTRACT: Copolymerizations of nonpolar methacrylic esters followed by functional group conversions were employed to produce random polyampholytes. Random terpolymers of Solketal methacrylate (SMA):*tert*-butyl methacrylate (tBMA):*N,N*-dimethylaminoethyl methacrylate (DMAEMA) were prepared from 80:10:10 and 54:23:23 mol % mixtures of monomers by RAFT polymerization in 1,4-dioxane. The terpolymers were treated with iodomethane to convert the DMAEMA units to quaternary ammonium ions and then with concentrated aqueous HCl/1,4-dioxane to convert the SMA units to glyceryl methacrylate units and the tBMA units to methacrylic acid units. ^{1}H NMR analyses of the unreacted monomers in reaction mixtures after partial polymerization and compositions of the terpolymers calculated from reactivity ratios support random structures for the terpolymers. ^{1}H NMR analyses of the polymers support complete conversions of the nonpolar monomer units in the terpolymers to ionic and hydrophilic monomer units in the polyampholytes. SEC analyses gave $M_w/M_n = 1.3-1.4$ for terpolymers having $DP_n < 300$ and $M_w/M_n > 3$ for terpolymers having higher DP_n. SEC analyses of the derived polyampholytes gave $M_w/M_n = 2.2-3.2$ for all samples. Isoelectric points of polyampholytes were determined by potentiometric titrations and measurements of aqueous solution viscosity as a function of pH.

INTRODUCTION

Polyampholytes have both positively and negatively charged repeat units on one polymer chain, in contrast to the more common polyelectrolytes, which have charge of one sign.[1−5] Consequently, aqueous solutions of polyampholytes and polyelectrolytes behave much differently. Polyelectrolytes have expanded coil structures and high solution viscosities in pure water due to intramolecular electrostatic repulsions. Addition of an electrolyte such as NaCl to a polyelectrolyte solution screens the intramolecular repulsions, causing the coil to contract and the solution viscosity to decrease. On the other hand, a polyampholyte in pure water has a compact coil structure due to intramolecular electrostatic attractions.[1−7] Addition of NaCl expands the polyampholyte coil and increases the solution viscosity due to screening of charge attraction. Proteins are charge-balanced polyampholytes at the isoelectric point pI (pI = pH of zero net charge), polycations at pH < pI, and polyanions at pH > pI. Synthetic polyampholytes were reported first in the 1950s as analogues of proteins.[8−14]

Recent theory predicts the following behavior of random polyampholytes in aqueous solution as functions of fraction of charged repeat units, net charge, added salt, and chain length.[15] A charge-balanced polyampholyte in pure water collapses to a globule. As the fraction of charged monomers in the chain increases, the size of the globule decreases. As the degree of polymerization increases, the globule collapses. The transition is different for alternating and block polyampholytes. Net charge converts a polyampholyte to an elongated globule and at greater charge imbalance into a beaded chain. The goal of our research is to prepare well-characterized random polyampholytes in order to test the recent theory.

It is questionable as to whether any truly random synthetic polyampholyte suitable to test the theory has ever been synthesized. Polyampholytes synthesized from positively and negatively charged monomers tend to have alternating structures.[10,16−18] In principle, the electrostatic attractions causing the alternating structure can be screened by a high concentration of low molar mass electrolyte during solution polymerization,[19] but proof that any known synthetic polyampholyte has a completely random structure is lacking.

We used free radical polymerization and three important strategies to prepare random polyampholytes. The first strategy is to prepare terpolymers from uncharged monomers that copolymerize randomly without change in monomer composition and then convert the terpolymers to polyampholytes by postpolymerization reactions that create positively charged, negatively charged, and hydrophilic uncharged repeat units. The method is shown in Scheme 1. Previously, we made binary copolymers of the monomers *N,N*-dimethylaminoethyl methacrylate (DMAEMA), *tert*-butyl methacrylate (tBMA), and Solketal methacrylate (SMA) and measured all of the binary reactivity ratios to be in the range 0.77−1.40, which means there is no large deviation from random copolymers and little change in

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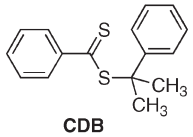
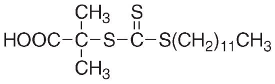
monomer composition during polymerization.[20] The second strategy is to prepare the terpolymers by controlled RAFT polymerization so that the solution properties of different polyampholytes are not affected by differences in molecular weight distributions. The third strategy is to carry the copolymerizations to <40% conversion to maintain nearly constant comonomer composition and to produce RAFT polymers having the narrowest possible molecular weight distributions.

