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Synthesis and Properties of Low-Polydispersity Poly(sulfopropylbetaine)s and Their Block Copolymers

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ABSTRACT: A series of near-monodisperse sulfopropylbetaine homopolymers have been prepared by reaction of 1,3-propanesultone with poly(2-(dimethylamino)ethyl methacrylate)s produced by group-transfer polymerization. Block copolymers of 2-(dimethylamino)ethyl methacrylate and *n*-alkyl methacrylates gave sulfobetaine block copolymers when treated with 1,3-propanesultone. Betaine formation dramatically reduces the surface activity of both the homopolymers and the block copolymers. Chromatography and light scattering show that the betaine copolymers form polydisperse micelles on direct dissolution in water, and preliminary dissolution in a nonselective solvent (2,2,2-trifluoroethanol) is needed to give near-monodisperse micelles. Micelle aggregation numbers are controlled by the length of the hydrophobic block and are essentially independent of the hydrophilic block. The betaine homopolymers show chain expansion in aqueous NaCl solutions up to 0.1 M, due to the anti-polyelectrolyte effect. A similar effect is also observed for the block copolymer micelles, which expand significantly with increasing salt concentration up to 0.1 M.

Introduction

Polysulfobetaines are zwitterionic polymers, which have both cationic and anionic charges on every monomer residue. They are generally synthesized by the alkylsulfonation of a tertiary amine monomer with a sultone[1] followed by free-radical polymerization of the zwitterionic monomer. The most widely used sultone is 1,3-propanesultone, although many others are known.[1]

The first polybetaine was a polycarboxybetaine based on poly(4-vinylpyridine), reported by Ladenheim and Morawetz.[2] The first polysulfobetaines, also based on poly(2-vinylpyridine) and poly(4-vinylpyridine), were reported by Hart and Timmerman.[3] The monomers were betainized with 1,4-butanesultone and polymerized by free-radical initiation.

The majority of betaine (co)polymers are based on vinylpyridines or tertiary amine (meth)acrylates.[4] For example, Laschewsky and Zerbe[5] and Galin and Soto[6] have synthesized and polymerized a wide range of sulfobetaine monomers, predominantly (meth)acrylates. The polymers were made by free-radical chemistry after betainization of the monomer with 1,3-propanesultone in acetonitrile at 70 °C for 3 days.[7] Galin and Soto[6] have also obtained polysulfobetaines from preformed polymers. Vinylpyridines,[6] *N*-vinylimidazole,[8] (meth)acrylamides,[9] and phosphazenes[10] can all be functionalized to yield betaines. Galin et al. have reported the synthesis of poly(aminoalkoxydicyanoethenolates),[11,12] a phosphobetaine has been reported by Chevalier et al.,[13] and the betaine derived from 4,5-dicyanoimidazole has been reported by Apen and Rasmussen.[14]

A unique property of polyzwitterions is the anti-polyelectrolyte effect, i.e., chain expansion in aqueous solution on addition of low molecular weight electrolyte. It is sometimes claimed[15] that polybetaines are insoluble in pure water, due to the formation of intra- and interchain ion contacts resulting in an ionically cross-linked network, and that they become soluble on addition of low molecular weight electrolyte, e.g., NaCl. The electrolyte screens electrostatic interactions between polymer chains and promotes solubility.[16] The effects of salt have been studied by light scattering, with the conclusion that solvent quality increases with salt concentration.[17] However, polymeric sulfobetaines that are freely soluble in water are well-known. They can pass a minimum in solubility on addition of small amounts of salt, before showing strongly increased solubility.[18] This effect presumably arises because they are at the point of zero charge in pure water but not at the isoelectric point, as they are not point dipoles. Since, in most publications, the authors did not exclude traces of inorganic salts, it is difficult to interpret the often cited insolubility in pure water. Hart and Timmerman[3] and Schulz et al.[17] have also shown that dissolution by electrolytes depends on the type of salt, with anions and cations of soft salts being more effective solubilizers than those of hard salts.

Salamone et al.[8] studied the aqueous solution properties of a poly(*N*-vinylimidazolium sulfobetaine). This particular class of polybetaine is water-insoluble, except in the presence of electrolyte. Pujol-Fortin and Galin[11] have studied the solution properties of several poly(ammonioalkoxydicyanoethenolates). These polybetaines are not water-soluble between 0 and 100 °C but become soluble on addition of either very strong acids, e.g., 40−60 wt % H_2SO_4, or salt. In this case the acid can partially protonate the anionic segment of the chain, converting the polyzwitterion into a cationic polyelectrolyte. A unique feature of this class of polybetaines, as compared to poly(sulfopropylbetaine)s, is the very high electrolyte concentration required to promote solubility. For example, the polymer remains insoluble in 6 M NaCl and 7 M NaBr. Even for the more efficient anions, such as I^-, concentrations must be increased by a factor of 10^3 compared to those required for the solubilization of poly(sulfopropylbetaine)s.

Despite much interest in polysulfobetaines, the use of free-radical chemistry means that there have been very few reports of the synthesis of these polymers with low polydispersity. In recent work[19] we have shown that

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2-(dimethylamino)ethyl methacrylate (DMAEMA) undergoes group-transfer polymerization (GTP) to give polymers of low polydispersity and that well-defined block copolymers with methyl methacrylate (MMA) and higher alkyl methacrylates can be readily synthesized by this route. In preliminary reports, we have also shown[20] that poly(DMAEMA) very easily undergoes betainization with 1,3-propanesultone and that betainized DMAEMA block copolymers form spherical micelles[21] in water. In this paper we report a study of the synthesis and solution properties of a series of sulfobetaine polymers derived from PDMAEMA homopolymers and P(DMAEMA-*block*-alkyl methacrylate) copolymers, where the alkyl component is either methyl (MMA), *n*-octyl (OCMA), *n*-lauryl (LAMA), or allyl methacrylate (ALMA). The *n*-alkyl groups were chosen to give varying hydrophobicity. The allyl group was chosen for two reasons: (1) for its potential for derivatization to create hydrophilic second blocks and (2) to act as a reactive stabilizer in dispersion polymerizations.[22]

Experimental Section

Polymerizations. All polymerizations were carried out under dry nitrogen in glassware dried overnight at 120 °C. Glassware was assembled hot and heated under vacuum to remove any residual moisture. Unless stated otherwise, all reagents were purchased from Aldrich.

