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Polymer 48 (2007) 1193–1202
polymer
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Esterification of hydroxylated polymers with 2-sulfobenzoic acid cyclic anhydride: A facile approach for the synthesis of near-monodisperse strong acid homopolymers and diblock copolymers

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Received 30 August 2006; received in revised form 21 December 2006; accepted 27 December 2006
Available online 24 January 2007

Abstract

A convenient two-step route was developed to prepare a range of low polydispersity strong acid homopolymers and several examples of well-defined diblock copolymers. Atom transfer radical polymerization (ATRP) of either 2-hydroxypropyl methacrylate, 2-hydroxyethyl methacrylate or glycerol monomethacrylate afforded the corresponding near-monodisperse hydroxylated homopolymers, while several diblock copolymer precursors were prepared by either (1) the one-pot ATRP of 2-hydroxypropyl methacrylate and 2-(diethylamino)ethyl methacrylate using sequential monomer addition or (2) the ATRP of either 2-hydroxypropyl methacrylate or glycerol monomethacrylate using a poly(ethylene oxide)-based macro-initiator. Excess 2-sulfobenzoic acid cyclic anhydride was used to fully esterify the hydroxy groups of these homopolymers and diblock copolymers under mild conditions. The resulting zwitterionic diblock copolymers undergo micellar self-assembly on adjusting the pH of the solution, while one of the anionic poly(ethylene oxide)-based diblock copolymers formed colloidal polyelectrolyte complexes in aqueous solution when mixed with a cationic poly(ethylene oxide)-based diblock copolymer.

Keywords: Controlled radical polymerization; Polyelectrolytes; Esterification

1. Introduction

Polyacids have been used in numerous industrial applications, such as scale inhibition, coatings, food, cosmetics, textile finishing, and paper making [1–3]. Near-monodisperse polyacids are of particular interest as dispersants for pigments [4–7] and other inorganic materials [8–10], as crystal habit modifiers [11–16], for the synthesis of shell cross-linked micelles via polyelectrolyte complexation [17,18], and as components of glass–ionomer dental cements [19]. The synthesis of well-defined, low polydispersity polyacids has traditionally involved living ionic polymerization combined with protecting group chemistry. For example, Ishizone et al. [20] obtained well-defined poly(4-vinylbenzoic acid) (PVBA) by the hydrolysis of a protected poly(*t*-butyl 4-vinylbenzoate) (P*t*BVB) that had been prepared by anionic polymerization. Similarly, poly(methacrylic acid)-based (PMAA) diblock copolymers [5,10,11,14–16,21] were obtained from selective hydrolysis of diblock copolymer precursors comprising various methacrylic blocks and poly(*t*-butyl methacrylate) (P*t*BMA). Various PMAA precursors have been synthesized using group transfer polymerization (GTP), such as P*t*BMA [22], poly(2-tetrahydropyranyl methacrylate) (PTHPMA) [23–27], poly(benzyl methacrylate) (PBzMA) [28,29], and poly(trimethylsilyl methacrylate) (PTMSMA) [23,26]. Unfortunately, conversion of P*t*BMA to give PMAA typically requires the use of harsh acidic reaction conditions [7,21,22,28,30] and such protecting group chemistry is always intrinsically atom-inefficient. Moreover, the incomplete removal of *t*-butyl groups from methacrylic copolymers has been claimed to be a source of irreproducibility in mineral dispersion experiments [9].

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0032-3861/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.polymer.2006.12.047

In principle, recent advances in controlled radical polymerization now allow the *direct* polymerization of various acidic monomers. For example, Georges and co-workers used nitroxide-mediated polymerization for the synthesis of poly(sodium 4-styrenesulfonate) with relatively low polydispersities and high conversions [31]. We recently used ATRP in aqueous and mixed aqueous media to polymerize sodium 4-styrenesulfonate [32], but polydispersities were higher than those reported by Choi and Kim [33]. However, an Italian group has reported some success in the polymerization of potassium 3-sulfopropyl methacrylate in 1:1 DMF/water mixtures [34]. Reversible addition-fragmentation transfer (RAFT) polymerization appears to be a promising approach for various acidic monomers in their sodium salt form [35–37], but some RAFT agents can be prone to hydrolysis under certain reaction conditions [38]. Thus the direct synthesis of controlled-structure polyacids by living radical polymerization actually remains somewhat problematic, although progress continues to be made in this area.