■ RESULTS

Synthesis of Terpolymers. Terpolymers of SMA, tBMA, and DMAEMA were synthesized by the RAFT method using either cumyl dithiobenzoate (CDB) or 2-methyl-2-(dodecylsulfanylthiocarbonyl)sulfanylpropanoic acid[21] (MDSP) as a chain transfer agent (CTA) in 1,4-dioxane at 75 °C. The conditions are reported in Table 1. CDB is reported to decompose slowly during storage to dithiobenzoic acid, which reduces polymer molecular weights by hydrogen atom chain transfer in radical polymerization.[22] The CDB in this research was freshly purified by alumina chromatography. Because of the known difficulties with purity of CDB, we used the trithiocarbonate MDSP for the synthesis of high molecular weight terpolymer, even though MDSP is reported to give less control of molecular weight distribution than CDB in RAFT polymerization of methyl methacrylate.[23,24]



CDB

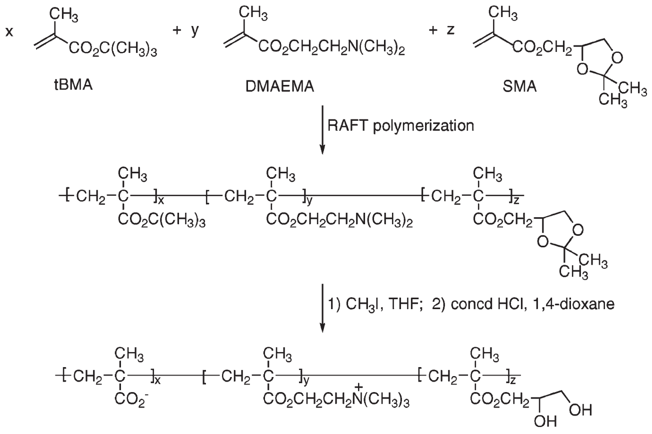


$HOOC{-}C(CH_3)_2{-}S{-}C({=}S){-}S(CH_2)_{11}CH_3$

MDSP

Initially, 80/10/10 (molar) mixtures were polymerized in NMR tubes in search of conditions for the larger scale polymerizations.

Scheme 1. Synthesis of Polyampholytes



Dioxane-d_8 was the best solvent found for analysis of the compositions of mixtures of monomers because the vinyl proton signals in NMR spectra of the three monomers were clearly resolved, as shown in Figure 1. The amounts of monomers in the mixture were measured relative to *p*-xylene as an internal standard before the start of polymerization and after partial conversion in order to calculate the composition of the terpolymer.

The terpolymers were isolated by precipitation in hexane. The ^1H NMR spectra of the terpolymers did not permit accurate analysis of polymer composition because of overlap of the *tert*-butyl signal of tBMA with the broad polymer backbone signals and because of partial overlap of the OCH_2 signals of the SMA and DMAEMA units (see Figure S1 in the Supporting Information.) The terpolymers were pink due to the dithiobenzoate or trithiocarbonate groups. Terpolymers B10 with 80:10:10 composition and B11 with 54:23:23 composition were synthesized using MDSP as the CTA. Attempts to reach higher DP_n by RAFT polymerization with MDSP in bulk rather than in 1,4-dioxane produced insoluble polymers.

In the absence of termination, DP_n by the RAFT method is equal to the molar ratio of monomers consumed (M) to chain transfer agent (CTA).[24,25] Aiming for 40% conversion of monomers to get DP_n of 300 and 1000, we started with $[M]_0/[CTA] = 750$ for samples B1−B4 and 2500 for samples B10−B11, where $[M]_0$ is the sum of the initial concentrations of the monomers. We are aware of only two previous attempts to synthesize such high molecular weight methacrylate polymers by the RAFT method.[23,26] The conversions of the three monomers were determined from proton NMR spectra of the reaction mixtures, and the degree of polymerization was calculated as $DP_n(\text{calcd}) = ([M]_0/[CTA])$(weighted average fractional conversion of the three monomers). The compositions of the initial monomer mixtures and of the terpolymers isolated after partial conversion are reported in Table 2.

Compositions from Binary Copolymer Reactivity Ratios. Reactivity ratios from conventional radical polymerizations were determined previously for the binary monomer mixtures of SMA,

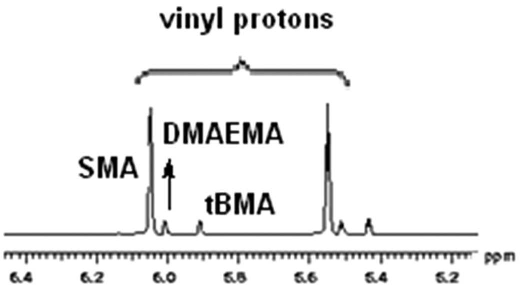


Figure 1. ^1H NMR spectrum of an 80:20:20 SMA:DMAEMA:tBMA mixture in dioxane-d_8.