Tetrahydrofuran (THF) (Fisons) was initially dried over sodium wire and then refluxed over potassium metal for 3 days prior to use. It was stored over 4 Å molecular sieves under dry nitrogen and transferred into the reaction vessel via a double-tipped needle.

Monomers were passed down a column of basic alumina to remove inhibitor. They were dried by stirring over calcium hydride for 24 h, stored below 0 °C, and freshly distilled before use. To prevent spontaneous polymerization upon distillation, diphenylpicrylhydrazyl (DPPH) was added to the higher boiling monomers (*n*-octyl and *n*-lauryl methacrylates) at the drying stage.

The initiator for all reactions was 1-methoxy-1-trimethylsiloxy-2-methyl-1-propene (MTS). It was distilled and stored under dry nitrogen below 0 °C.

Tetra-*n*-butylammonium bibenzoate (TBABB) was used as catalyst for all reactions. It was prepared by the method of Dicker et al.[23] and stored under dry nitrogen. 1,3-Propanesultone was used as received.

Synthesis of PDMAEMA Homopolymers. In a typical polymerization, THF (120 mL) was transferred, via a double-tipped needle, into a 250 mL three-necked round-bottomed flask equipped with a magnetic stir bar. The catalyst (TBABB, 0.01 g) was added under a nitrogen purge, through a sidearm of the reaction vessel which was then sealed with a rubber septum. The initiator (MTS, typically 0.20 mL) was then added via a double-tipped needle. The solution was stirred for approximately 30 min, after which DMAEMA (typically 10−15 mL), vacuum distilled from calcium hydride, was added dropwise. The polymerization exotherm was monitored. The polymer was recovered by removing the solvent and then dried in vacuo for 2 days at room temperature. The first stage of a block copolymer synthesis was carried out in the same way. Once the initial exotherm had abated, a homopolymer sample was extracted for GPC analysis, before slow addition of the second monomer. Once the second exotherm had abated, the reaction solution was stirred for approximately 30 min before being quenched with methanol (2 mL). The copolymer was recovered by removing the solvent and dried in vacuo for 2 days at room temperature.

Betainization of PDMAEMA. Typically, the precursor homopolymer or block copolymer (2−3 g) was dissolved in THF (~50 mL) in a single-necked 100 mL round-bottomed flask, equipped with a magnetic stir bar and a rubber septum. 1,3-Propanesultone was added to give a 1:1 molar ratio to the tertiary amine groups. Derivatization was apparent because the resulting poly(sulfopropylbetaine)s are insoluble in THF and the reaction solution gels. Precipitation of the polybetaine occurs at near 100% conversion as indicated by ^{1}H NMR spectroscopy and elemental microanalyses. The (co)polymer was purified by Soxhlet extraction with THF, to remove unreacted 1,3-propanesultone, and freeze-dried overnight from water.

Table 1. Characterization Results for DMAEMA-*block*-alkyl methacrylate Copolymers

sample ID	co-monomer	theor DMAEMA content/ mol %	obsd DMAEMA content/ (mol %)[b]	measd M_n of copolymer/ g mol^{-1} [a]	M_w/M_n
AB3-30	MMA	80	80	10 700	1.11
AB3-32	MMA	70	71	10 500	1.12
AB3-34	MMA	60	59	10 400	1.11
AB3-36	MMA	50	48	3 900	1.10
AB3-40	MMA	40	42	9 300	1.10
AB3-42	MMA	30	29	10 300	1.10
AB3-44	MMA	20	16	10 700	1.05
AB3-50	LAMA	80	85	8 200	1.12
AB3-57	LAMA	20	20	10 400	1.08
AB3-51	OCMA	80	85	9 700	1.08
AB3-53	OCMA	70	72	8 800	1.09
AB3-22	ALMA	80	81	4 700	1.70
AB3-28	ALMA	40	43	5 800	1.70

[a] All samples were synthesized with a theoretical overall M_n of 8000, except for AB2-50 and AB2-57 where the theoretical M_n was 7000. [b] Determined by ^{1}H NMR spectroscopy.

Polymer Characterization. Molecular weights of the precursor (co)polymers were estimated by size exclusion chromatography (SEC), using a Polymer Labs mixed D polystyrene column, with RI and UV detectors. The mobile phase was HPLC grade THF at flow rate of 1 mL min^{-1}. Calibration was with PMMA standards.

The molecular weights of the poly(sulfopropylbetaine)s were estimated using aqueous size exclusion chromatography (ASEC), with a Pharmacia Biotech "Superose" column and RI and UV detectors. The column temperature was controlled using a Polymer Labs 505 LC column oven. The mobile phase was a buffered 0.05 M solution of tris(hydroxymethyl)aminomethane (TRIZMA) in 1.0 M aqueous NaCl at a flow rate of either 1.0 or 0.5 mL min^{-1}. Calibration was with poly(ethylene oxide) standards.