We recently described the esterification of various hydroxy-functional polymers using succinic anhydride (SA). This atom-efficient route allowed the synthesis of a wide range of well-defined *weak* polyacids [39] and also their corresponding zwitterionic diblock copolymers [40]. In the present work, near-monodisperse poly(2-hydroxyethyl methacrylate) (PHEMA), poly(2-hydroxypropyl methacrylate) (PHPMA) and poly(glycerol monomethacrylate) (PGMA) precursors were synthesized via ATRP and subsequently esterified using 2-sulfobenzoic acid cyclic anhydride (SBA) to produce a wide range of well-defined *strong* polyacids. Several diblock copolymers (containing one hydroxylated polymer block) have also been esterified using SBA. To the best of our knowledge, no examples of fully sulfonated polyacids prepared by esterification of hydroxylated polymers have been reported in the literature. This approach does not involve protecting group chemistry, requires only mild reaction conditions and is relatively atom-efficient.

2. Experimental

2.1. Materials

2-(Diethylamino)ethyl methacrylate (DEA) (Aldrich) was passed through a basic alumina column (Aldrich) to remove inhibitor, and then stored in a refrigerator before use. 2-Hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA) and glycerol monomethacrylate (GMA) were kindly donated by Cognis Performance Chemicals (Hythe, UK) and were used as received. Silica gel 60 (0.063–0.2 mm) was obtained from Merck (Darmstadt, Germany). Spectra/Por 6 regenerated cellulose dialysis membrane (molecular weight cut-off 1000 Da) was acquired from Sigma. D_2O, CD_3OD, $CDCl_3$, and DCl were obtained from Goss Scientific (UK). Acetone, dichloromethane, methanol and THF (all HPLC grade) were purchased from Fisher. Acetone was dried over molecular sieves (3 Å, 8–12 mesh) before use. 2-Sulfobenzoic acid cyclic anhydride (SBA) and other reagents were supplied by Aldrich and were used as received. The deionized water used in these experiments was obtained using an Elga Elgastat Option 3 water purification apparatus. The ME–Br and PEO_{45}–Br ATRP initiators were synthesized according to previously reported protocols [40].

2.2. Syntheses

2.2.1. Synthesis of hydroxylated homopolymers via ATRP

Homopolymerizations of HEMA, HPMA and GMA were conducted in 50 w/v% methanolic solutions at 20 °C. Each polymerization was carried out according to the following procedure: ME–Br initiator (2.9–2.4 mmol; target DP = 50) together with either HEMA (19.18 g, 147 mmol), HPMA (19.25 g, 134 mmol), or GMA (19.33 g, 121 mmol) was added to a round-bottomed flask. The mixture was degassed by purging the flask with nitrogen gas for 30 min. Nitrogen-degassed methanol (HPLC grade; 20.0 mL) was then added to the flask using a nitrogen-purged syringe, and the solution was purged for an additional 5 min. The copper catalyst (Cu(I)Cl; one molar equivalent relative to the ME–Br initiator) and 2,2′-bipyridine (bpy) ligand (two molar equivalents relative to Cu(I)Cl) were quickly added to the flask, while maintaining a slow nitrogen purge. The reaction mixture turned dark brown, indicating the onset of polymerization. The reaction mixture was magnetically stirred for 18 h at 20 °C in the case of HEMA and HPMA monomers, and for 4 h at 20 °C in the case of GMA monomer. Each polymerization was terminated by dilution with aerated methanol. The reaction solution turned from brown to blue-green, indicating aerial oxidation of the Cu(I) to Cu(II). This solution was then passed through a silica gel column to remove the copper catalyst, resulting in a colourless solution. The solvent was removed under reduced pressure at 30 °C to give an off-white solid and a ^{1}H NMR spectrum was recorded in CD_3OD to determine the monomer conversion (at least 99% for all three homopolymers). The dried reaction products were then purified according to the following protocols. Crude PHEMA was ground to a fine powder and then washed five times using ice-cold THF (HPLC grade). Crude PHPMA was redissolved in methanol (HPLC grade) and then precipitated in water; this dissolution/precipitation cycle was then repeated. Crude PGMA was redissolved in methanol (HPLC grade) and then precipitated in THF (HPLC grade); this dissolution/precipitation cycle was then repeated. Each of these purified polymers was dried under vacuum and ^{1}H NMR spectra were recorded in CD_3OD in order to assess their purity.