Table 1. Terpolymers of SMA, tBMA, and DMAEMA

sample	monomers (mmol)[a]	CTA	CTA (μmol)	AIBN (μmol)	1,4-dioxane (mL)	temp (°C)	time (h)	product (g)	yield (%)
B1	52.8	CDB	70.4	23.4	4.4	75	1.05	3.02	30
B2	132.0	CDB	176.0	58.7	8.8	75	1.05	5.37	21
B4	56.8	CDB	75.0	25.2	4.4	75	1.05	2.40	24
B10	13.2	MDSP	5.28	0.52	1.1	85	4.00	1.40	56
B11	14.1	MDSP	5.64	0.56	1.1	85	1.50	0.90	36

[a] Monomer compositions are in Table 2.

Table 2. ^{1}H NMR and Reactivity Ratio Data for Compositions of Terpolymers

	feed composition[a] (NMR)			terpolymer composition[a] (NMR)			terpolymer composition[b] (reactivity ratio)				
sample	SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA	SMA	tBMA	DMAEMA	% conv[c]	DP$_n$ (calcd)[d]
B1	0.798	0.102	0.099	0.790	0.111	0.100	0.760	0.116	0.123	49	368
B2	0.804	0.094	0.101	0.789	0.108	0.102	0.760	0.110	0.131	30	225
B4	0.541	0.234	0.223	0.539	0.224	0.236	0.509	0.242	0.250	35	263
B10	0.866	0.070	0.065	0.800	0.101	0.100	0.842	0.080	0.079	73	1825
B11	0.544	0.231	0.226	0.538	0.229	0.232	0.486	0.255	0.258	43	1075

[a] Calculated from integrated ^{1}H NMR spectra acquired at room temperature. [b] Composition of all polymer formed up to specified % conversion calculated from reactivity ratios. [c] Weighted average percent conversion from ^{1}H NMR spectra. [d] Calculated from (% conversion)[M]/[CTA].

Table 3. SEC Molar Mass Measurements of Terpolymers

sample	M_n(calcd)[a]	M_n[b]	M_w[b]	M_w/M_n
B1	57 300	63 800	221 000	3.86
B2	38 000	42 600	56 500	1.33
B4	44 000	46 900	65 000	1.39
B10	300 000	183 000	1 200 000	6.56
B11	180 000	181 000	985 000	5.45

[a] From DP$_n$ of Table 2. [b] Samples B1, B2, B4, and B11 were measured in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP). Sample B10 was measured in *N*-methylpyrrolidinone (NMP)/0.01 M LiNO$_3$ at 80 °C. Absolute M_w and calculated M_n from light scattering detection.

tBMA, and DMAEMA.[20] Monomer feed composition, weighted average percent conversion of monomers, and binary reactivity ratios were used with ProCop[27,28] software to calculate compositions of the terpolymers corresponding to the experimental data in Table 2. The calculations assume that the random errors in the copolymer composition are normally distributed and statistically independent from run to run and that there are no errors in comonomer feed compositions. The results in Table 2 show that feed compositions of starting reaction mixtures, the polymer compositions determined from NMR spectra after partial conversion, and the polymer compositions calculated from reactivity ratios do not differ much from each other or from the target copolymer compositions of either 80:10:10 or 54:23:23 of SMA:tBMA:DMAEMA. Therefore, there was little drift in copolymer composition over the course of polymerizations.

From RAFT polymerization the theoretical number-average molecular weight ($M_{\mathrm{n,th}}$) is calculated by eq 1:[24]

$$M_{\mathrm{n,th}} = [\mathrm{M}]_0 M_{\mathrm{M}} C/[\mathrm{CTA}] + M_{\mathrm{CTA}} \qquad (1)$$

where $[\mathrm{M}]_0$ is the sum of the initial monomer concentrations, M_{M} the weighted average molecular weight of the reacted monomers, C the mole fraction conversion, [CTA] the initial concentration of CTA, and M_{CTA} the molecular weight of the CTA. Table 3 shows the results of SEC analyses of the terpolymers that were performed using light scattering detection for determination of absolute M_w, M_n, and M_w/M_n. (Note: in a preprint we reported SEC data from differential refractive index detection and calibration standards.[29] The light scattering results here are more reliable.) The M_n values that were calculated from compositions measured from NMR spectra of unreacted monomers and eq 1 are in reasonable agreement with the M_n values determined by SEC for samples B1, B2, and B4, which is consistent with a controlled RAFT polymerization. The M_w/M_n values of 1.33 and 1.39 for samples B2 and B4 indicate controlled polymerization. The molecular weight distribution of B1 has a narrow main mode also consistent with controlled polymerization, but it possesses a second smaller, high-molecular-weight mode that increases the polydispersity index. Control of DP$_n$ by RAFT apparently was lost in samples B10 and B11, which were designed to be terpolymers having DP$_n$ = 1000.