Surface tension measurements were made using a White Electrical Instrument Co. torsion balance and a platinum ring. All measurements were performed at 21 ± 1 °C, and reproducibility was checked by frequent determination of the surface tension of doubly distilled deionized water (72.7 mN m^{-1}).

Dynamic light scattering experiments were performed using a Malvern PCS 4700 spectrometer, with a 40 mW He−Ne laser operated at $\lambda_0 = 632.8$ nm or a variable power (9−175 mW) argon ion laser operated at $\lambda_0 = 488$ nm. Measurements were made at 90°. Both monomodal cumulants and CONTIN analyses were used to fit the data. The (co)polymer samples were prepared as 1 w/v % solutions in either doubly distilled water or aqueous salt solution. Where 2,2,2-trifluoroethanol (TFE) was used as cosolvent, the (co)polymer was initially dissolved in TFE and the solution diluted with either aqueous salt or doubly distilled water to give 1 w/v % (co)polymer solutions containing approximately 4 v/v % TFE.

Results and Discussion

Polymer Synthesis and Characterization. GTP was used to synthesize a series of PDMAEMA homopolymers and P(DMAEMA-*block*-alkyl methacrylate) copolymers, where the alkyl component was either methyl (MMA), *n*-octyl (OCMA), *n*-lauryl (LAMA), or allyl (ALMA) methacrylate. The syntheses are summarized in Table 1. In block copolymer syntheses, the DMAEMA was usually polymerized first, because any homopolymer contamination resulting from polymer-

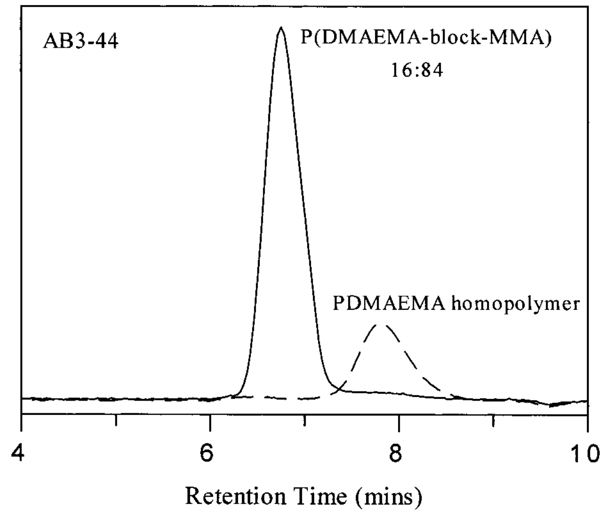


Figure 1. Typical SEC (THF) chromatogram of a P(DMAEMA-*block*-MMA) copolymer.

izing the hydrophobic alkyl MA first would be undesirable when studying the aqueous solution properties of the block copolymers. For each series, the chain length was kept constant, while the molar ratio of DMAEMA to alkyl methacrylate was varied. All syntheses gave quantitative yields (>95% after workup). Throughout this paper the notation *x*:*y* is used to represent molar copolymer composition, on the order of addition. For example, 20:80 represents a copolymer with 20 mol % DMAEMA, polymerized first, and 80 mol % of the comonomer.

Figure 1 shows a typical SEC chromatogram. The peak labeled “PDMAEMA homopolymer” represents a sample removed from the “living” PDMAEMA solution prior to the addition of the MMA monomer. There is no detectable PDMAEMA homopolymer contamination in the block copolymer. However, in copolymers where PDMAEMA is the major component, e.g., AB3-30 in Table 1, such contamination may not be resolved given the small difference between the molecular weights of the PDMAEMA first block and the final copolymer.

Table 1 shows typical SEC results (calculated as PMMA equivalents) for some of the copolymers. They all have narrow molecular weight distributions ($M_w/M_n < 1.25$), which is typical of (co)polymers synthesized via GTP.[19] The molecular weights from SEC are always higher than the value calculated from the monomer:initiator ratio, almost certainly because the hydrodynamic volumes of the homo/block copolymers in THF are different from the PMMA standards.[19]

Some problems were encountered when ALMA was the second monomer. The block copolymers have elution volumes virtually identical to that of the DMAEMA homopolymer, with significant tailing to low molecular weight (high retention time). Block copolymer formation at the expected composition was verified via ^{1}H NMR spectroscopy, and we have encountered similar tailing when analyzing ALMA hompolymers by SEC. We therefore attribute the similar elution times to adsorption of the ALMA block onto the GPC columns.

^{1}H NMR spectroscopy was used to determine the relative copolymer compositions, by comparing the integrals of signals associated with DMAEMA residues and an appropriate signal from the alkyl methacrylate block as described previously;[19] the error is estimated to be ±2%. There is good agreement between the theoretical and measured compositions, as shown in Table 1.

Betainization of Homopolymers and Block Copolymers. Betainization of the DMAEMA homopolymers and the DMAEMA-*block*-alkyl methacrylate copolymers was achieved at room temperature in THF, under normal air, using 1,3-propanesultone as described previously;[20] see Scheme 1. Betainization of DMAEMA homopolymers and DMAEMA-rich block copolymers is easily detected, since the polybetaines are insoluble in THF. Gelation occurs even with block copolymers of relatively low DMAEMA content, e.g., 29 mol %. In a 16:84 block copolymer with MMA the reaction solution does not gel, but its viscosity increases significantly. Gelation often occurred within 5−8 h, although reactions were generally left overnight (12−16 h).

The extent of betainization was measured by ^{1}H NMR and elemental microanalyses.[20] Both methods indicated >95% conversion in every case.