2.2.2. Esterification of hydroxylated homopolymers using SBA in either THF or acetone

For PHEMA and PHPMA, the previously reported protocol [39] for the succinic anhydride esterification of hydroxylated homopolymers in pyridine was employed using anhydrous THF (20 mL) instead of pyridine. Once the homopolymer (0.5 g, 3.65 mmol for PHEMA; 0.5 g, 3.47 mmol for PHPMA) had dissolved/become swollen in the solvent, TEA (either 1.02 ml, 7.30 mmol for PHEMA or 0.97 mL, 6.94 mmol for PHPMA; 2.0 equivalents) was added, followed by the addition

of SBA. For the esterification of PGMA, dry acetone (HPLC grade; 20 mL) was employed instead of pyridine. Once the homopolymer had become swollen in the solvent, TEA (1.40 mL, 10.1 mmol, 2.0 equivalents) was added, followed by the addition of SBA. Since GMA monomer has two hydroxyl groups, 2 equivalents of TEA or SBA per hydroxyl group was equal to 4 equivalents per GMA repeat unit. The terminated reaction mixture was reduced in volume by rotary evaporation under vacuum at 30–40 °C, sealed within a tube of benzoylated cellulose membrane tubing (molecular weight cut-off 1200–2000 Da) and then immersed in deionized water. Dialysis was performed for at least five days with daily changes of the mother liquor for fresh deionized water. After dialysis, the solution was dried under vacuum to give a solid polymer that ranged in colour from off-white to tan (esterifications conducted in either THF or acetone tended to give more coloured products). ^{1}H NMR in either D_2O or a D_2O/CD_3OD mixture confirmed the complete removal of 2-sulfobenzoic acid and free TEA or THF. However, depending on the solvent/base systems used, some fraction of TEA remained complexed with the new pendent sulfonate groups introduced during esterification. The same general protocols were employed for varying target degrees of esterification and also with differing amounts of added base.

2.2.3. Synthesis of hydroxylated PHPMA–PDEA diblock copolymer precursors

We recently reported the synthesis of PHPMA–PDEA diblock copolymers [40]. In the present work, HPMA (7.71 g, 53.48 mmol) was polymerized first in methanol at 20 °C using the following relative molar ratios: HPMA:ME–Br:Cu(I)Cl:bpy = 50:1:1:2 (i.e. target DP = 50). The monomer conversion reached 98% after 9 h. A 50 w/v% degassed solution of DEA (5.95 g, 32.11 mmol; target DP = 30) in methanol was then added at 20 °C. After the required reaction time, the reaction mixture was diluted with methanol and passed through a silica column to remove the spent ATRP catalyst. The resulting solution was then concentrated and the copolymer was precipitated into excess *n*-hexane to remove unreacted monomer(s). The obtained copolymer was finally dried under vacuum to provide an off-white solid $PHPMA_{49}$–$PDEA_{26}$ diblock copolymer (yield: 9.74 g, 74%). This protocol was repeated with varying amounts of HPMA and DEA comonomers to obtain a $PHPMA_{50}$–$PDEA_{72}$ diblock copolymer.

2.2.4. Esterification of PHPMA–PDEA diblock copolymers using SBA

In a typical experiment, $PHPMA_{49}$–$PDEA_{26}$ diblock copolymer (2.0 g) was first dissolved in 50 mL anhydrous THF under nitrogen. Two molar equivalents of TEA and two molar equivalents of SBA relative to the hydroxy groups of the PHPMA block were then added. The reaction was allowed to proceed under nitrogen at 20 °C for 72 h before termination with deionized water. THF was removed under vacuum and the resulting zwitterionic diblock copolymers were purified by dialysis, whereby the mother liquor was replaced with alternating cycles of either deionized water or saturated aqueous NaCl, prior to freeze-drying (yield: 2.62 g, 71%).

2.2.5. Synthesis of PEO_{45}–$PHPMA_{50}$ and PEO_{45}–$PGMA_{50}$ diblock copolymers

To a 50 mL one-necked flask was added PEO_{45}–Br macro-initiator (2.00 g, 0.9255 mmol). The macro-initiator was first degassed by three vacuum/nitrogen cycles, followed by the addition of HPMA (6.67 g, 46.27 mmol) or GMA (7.41 g, 46.27 mmol) and bpy (0.289 g, 1.85 mmol). The mixture was purged with nitrogen and stirred for 20 min. Then degassed methanol (either 8.8 or 10 mL for the polymerization of HPMA or GMA, respectively) was added and the solution was stirred until it became homogeneous. Cu(I)Cl (91.6 mg, 0.925 mmol) was added and the reaction mixture was heated at 50 °C using an oil bath for 6 h under nitrogen atmosphere with continual stirring. The conversion of the former monomer was 98% after 6 h and that of the latter monomer was 100% after 15 h, as determined by ^{1}H NMR spectroscopy. The polymerization was terminated by exposing to the air. The diblock copolymer solution was diluted with methanol (200 mL) and passed through a silica column to remove the spent catalyst. The solvent was then evaporated under vacuum. The solid PEO_{45}–$HPMA_{50}$ copolymer was dissolved in THF and precipitated into excess *n*-hexane so as to remove residual monomer. Yield: PEO_{45}–$PHPMA_{50}$ (7.5 g, 87.8%), PEO_{45}–$PGMA_{50}$ (7.9 g, 83.9%).