Conversion of the Terpolymers to Polycations. The DMAEMA in the terpolymers was treated with iodomethane in tetrahydrofuran at room temperature to produce the polycations as shown in Scheme 1. The experiments are reported in Table S1. Complete conversion to quaternary ammonium groups was confirmed by ^{1}H NMR spectra which had a new peak at 3.60 ppm corresponding to the $\mathrm{N^+(CH_3)_3}$ group and no peak at 2.35 ppm for the $\mathrm{N(CH_3)_2}$ group. Figure S2 shows a ^{1}H NMR spectrum of a quaternized terpolymer.

Conversion of Polycations to Polyampholytes. The conversions of the tBMA units to methacrylic acid (MA) units and the SMA units to glyceryl methacrylate (GMA) units, as shown in Scheme 1, were carried out in 1:1 mixtures of concentrated HCl and 1,4-dioxane at room temperature by a modification of a literature procedure.[30] The experiments are reported in Table S2.

A ^{1}H NMR spectrum of the purified water-soluble polyampholyte PA1-1 in $\mathrm{D_2O}$ is shown in Figure S3. The *tert*-butyl peak at 1.4 ppm and the peaks at 1.34 and 1.38 ppm from the methyl groups of the ketal ring of SMA, which appeared in the spectra of the terpolymers and the quaternary ammonium ion polymers (Figures S1 and S2), were absent from all spectra of isolated polyampholytes. We estimate that <5% of residual methyl peaks would not be detected. The complete compositions of the isolated polyampholytes could not be determined by ^{1}H NMR analysis because there was no unique signal from the methacrylic acid/methacrylate ion units, and the signals from the GMA and quaternized DMAEMA repeat units overlapped.

The molar mass distributions of the water-soluble polyampholytes were measured by SEC analysis and are reported in Table 4. The polyampholytes should have somewhat lower molar masses than the terpolymers due to loss of the ketal and *tert*-butyl protecting groups. Loss of low molecular weight material in the isolation of the solid polyampholytes may explain the increase in M_n of the polyampholytes derived from the B10 and B11 terpolymers. All samples exhibited shoulders and prepeaks to varying degrees that were most apparent in the light scattering chromatograms. The prepeaks result in higher than expected values of M_w for some of the samples and also affected M_n and polydispersities in complex ways. This behavior is consistent with aggregate structures. We attribute the inconsistent changes in M_w(LS) to aggregation of the polyampholytes in the aqueous buffered electrolyte solutions used for SEC analyses. (Note: in a

Table 4. SEC Analyses of Polyampholytes

polymer[a]	M_n(terpolymer)[b]	M_n[c]	M_w[c]	M_w/M_n
PA1-1	63 800	40 000	101 400	2.65
PA1-2	63 800	52 200	114 000	2.44
PA2-1	42 600	32 900	64 800	2.25
PA2-2	42 600	36 400	87 000	2.46
PA4	46 900	64 800	162 500	2.53
PA10	183 000	242 000	779 000	3.16
PA11	181 000	536000[d]	1 090 000	2.46

[a] For example, PA1-1 is one polyampholyte sample prepared from terpolymer B1. [b] SEC results from Table 3. [c] Absolute M_w and calculated M_n from light scattering detection in 0.15 M $NaNO_3$ and 0.01 M pH 7 phosphate buffer. [d] Bimodal distribution.

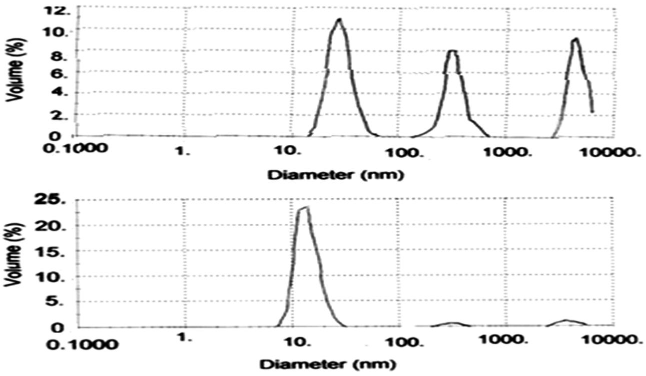


Figure 2. Sample PA4 size distribution in water by volume at (a) 1 and (b) 0.1 mg/mL.

preprint we reported SEC data from differential refractive index detection and calibration standards.[29] The light scattering results here are more reliable.)

Aggregation of Polyampholytes in Water. Dynamic light scattering analysis showed partial aggregation of the polyampholyte PA4 in pure water at 25 °C and decreased aggregation after dilution. The results are in Figure 2. At a 1 mg/mL concentration there were major peaks in the distribution of particle diameters at about 25, 300, and 4000 nm. After dilution to 0.1 mg/mL a peak at about 12 nm, which is consistent with unimolecularly dissolved polymer, accounted for more than 90% of the sample on volume basis.