Solution Properties of the Poly(sulfopropylbetaine)s. The betaine homopolymers and copolymers reported here are all directly soluble in distilled water. The copolymers are the first known examples of low-polydispersity sulfopropylbetaine-based block copolymers.[21]

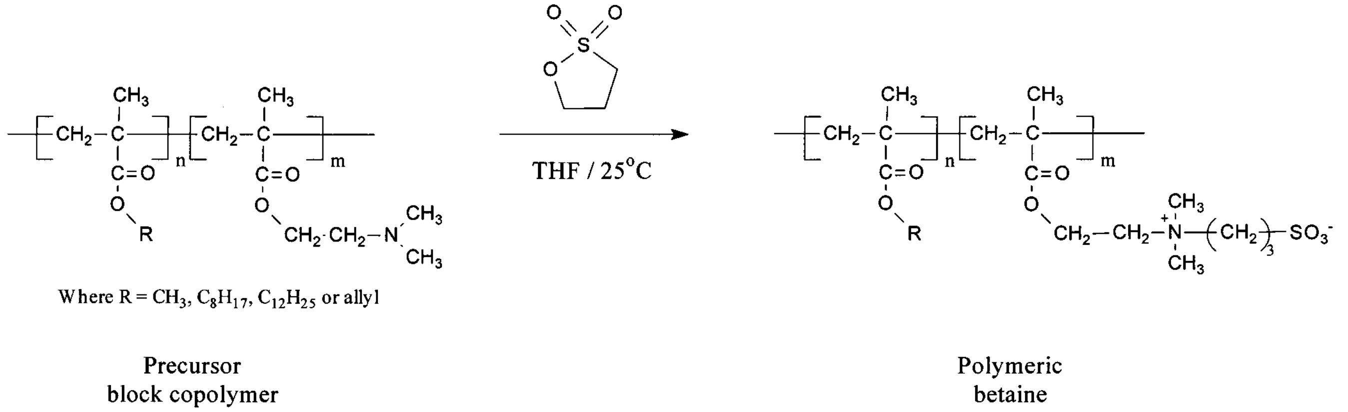
In previous preliminary work[21] we have shown that the betaine copolymers form micelles when dissolved in water; their aqueous solution properties were therefore investigated by surface tensiometry, aqueous size exclusion chromatography (ASEC), and dynamic light scattering (DLS).

In any discussion of surface activity and micelle formation in copolymers of this type, it must be recognized that there is unlikely to be a dynamic equilibrium between micelles and unimers, since PMMA has a glass transition temperature of ∼50−100 °C depending on chain length, and the micelle core will have, at most, only very limited mobility at 25 °C. This problem has been extensively discussed for block polyelectrolytes by, among others, Eisenberg et al.,[24] who concluded that, although the micelles are not in dynamic equilibrium, they probably pass close to equilibrium during their formation and can often be well described as equilibrium structures.

Surface Tension. Surface tension measurements were made on (co)polymers dissolved directly into doubly distilled deionized water. Figure 2 shows the results for a DMAEMA homopolymer and the corresponding polybetaine. The surface tension of the homopolymer solution falls rapidly with increasing concentration up to ∼0.075 w/v % and then remains roughly constant at ca. 50 mN m^{-1}. This shows that the homopolymer is significantly surface active, presumably due to the presence of both protonated (hydrophilic) and nonprotonated (hydrophobic) segments. After betainization, the homopolymer shows little surface activity, the surface tension remaining virtually constant at ca. 72 mN m^{-1}. In view of the ionic nature of the polybetaines, their lack of surface activity is not surprising.

Figure 3 shows the curves for an 80:20 (DMAEMA-*block*-MMA) copolymer and the corresponding betaine copolymer. As expected,[19] the precursor copolymer shows surface activity, the surface tension falling rapidly over a narrow concentration range to a minimum at ca. 0.05 w/v %; above this concentration it is constant at ca. 45 mN m^{-1}. The corresponding poly(sulfopropylbetaine) is more surface active than the

Scheme 1. Conversion of the Precursor (Co)polymers to the Corresponding Poly(sulfopropyl betaine)



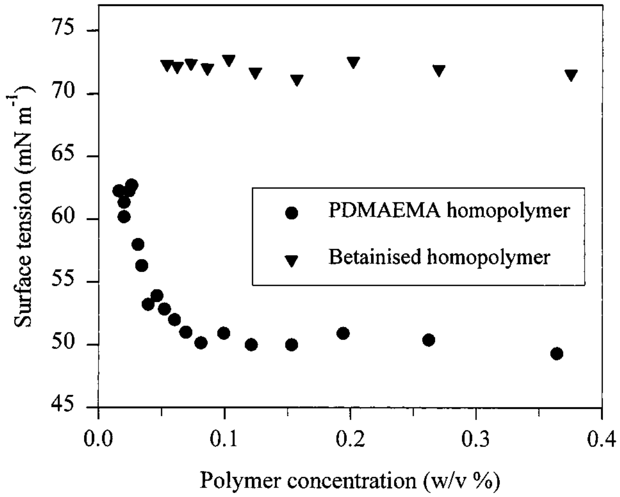


Figure 2. Surface tension data for PDMAEMA homopolymer (M_n = 32 000) and the corresponding polybetaine in distilled water at 21 °C.

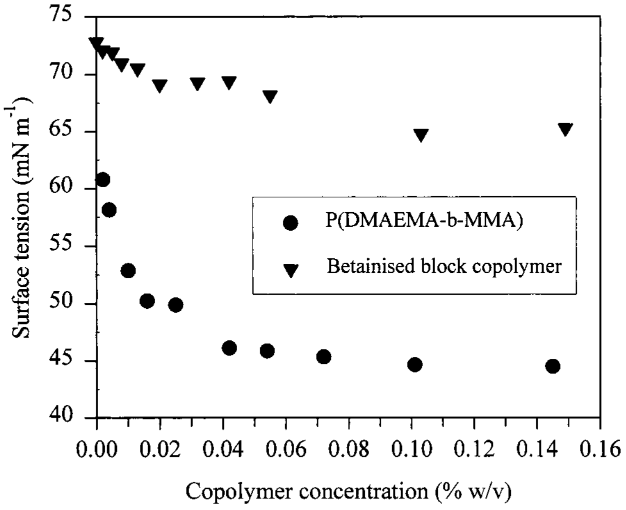


Figure 3. Surface tension data for a 80:20 DMAEMA:MMA block copolymer and the corresponding betaine in distilled water at 21 °C.