2.2.6. Esterification of PEO_{45}–$PHPMA_{50}$ and PEO_{45}–$PGMA_{50}$ diblock copolymer using SBA

In a typical experiment, PEO_{45}–$PGMA_{50}$ diblock copolymer (6.0 g) was first dissolved in 250 mL anhydrous acetone under nitrogen. Three molar equivalents of TEA and SBA relative to the hydroxy groups of the PGMA block were then added. The reaction was allowed to proceed under nitrogen at 20 °C for five days before termination with deionized water. Acetone was removed under vacuum and the resulting diblock copolymers were purified by dialysis, whereby the mother liquor was replaced with alternating cycles of either deionized water or saturated aqueous NaCl, prior to freeze-drying (yield: 8.1 g, 48%). The esterification of PEO_{45}–$PHPMA_{50}$ with SBA was conducted under similar conditions using anhydrous THF as a solvent (yield: 1.25 g, 63%).

2.2.7. Polyelectrolyte complexation of PEO_{45}–SBA:$PHPMA_{50}$ with PEO_{45}–$PQDMA_{30}$

Binary mixtures of 1.0 w/v% aqueous solutions of an anionic-based diblock copolymer (PEO_{45}–SBA:$PHPMA_{50}$) and a cationic-based diblock copolymer (PEO_{45}–$PQDMA_{30}$) were prepared in deionized water. This latter copolymer was synthesized by ATRP of methyl chloride-quaternized 2-(dimethylamino)ethyl methacrylate (QDMA) in a mixed aqueous alcohol solution according to the protocol described in [41]. The resulting binary copolymer solutions were ultrafiltered using 0.20 μm Nylon filters (Fisher Scientific). The cation/anion molar ratio was systematically varied and its effect on the size of the resulting colloidal complexes was examined by DLS measurements.

2.3. Polymer characterization

2.3.1. NMR spectroscopy

All ^{1}H NMR spectra were recorded in either D_2O, CD_3OD, $CDCl_3$ or d_5-pyridine using a Bruker AC-250 MHz spectrometer.

2.3.2. GPC analyses of precursors and the corresponding esterified homopolymers

Molecular weight distributions of hydroxylated homopolymers were analyzed by DMF GPC at 70 °C using three PL gel 10 μm 'Mixed B' columns (Polymer Laboratories, UK) in series with a Viscotek TriSEC Model 302 refractive index detector. The mobile phase contained 10 mmol LiBr and was used at a flow rate of 1.0 mL min^{-1}. The GPC columns were calibrated using 10 near-monodisperse poly(methyl methacrylate) homopolymer standards ($M_p = 2000-300{,}000$ g mol^{-1}). The data were analyzed using Viscotek TriSEC 3.0 software.

Molecular weight distributions of selected esterified polymers were assessed by aqueous GPC at 35 °C using one PL Aquagel OH 40 and one Aquagel OH 30 columns in series connected to a Polymer Labs ERC 7517A refractive index detector at 20 °C. Poly(sodium 4-styrenesulfonate) standards ($M_p = 1100-148{,}500$ g mol^{-1}) were used with an eluent of 40/60 (v/v) of methanol and 0.2 M $NaNO_3$ + 0.01 M NaH_2PO_4 aqueous solution at pH 7.0 at a flow rate of 1.0 mL min^{-1}.

2.3.3. GPC analyses of the diblock copolymer precursors

Molecular weight distributions of the PHPMA and PHPMA-based diblock copolymer precursors were determined using a THF GPC set-up comprising two Polymer Laboratories PL gel 5 μm 'Mixed C' columns (Polymer Laboratories, UK). Calibration was carried out using a series of near-monodisperse poly(methyl methacrylate) standards. The GPC eluent was of HLPC grade THF with added 2% TEA and using the BHT stabilizer as an internal standard, at a flow rate of 1.0 mL min^{-1}. The column temperature was set at 30 °C.