Titrations and Viscosities of Polyampholyte Solutions. Dialyzed polyampholyte sample PA1-2 was titrated with acid and with base, and its solution viscosity was measured as a function of pH. Figure 3 shows that dialyzed PA1-2 in water gave a pH 6.6 solution. Standard HCl was added to pH 3.6, and then the solution was titrated with standard KOH solution to pH >11. In a second experiment, shown in Figure 4, a pH 6.6 solution of PA1-2 was adjusted to pH 11 and then titrated with HCl solution. The inflection points of the titration curves measured from the derivatives gave end point pH values of 8.14 and 8.50. The viscosity of a PA1-2 solution as a function of pH by adding KOH, as shown in Figure 5, had a minimum at pH 8.5. We interpret the results as follows: At pH 6.6, PA1-2 is a poly(tetraalkylammonium) cation (N^+) that contains both COO^- groups and COOH groups. A titration end point and minimum viscosity were reached when all of the COOH groups were ionized at pH 8.5.

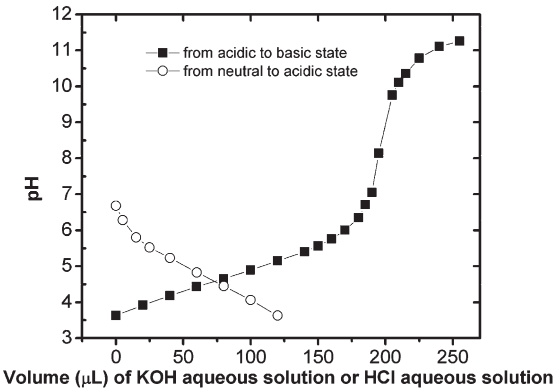


Figure 3. Acidic to basic titration of sample PA1-2. Starting from 0.03 g of polymer in 1.5 mL of deionized water at pH 6.6, the sample was first titrated with 120 μL of 0.1547 M HCl to pH 3.56 (open circles) and then titrated with 260 μL of 0.1000 M KOH (filled squares).

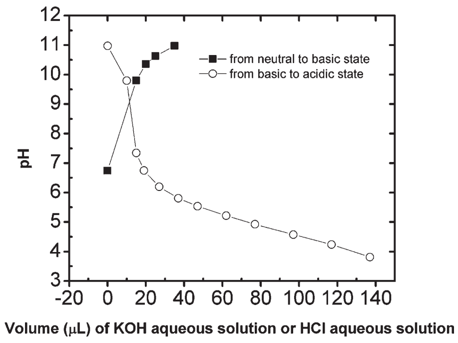


Figure 4. Basic to acidic titration of sample PA1-2. Starting from 0.03 g of polymer in 1.5 mL of deionized water at pH 6.6, the sample was first titrated with 36 μL of 0.1000 M KOH to pH 11 (filled squares) and then titrated with 139 μL of 0.1547 M HCl (open circles).

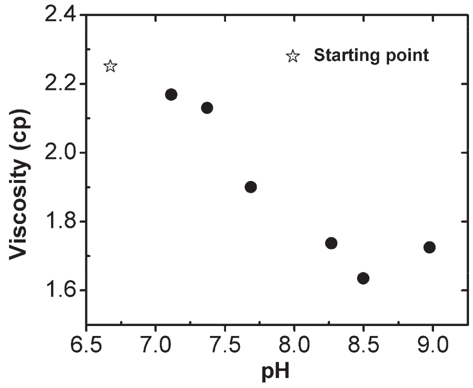


Figure 5. Dependence of solution viscosity of PA1-2 on pH at 25 °C. Starting from 0.5414 g of polymer in 18.05 mL of deionized water, a 30 mg/mL solution was prepared that had pH 6.6 (open star), and pH was adjusted by adding 0.1000 M KOH to 2.5 mL aliquots of this master solution (filled circles).

The increased viscosity at higher pH is a polyampholyte effect, as additional KOH simply adds electrolyte, screening the charge attraction that makes the polyampholyte coil (and viscosity) small.

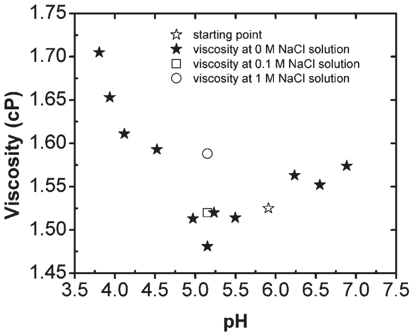


Figure 6. Dependence of solution viscosity of 30 mg/mL PA2-2 on pH at 25 °C. The starting solution in deionized water had pH 5.9 (open star). The pH of 2.5 mL aliquots of this master solution was adjusted by adding either 0.1547 M HCl or 0.1000 M KOH (filled stars). The salt concentration of 2.5 mL aliquots of the pH 5.17 solution also was increased to 0.1 M NaCl (open square) and 1.0 M NaCl (open circle).