Table 2. Characterization Data for PDMAEMA Homopolymers and the Resulting Polybetaines

	PDMAEMA precursors		poly(sulfopropylbetaine)	
sample	M_n[a]	M_w/M_n[a]	M_n[b]	M_w/M_n[b]
HOMO 2	5 100	1.15	3 700	1.13
HOMO 4	10 000	1.15	5 300	1.11
HOMO 5	32 000	1.17	28 400	1.05
HOMO 6	71 000	1.21	45 000	1.16

[a] By SEC (THF), calibrated with PMMA standards. [b] By SEC (aqueous 1.0 M NaCl/TRIZMA buffer at pH 9), calibrated with PEO standards.

homopolymer, but much less than the parent copolymer. This is attributed to the combination of the hydrophobic MMA segments and the ionic betaine units. There is no well-defined cmc; the surface tension falls steadily to ca. 65 mN m^{-1} over the concentration range studied. The adsorption of the block copolymers, whether betainized or not, is complicated by the lack of dynamic equilibrium between micelles and unimers; we have recently shown that the DMAEMA–MMA block copolymers can adsorb as micelles at the air–water interface.[25] The shape of the surface tension–concentration curves and the absence of a well-defined cmc reflects saturation of the surface with adsorbed polymer rather than a true micelle–unimer equilibrium.

Aqueous Size Exclusion Chromatography. The DMAEMA homopolymers were analyzed in a buffered aqueous solution (TRIZMA buffer at pH 9) of 1.0 M NaCl to screen any inter- and intrachain electrostatic interactions. Table 2 lists the data for the homopolymers before and after betainization. All ASEC traces were unimodal, with no indication of high molecular weight aggregates. It is clear that the narrow molecular weight distributions of the precursors are retained in the polybetaines. This is not surprising, since chain scission would not be expected under the mild conditions used for betainization. The anomalously low molecular weights obtained for the polybetaines are almost certainly due to their hydrodynamic volumes being significantly different from the nonionic PEG/PEO calibration standards.

Sun et al.,[26] Xu et al.,[27] and Patrickios et al.[28] have used ASEC for characterization of block copolymer micelles, and we applied the same method to some of our betainized DMAEMA–MMA copolymers. We found that choice of column is critical to obtaining good ASEC data for the polybetaines, and the best results were obtained using an agarose column (Pharmacia Biotech "Superose"). Figure 4 is a typical chromatogram, showing clear resolution of the block copolymer into two fractions. The peak at high retention time could be due to either unimer chains or homopolymer contamination, whereas the high molecular weight peak is due to micellar aggregates. Homopolymer contamination might arise from the synthesis of the precursor DMAEMA–MMA block copolymers if cross-initiation from a "living" PDMAEMA homopolymer to MMA monomer is not

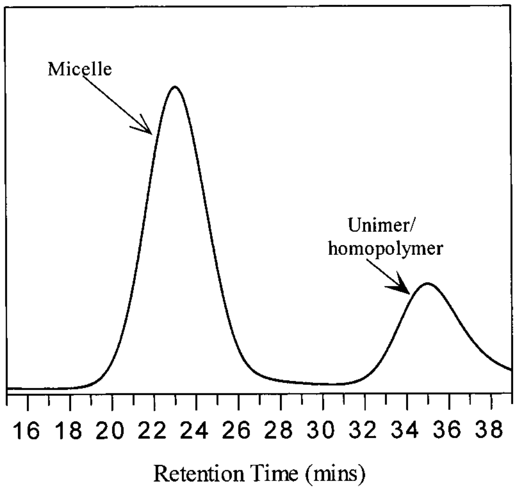


Figure 4. Typical aqueous SEC trace of a betainized 70:30 DMAEMA–MMA block copolymer.

Table 3. Characterization of Unimers and Micelles by Aqueous SEC

sample	micelle		unimer/homopolymer	
(mol composn)	M_n	M_w/M_n	M_n	M_w/M_n
80:20	38 650	1.04	7200	1.39
71:29	46 350	1.09	4800	1.20
59:41	115 850	1.34	5300	1.14
48:52			4200	1.11

100% efficient. In one experiment a betaine block copolymer was produced by betainization of a 30:70 MMA–DMAEMA block copolymer in which the MMA was polymerized first. Any homopolymer would then be PMMA, which will be readily removed during purification (Soxhlet extraction with refluxing THF) of the betainized block copolymer (or during the sample preparation for ASEC, since PMMA is not soluble in 1.0 M NaCl). The ASEC chromatogram showed the same fractionation effect; thus, the low molecular weight peaks observed for the other copolymers must represent unimeric block copolymers, rather than betaine homopolymer contamination.

Table 3 shows the molecular weights and polydispersities calculated for both peaks (using linear PEO calibration standards). Except for the block copolymer with 59 mol % betaine residues, the polydispersities of the micellar species are reasonably narrow, which implies well-defined micelles of a similar aggregation number. The low molecular weight species all have $M_w/M_n > 2.25$. It is likely that this results from distortion of the chromatogram because the hydrophobic MMA segments adsorb on the column packing, resulting in retention and broadening of the peak.

The betaine block copolymer of composition 48:52 eluted beyond the upper limit of the column and could not be analyzed. For the remaining block copolymers the M_n of the micelles increases with increasing mole percent of hydrophobic MMA comonomer and decreasing mole percent of hydrophilic betaine, with a large increase observed at 41 mol % MMA. Although calculation of aggregation numbers from these data is not expected to be reliable due to calibration problems, the general trend of increasing aggregation number with hydrophobic block content and block length is typical of hydrophilic–hydrophobic block copolymers in aqueous media. For example, Khougaz et al.[24] studied block copolymers of polystyrene (insoluble block) with poly(sodium acrylate) (soluble block) in aqueous salt solution. It was found that, for a constant block length of 160 units of sodium acrylate, the aggregation number increased from 63 to 150 when the insoluble polystyrene block length was increased from 11 to 23 units. For a constant polystyrene block length of 11 units and an increase from 69 to 160 units of sodium acrylate, the aggregation number was constant at 65. For our betaine block copolymers, the aggregation numbers lie roughly in the range 5–20 chains per micelle. This is very similar to the micelles formed by the precursor polymers with MMA as the hydrophobic block,[29] though the relation of aggregation number to chain structure was less clear in the precursor polymers. It is therefore likely that the observed increases in the M_n values for the polybetaines reported here are due to their increasing MMA content, rather than to the decreasing content of hydrophilic betaine.

Table 4. Effect of Block Copolymer Composition on Hydrodynamic Diameters of Micelles in 1 W/v % 1 M NaCl at 25 °C

sample	d_h from	cumulants	CONTIN	
(betaine:MMA)	SEC/nm[a]	d_h micelle	d_h aggregate	d_h
80:20	18.9	17.8 (0.185)	19.3	
71:29	22.9	22.9 (0.086)	24.4	
59:41	43.4	39.5 (0.130)	26.9	54.4
48:52	71.3	87.8 (0.381)	39.8	155.6

[a] Estimated from SEC data assuming universal calibration.

Dynamic Light Scattering. In initial experiments the polybetaine block copolymers characterized via ASEC were studied. The 1 w/v % solutions of the copolymers (80:20, 71:29, 59:41, and 48:52, betaine: MMA) were prepared by direct dissolution in 1.0 M NaCl. Measurements were made at 25 ± 0.1 °C. Table 4 shows the hydrodynamic diameters of the micelles as determined via DLS. There are two sets of DLS data, obtained using different methods of analysis. The cumulants method shows one population for all samples. (The numbers in brackets represent the polydispersities of the micelle populations; values of less than 0.10 indicate reasonably well-defined micelles.) CONTIN analysis is able to resolve two (or more) distinct populations. While CONTIN analysis of the 80:20 and 71:29 copolymers indicates only one population, whose sizes are in excellent agreement with those determined via cumulants, bimodal distributions are observed for the 59:41 and 48:52 copolymers. (Cumulants analyses yielded values that were intermediate between these two populations.) The smaller values are most likely micelles, while the larger values indicate either nonequilibrium aggregates or micelle clusters. For the 59:41 block copolymer, the smaller size represented ~90% (by volume) of the total population, while for the 48:52 the smaller size represented ~99% of the population. Given the more sophisticated data analysis by CONTIN, these values are considered to be more representative of the micellar solutions.

Hydrodynamic diameters of the micelles can also be estimated from the ASEC data. Since the Mark Houwink parameters of the PEO standards in water are known[26] ($[\eta] = 0.0125\ M^{0.78}$), the value of $[\eta]M$ can be calculated for the PEO at any retention volume, where $[\eta]$ is the limiting viscosity number. If universal calibration is assumed, the micelle will elute at the same retention volume as a PEO standard with the same

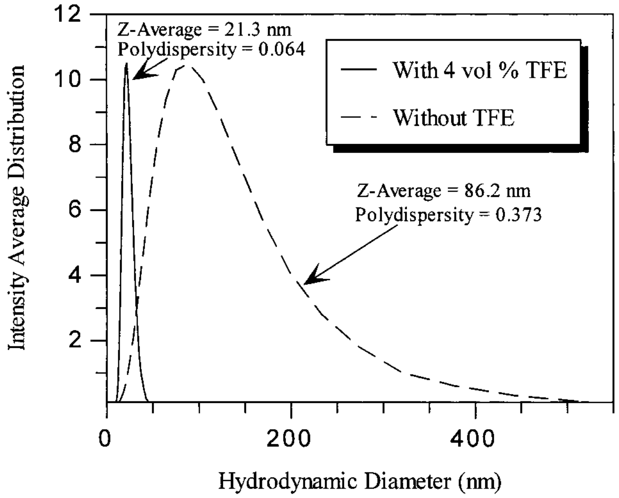


Figure 5. Hydrodynamic diameter (via monomodal analysis) of the sulfopropylbetaine block copolymer of mole composition 48:52 (betaine:MMA), with and without initial dissolution in TFE.

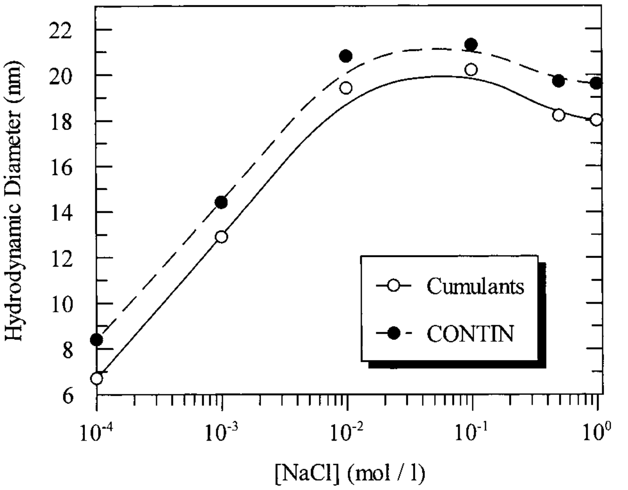


Figure 6. Variation in hydrodynamic diameter with NaCl concentration for betainised PDMAEMA (M_n= 71 000).

value of $[\eta]M$, and an equivalent hard-sphere hydrodynamic volume for the micelle can be calculated from the Einstein equation $V_h = [\eta]M/2.5N_A$, where N_A is Avogadro's constant.