Sample PA2-2 behaved differently, as shown in Figure 6. The dialyzed polymer dissolved to pH 5.9, addition of KOH increased the viscosity, and addition of standard HCl decreased the viscosity to a minimum at pH 5.17 and then increased the viscosity with further decrease of pH. Thus, PA2-2 is charge balanced and has minimum coil size at pH ~5.17. The dialyzed sample had a small excess of COO^- ions over N^+ ions. Adding NaCl to the solution of lowest viscosity at pH 5.17 increased the viscosity (open square, 0.1 M NaCl; open circle, 1 M NaCl) because electrolyte screens the charge attraction that makes the polyampholyte coil (and viscosity) small.

The differences between PA1 and PA2 are due to the relative amounts of quaternary ammonium ions and methacrylate ions in the polymers. PA1 has an excess of N^+ groups over COO^- groups at all pH values at least up to pH 8.5, and either is charge balanced at pH 8.5 or still has an excess of N^+ groups at pH >8.5. PA2 is charge balanced at pH 5.17. The terpolymer composition data in Table 2 and the assumption of quantitative transformations of copolymer functional groups to polyampholyte functional groups are not accurate enough to predict the differences between PA1 and PA2.

■ DISCUSSION

Terpolymers. The compositions of the terpolymers calculated from NMR spectra of the three unreacted monomers in most cases were within 3% of the compositions predicted from binary copolymer reactivity ratios and within 3% of the initial feed compositions of monomers. There are slightly more of the tBMA and DMAEMA components in the terpolymer formed early than in the initial monomer feed and slightly less tBMA and DMAEMA in the monomer feed after substantial conversion. Thus, the terpolymer compositions and sequence distributions are statistical and close to random. In contrast, copolymerization of oppositely charged monomers tends to form alternating copolymers, even in aqueous electrolyte solutions.[10,16−18]

The M_w/M_n values of 1.33 and 1.39 for terpolymers B2 and B4 indicate substantial control of polymerization by the RAFT agent CDB at 30−35% conversion and $DP_n < 300$. The higher M_w/M_n values for terpolymers B10 and B11 indicate a lack of RAFT control when the target $DP_n > 1000$, which could be due to the use of MDSP as the RAFT agent.[23,24] For terpolymer B1 $M_w/M_n = 3.86$ indicates a lack of complete RAFT control using CDB, although the breadth of the main mode of the molecular weight distribution is consistent with controlled radical polymerization. Thus, to a first approximation terpolymers B2 and B4 were formed with substantial RAFT control, B1 likely was under control for at least some portion of the polymerization, and the B10 and B11 terpolymers were formed by conventional free radical polymerization.

Polyampholytes. The SEC M_w/M_n values of polyampholytes PA1-1 and PA1-2 are slightly lower than that of terpolymer B1 from which they were prepared. This surprising result may be due to random error, to partial aggregation of the terpolymer during SEC analysis, or to fractionation either during isolation of a polymer or during preparation of solutions for SEC analysis. In contrast, the polyampholytes PA2-1 and PA2-2 have higher M_w/M_n values than that of their terpolymer precursor B2. Note that the solution viscosity and acid−base titrations show that PA1-2 is a polycation and PA2-2 is a polyanion at pH 7, the pH of the SEC analyses. The charge differences could affect aggregation in solution and adsorption to the SEC column packing and thereby affect both the measured values of the molecular weights and the molecular weight distributions.

Some polyampholyte samples not reported here and having the same approximate compositions were insoluble gels rather than solutions after dialysis in pure water. Two possible reasons for insolubility are chemical cross-linking and aggregation. Under the strongly acidic conditions of hydrolysis of the tBMA and SMA to form the MAA and GMA repeat units possibly alcohol groups of the GMA units transesterified intermolecularly to form branched and cross-linked polymers. After dialysis the polyampholyte samples could be polycations, polyanions, or nearly charge balanced polyampholytes, depending on the relative numbers of quaternary ammonium cation and methacrylate anion repeat units. Charge balanced polyampholytes are less soluble than polymers having net charge because intramolecular ion aggregation reduces hydration of the ions and decreases polymer coil size and solubility and because a charge-balanced sample contains both polycations to polyanions, which aggregate. During preparation of samples for SEC experiments sometimes small amounts of gels were separated from the solution and not injected into the chromatograph. Also, many chromatograms had a small high molecular weight "prepeak" suggestive of either aggregation of a minor fraction of the polyampholyte or to reversible adsorption of part of the polymer to the column.