Table 3 shows the hydrodynamic diameters calculated from ASEC data. The values can only be regarded as semiquantitative since the mobile phase was a buffered 1.0 M solution of NaCl and not pure water. Given this, the agreement between ASEC and DLS data is gratifying.

The presence of the larger "aggregates" is most likely a result of residual solid-state morphology,[30] which should be minimized if the polymer is initially molecularly dissolved in a solvent for both blocks. In general, polybetaines are only soluble in aqueous salt solution or solvents of high hydrogen-bonding donating power. Monroy-Soto and Galin[31] and Huglin and Radwan[32] have shown that 2,2,2-trifluoroethanol (TFE) (which is a strongly hydrogen-bonding solvent) is a thermodynamically good solvent for betainized DMAEMA homopolymer.

To verify molecular dissolution in TFE, the 71:29 copolymer was analyzed at Optokem Instruments Ltd. by static light scattering in pure TFE, using a DAWN instrument. This gave $M = 18\ 500 \pm 400$ as compared to the expected value of 19 000 g mol^{-1}, thus confirming molecular dissolution.

The advantage of using TFE as a cosolvent in the preparation of well-defined micellar solutions is shown in Figure 5, which shows the intensity average size distribution for the micelles of the 48:52 betaine copolymer prepared by direct dissolution in 1.0 M NaCl or by initial dissolution in TFE, followed by dilution with 1.0 M NaCl to achieve a final TFE content of 4 vol %. Direct dissolution in 1.0 M NaCl results in a broad distribution of aggregate sizes, ranging from ca. 25 to ca. 500 nm, with a *z*-average size of 86 nm. However, initial dissolution in a small volume of TFE with subsequent dilution results in a much narrower distribution of micelle sizes and a significantly lower *z*-average of 21 nm. The cosolvent is only necessary when the mole percent of MMA is greater than 30. For example, the 71:29 copolymer has a hydrodynamic diameter of 23 nm (by cumulants analysis) on direct dissolution in 1.0 M NaCl and 21 nm via the cosolvent. Increasing the MMA content to 41 mol % results in a hydrodynamic diameter of 39 nm by direct dissolution (polydispersity = 0.130) and 21 nm (polydispersity = 0.064) via the cosolvent.

Conventional polyelectrolytes, such as ionized poly(methacrylic acid), have highly expanded conformations in solution due to electrostatic repulsions from the high density of carboxylate anions. Addition of salt results in collapse of the chain due to screening of the repulsive interactions; this is known as the polyelectrolyte effect. Polybetaines have collapsed conformations due to net attractive electrostatic interactions. Addition of salt to a polybetaine solution also screens the electrostatic interactions, but since in this case the interactions are attractive, the polymer shows an anti-polyelectrolyte effect and expands. For example, Schulz et al.[17] studied the effect of increasing NaCl concentration on a sample of betainized PDMAEMA ($M_w = 4.35 \times 10^5$), by viscosity measurements and static and dynamic light scattering, and observed increases in reduced viscosity, hydrodynamic diameter (by DLS), and A_2 values (by static LS) with increasing salt concentration (0–20%). These observations imply not only chain expansion with increasing salt concentration but also increasing solvent quality (higher A_2).

Figure 6 shows the change in hydrodynamic diameter of a betainized homopolymer (initially molecularly dissolved in TFE) as a function of NaCl concentration, as determined by DLS. The observed size in water (initially molecularly dissolved in TFE; total TFE content ~8 vol %) was 5.6 nm. Increasing the concentration of NaCl from 10^{-4} to 1.0 M results in an increase in the hydrodynamic diameter from ~7.0 nm (cumulants analysis) to a maximum of ~20.0 nm at 0.1 M NaCl, after which the diameter falls to ~18.0 nm at 1 M NaCl. The initial very rapid increase is direct evidence for the anti-polyelectrolyte effect, although it is worth noting that, since the solvent quality is also increasing, the observed increase in hydrodynamic diameter may be due, in part, to increased polymer–solvent interactions. Our results indicate that the (co)polymer chains collapse slightly as the salt concentration exceeds 0.1 M, suggesting the onset of a "salting-out" effect.

The effect of salt concentration on the micellar solutions formed by the betaine block copolymers is shown in Figure 7. The trend is the same as that observed for the betaine homopolymer. An initial very sharp increase in micellar hydrodynamic diameter is observed at low

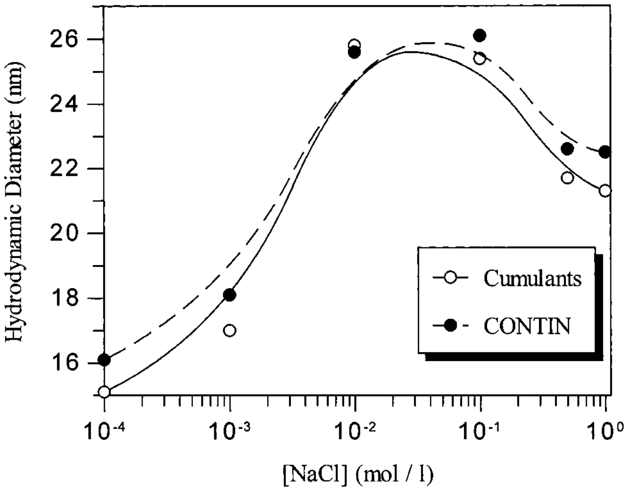


Figure 7. Variation in hydrodynamic diameter with NaCl concentration for a 71:29 poly(sulfopropylbetaine) block copolymer with MMA.

salt concentration; this reaches a maximum value of ca. 26 nm, after which the diameter falls slightly. Block copolymer composition has relatively little effect on the maximum hydrodynamic diameter for a constant precursor M_n of ca. 10 000. Even changing the hydrophobic comonomer from MMA to OCMA has no discernible effect. However, block copolymer composition does affect the salt concentration at which the maximum diameter is observed. For the homopolymer, the 80:20, 71:29 (betaine:MMA), and the 70:30 (betaine:OCMA) block copolymers, the maximum is observed at ca. 0.1 M NaCl, while increasing the mole percent of hydrophobe above ca. 30% results in the critical salt concentration falling by an order of magnitude to ca. 0.01 M. At salt concentrations higher than the critical value, the hydrodynamic diameters fall to ca. 21 nm, irrespective of copolymer composition or hydrophobic comonomer.

Although the initial increase in observed hydrodynamic diameter is almost certainly due to the anti-polyelectrolyte effect and increasing corona−solvent interactions, it is also possible that it is a result of an increase in the aggregation number of the micelles or induced aggregation of micelles to form micelle clusters. However, this is unlikely since the same trend is seen in the homopolymer. Moreover, it is hard to envisage the formation of micelle clusters since the solvent quality for the betaine coronas increases with increasing salt concentration. A change in aggregation number requires a dynamic equilibrium between unimers and micelles which is unlikely in the present case. This suggests that any observed swelling is due to the corona. Since the TFE (a good solvent for PMMA) will partition between the PMMA core, the corona, and the solvent, at 4 vol % it is unlikely that there is a sufficient amount of TFE in the micelle cores to significantly alter the glass transition temperature of the PMMA chains. Also, the same behavior is observed in the 80:20 (betaine: MMA) block copolymer, which was analyzed by direct dissolution in aqueous salt solution. We have previously suggested that the micelles formed by the precursor copolymers are “locked” and unable to alter their aggregation number once they are formed.[19]

Guenoun et al.[33] have recently reported the effect of added salt (NaCl) on the block polyelectrolyte poly(sodium 4-styrenesulfonate-*block*-*tert*-butylstyrene) (P(SS-*b*-TBS)). For a block copolymer rich in PSS (M_w PSS = 83 000 and M_w PTBS = 4200), dissolution in aqueous media results in the formation of micelles, with the hydrophobic PTBS block forming the micelle core and the corona consisting of highly expanded PSS chains. The effect of added salt on hydrodynamic diameter and aggregation number was studied by light scattering. Increasing the salt concentration from 10^{-4} to 10^{-2} M NaCl resulted in the hydrodynamic diameter falling from ca. 160 to ca. 90 nm, while the aggregation number remained constant at ca. 40. The fall in hydrodynamic diameter was attributed to the polyelectrolyte effect. By analogy, the betaine block copolymers exhibit chain *expansion* over this concentration range due to the anti-polyelectrolyte effect. Increasing the NaCl concentration from 10^{-2} to 1.0 M resulted in a monotonic decrease in the hydrodynamic diameter from ca. 90 nm (10^{-2} M NaCl) to ca. 50 nm (1.0 M NaCl). However, a simultaneous decrease in aggregation number was also observed, falling from ca. 40 (10^{-2} M NaCl) to ca. 15 at 1.0 M NaCl.

Conclusions

We have reported the first examples of directly synthesized narrow molecular weight distribution poly(sulfopropylbetaine) homopolymers and block copolymers, where the comonomer can, in principle, be any alkyl methacrylate. The direct synthesis takes advantage of the ease of betainization of the tertiary amine residues of preformed homo/block copolymers of DMAEMA with an alkyl methacrylate to high conversions under mild conditions.

The homo and block poly(sulfopropylbetaine)s exhibit no or little surface activity, respectively, while the corresponding precursor (co)polymers show marked activity. Aqueous SEC confirmed that the narrow molecular weight distributions of the precursors are retained on conversion to the poly(sulfopropylbetaine)s and also indicated micelle formation for the block copolymers. The observed bimodal size distributions for the block copolymers represent a mixture of micelles and unimers. Dynamic light scattering confirmed the formation of micelles, with hydrodynamic diameters in the 20−40 nm range, and indicated the need for a nonselective cosolvent, such as 2,2,2-trifluoroethanol, for the preparation of well-defined micellar solutions when the hydrophobic comonomer content exceeds 30 mol %.

Aggregation numbers for the micelles produced by the betaine blocks are very similar to those obtained for the precursor copolymers in earlier work. Since the ionic betaine residues are much more hydrophilic than the precursor DMAEMA chains, this suggests that the aggregation is largely controlled by the hydrophobic block length, as suggested in other studies of micelle formation.

The effect of increasing salt concentration for both the homopolymers and the block copolymer micelles shows anti-polyelectrolyte behavior at low salt concentrations, reaching a maximum at ca. 10^{-2}−10^{-1} M NaCl. For the block copolymer micelles this is due to expansion of the corona, and the effect is compensated to some extent at higher (>0.10 M) salt concentrations by the onset of salting-out effects. Thus, at low salt contents the micelles are smaller than those of the precursor copolymers because of their compact polybetaine corona, whereas at higher concentrations they are much more expanded.

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