Advantages and Limitations of the Polyampholytes. The method of RAFT terpolymerization of methacrylic esters and functional group conversions to polyampholytes reported here produces the most nearly random synthetic polyampholytes known. ^1H NMR spectra showed no evidence of unreacted tertiary amine, *tert*-butyl ester, or acetone ketal groups in the polyampholytes. Likewise the ^1H NMR spectra of the quaternary ammonium ion polymers showed no evidence of tertiary amine groups. Analyses of the contents of the polyampholytes from their ^1H NMR spectra are not possible because there is no unique signal of the methacrylate ion.

Better control of DP_n and M_w/M_n of the polyampholytes would facilitate interpretation of solution property measurements in terms of ideal structures. Much higher molecular weight polyampholytes, such as $DP_n > 1000$ with narrower distributions, would enable investigation of viscosities of solutions in the semidilute regime and require less sample. At this time the synthetic method does not allow fine control of the relative amounts of positively and negatively charged repeat units. Consequently, the polyampholytes must be analyzed by acid−base titrations to establish their cation and anion contents. Nonetheless, these model random polyampholytes are the most promising available for determination of the solution properties that are predicted by theory.

EXPERIMENTAL SECTION

Materials. Tetrahydrofuran (Aldrich, HPLC grade), 1,4-dioxane (Aldrich, anhydrous, 99.8%), *p*-xylene (Eastman Chemicals), hexane (Aldrich, 98%), iodomethane, and hydrochloric acid (Fisher Scientific) were used as received. 2-Methyl-2-(dodecylsulfanylthiocarbony)-sulfanylpropanoic acid was provided by Dr. John Lai of the Lubrizol Corp. Solketal methacrylate was prepared by a known method.[20,31] 2-(Dimethylamino)ethyl methacrylate (Polysciences, Inc.) and *tert*-butyl methacrylate (Aldrich) were purified before use by passing through a column of basic alumina. 2,2-Azobis(isobutyronitrile) (AIBN) (Aldrich) was recrystallized from methanol. $CDCl_3$ (Aldrich, 99.8 atom % D), 1,4-dioxane-d_8 (99 atom % D), and D_2O (99.9 atom % D) (Cambridge Isotope Laboratories, Inc.) were used as received. Water was purified with a Barnstead three column ion exchange and active carbon system. Dialysis tubing (molecular weight cutoff 1000, Spectra/Por, Spectrum Chemical Co.) was soaked and washed with water to remove the sodium azide preservative.

Instrumentation. ^{1}H NMR spectra were recorded at 400 MHz. Particle size distributions of polyampholytes were measured by dynamic light scattering at 25 °C using a Malvern HPPS 3.1 instrument equipped with a He−Ne, 3.0 mW, 633 nm laser.SEC. Terpolymers B1, B2, and B4 were analyzed in HFIP containing 0.01 M tetraethylammonium nitrate at 40.0 °C using two Agilent (formerly Polymer Laboratories) 7.5 mm × 300 mm PolyPore columns at a nominal flow rate of 0.6 mL/min. The flow rates were corrected using the retention time of an acetone internal flow marker peak. The DRI detector was a Model 410 from Waters Corporation, and the light scattering detector was a Model PD2020 from Agilent (formerly Precision Detectors). Injection volumes were 100 μL, and the injected sample concentration for samples was 2.0 mg/mL. The light scattering detector was calibrated with isotropically scattering narrow distribution PMMA 67 000 MW. Specific refractive index increments calculated from the calibrated DRI detector response were 0.186, 0.195, and 0.207 mL/g for B1, B2, and B4, respectively. Terpolymer B11 was analyzed in HFIP as above using three 8 mm × 300 mm KF-806 L columns from Shodex at a nominal flow rate of 1.0 mL/min. The specific refractive index increment of B11 was 0.198 mL/g. Terpolymer B10 exhibited abnormal late elution[32,33] using HFIP as the SEC eluent. The most common cause of late elution is adsorptive interaction of the sample with the SEC columns. Although B10 is compositionally similar to B1, it has much higher molecular weight, and adsorptive interactions with SEC columns worsen with increasing polymer molecular weight. Consequently, terpolymer B10 was analyzed in NMP containing 0.01 M $LiNO_3$ at 80 °C in a Waters Corporation GPC2000 outfitted with a PD2040 two angle light scattering detector. The columns were three Agilent O7.5 mm × 300 mm Olexis, operating at a nominal flow rate of 0.7 mL/min, the injection volume was 220 μL, and the injected sample concentration was 1.5 mg/mL. The specific refractive index increment of B10 in NMP at 80 °C was 0.017 mL/g. Polyampholytes were analyzed using two 8 mm × 300 mm Polymer Standards Service PSS-Suprema linear XL columns at 40 °C calibrated with narrow-molecular-weight distribution poly(ethylene oxide) standards. The eluent was aqueous 0.15 M $NaNO_3$/0.01 M dibasic sodium phosphate/0.002 M monobasic potassium phosphate. The nominal flow rate was 0.8 mL/min, injection volume was 100 μL, and the injected sample concentrations were 2 mg/mL. Specific refractive index increments were all close to 0.153 mL/g.

Dilute Solution Viscosity. A computerized Contraves Low Shear 30 viscometer, calibrated with standard Newtonian liquids of known viscosity (including water), was used to measure the viscosity of 30 mg/mL solutions in the shear rate range 30−100 s^{-1} at 25 °C, maintained with circulating water inside the cup assembly. A concentric cylinder geometry of outer diameter 12.0 mm and inner diameter 11.1 mm was used under steady shear. This sensitive instrument can reliably measure the viscosity of air to three significant figures[34] at 100 s^{-1}. All solutions reported were Newtonian, and the viscosities measured at different shear rates were simply averaged. The largest viscosity reported is 2.25 cP, suggesting that all solutions are near or below their overlap concentration.

Cumyl dithiobenzoate (CDB) was synthesized from 7.54 g of α-methylstyrene and 7.99 g of dithiobenzoic acid and purified by chromatography.[35] Alumina (200 g, activity III) was deactivated with 8.8 g of water and mixed for 3 h on a rotary evaporator before loading the column. Elution of the crude CDB with hexane gave a fast moving purple band and a yellow-orange band at the top of the column. The purple fractions were combined and evaporated to recover 6.1 g of CDB as a viscous oil. After 2 years, 2.0 g of the CDB was chromatographed again, and 1.26 g of purified CDB was recovered. ^{1}H NMR ($CDCl_3$) δ: 2.03 (s, 6H), 7.15−7.50 (m, 8H), 7.78 (m, 2H).

Terpolymer Synthesis. In a typical run (sample B1), stock solutions of AIBN (38 mg in 10 mL of 1,4-dioxane) and CDB (192 mg in 10 mL of 1,4-dioxane) were prepared. SMA (8.40 g, 42.0 mmol), DMAEMA (0.801 g, 5.1 mmol), and tBMA (0.807 g, 5.7 mmol) were weighed into a scintillation vial that had been rinsed with 1,4-dioxane and dried. AIBN (2.31×10^{-2} mmol, 3.8 mg) and CDB (7.03×10^{-2} mmol, 19.2 mg) were weighed from the stock solutions and transferred to the vial. *p*-Xylene (internal reference, 0.405 g, 3.81 mmol) and 1,4-dioxane (4.4 mL) were added. A ^{1}H NMR spectrum was obtained at 25 °C from 0.25 mL of the mixture in 0.50 mL of 1,4-dioxane-d_8. The rest of the mixture was transferred to a thick-walled glass tube by using a syringe with a long needle. The tube was degassed using three freeze−pump−thaw cycles and sealed under vacuum. The tube was enclosed in a wire-mesh basket and immersed completely in a bath of ethylene glycol at 75 °C. An ^{1}H NMR spectrum of the partially polymerized mixture (0.5 mL) was taken in 1,4-dioxane-d_8 (0.5 mL) to determine the percent conversion of the monomers. The pink terpolymer was precipitated into 800 mL of hexane, filtered, and dried under vacuum. ^{1}H NMR: see Figure S1. Terpolymers B10 and B11 were synthesized by the same method using MDSP as the RAFT agent.

Quaternization of Terpolymer. Terpolymer (1.00 g of B1, containing 2.45 mmol of DMAEMA) in 15 mL of THF and 19.8 mL of iodomethane was stirred at 25 °C for 48 h.[30] Liquids were removed by rotary evaporation, and the quaternized terpolymer Q1-1 (1.16 g) was dried under vacuum for 48 h. ^{1}H NMR: see Figure S2. Samples Q10 and Q11 were prepared with $[CH_3I]/[DMAEMA] \sim 2$ and also were completely quaternized.

Polyampholyte. Quaternized polymer Q1-1 (1.0 g) was dissolved in 5 mL of 1,4-dioxane, 5 mL of concentrated HCl was added, and the mixture was stirred for 8 h at 25 °C. A ^{1}H NMR spectrum was taken immediately. The sample was neutralized to pH 7 using 8 M NaOH. The neutralized mixture was dialyzed changing water every 6 h. The progress of dialysis was followed by measuring the conductivity of the dialysate. After 36 h the excess water was rotary-evaporated until the volume was 10 mL, and the remaining water was lyophilized to give PA1-1. ^{1}H NMR: see Figure S3.

ASSOCIATED CONTENT

Ⓢ Supporting Information. ^{1}H NMR spectra of representative polymers and tables of data on syntheses of quaternary ammonium ion polymers and polyampholytes. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: warren.ford@okstate.edu.

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