2.3.4. Dynamic light scattering (DLS)

DLS measurements were carried out at 20 °C using a Brookhaven BI-200SM goniometer equipped with a BI-9000AT digital correlator and a solid-state laser (125 mW, $\lambda = 532$ nm) at a fixed scattering angle of 90°. The intensity-average hydrodynamic diameter (D_h) and polydispersity index (μ_2/Γ^2) of the micelles were evaluated from cumulants analyses of the experimental correlation functions. Unless otherwise stated, 1.0 w/v% aqueous copolymer solutions in the presence of 5×10^{-3} M NaCl were used for all measurements (either NaOH or HCl was used to adjust the pH of the solution where appropriate). All solutions were ultrafiltered through 0.20 μm Nylon filters (Fisher Scientific) and were left unstirred overnight prior to measurements.

3. Results and discussion

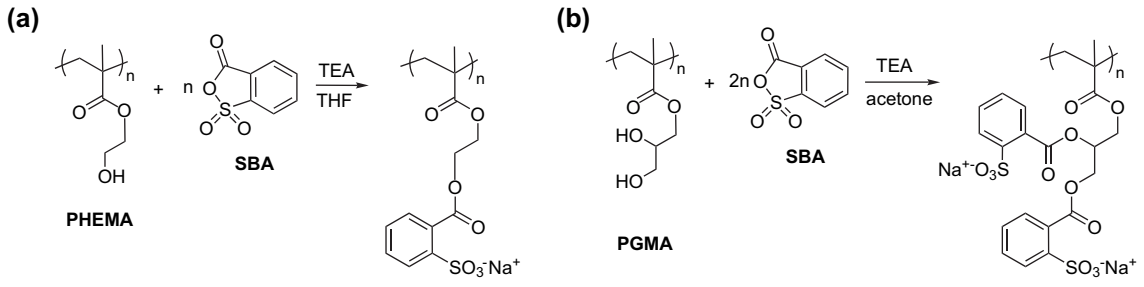
3.1. Esterification of hydroxylated homopolymers with SBA

Previously we reported the use of SA to esterify three hydroxylated homopolymers, namely PHEMA, PHPMA or PGMA, in either pyridine or THF [39]. In the present study, SBA was used to esterify the same three hydroxylated homopolymers, see Scheme 1 and Table 1. Despite the limited solubility of both SBA and the esterified product in pyridine, it was possible to achieve complete esterification of PHEMA within 48 h. However, significantly slower rates of esterification compared to those achieved using SA were observed for PHPMA and PGMA. Nevertheless, up to 87% esterification of PHPMA and essentially complete esterification of PGMA were achieved within one week at 20 °C. Preliminary results indicated that THF was a suitable solvent for the esterification of PHEMA- and PHPMA-based polymers, whereas acetone was preferred for PGMA-based polymers. Although SBA is

Table 1
Summary of the GPC molecular weight data obtained for the hydroxylated homopolymers and their corresponding strong polyacids after esterification using excess SBA

Sample ID	Hydroxy-functional homopolymer precursor		Final SBA-esterified polymer	
	M_n[a]	M_w/M_n[a]	M_n[b]	M_w/M_n[b]
SBA:PHEMA$_{45}$	13,000	1.27	16,600	1.34
SBA:PHPMA$_{50}$	12,400	1.34	19,300	1.35
2SBA:PGMA$_{50}$	13,800	1.31	16,500	1.31

[a] Determined by DMF GPC using poly(methyl methacrylate) standards.
[b] Determined by aqueous GPC using poly(sodium 4-styrenesulfonate) standards.



Scheme 1. Esterification of hydroxy-functional methacrylic homopolymer precursors using SBA at 20 °C: (a) poly(2-hydroxyethyl methacrylate) [PHPMA]; (b) poly(glycerol monomethacrylate) [PGMA].

soluble in both THF and acetone, only the PHPMA precursor is fully soluble in THF. PHEMA is only partially soluble in THF and acetone is a marginal solvent for PGMA, which is not soluble in THF. Moreover, the three homopolymers tended to precipitate at higher degrees of esterification, although the solid phase remained swollen in each case. In contrast to esterifications conducted in pyridine, which is sufficiently basic to catalyze esterification, the addition of a suitable base was required for esterifications conducted in either THF or acetone. Sodium carbonate and potassium carbonate both proved ineffective but good results were obtained with triethylamine (TEA). Thus TEA was chosen as the basic catalyst for esterifications conducted in THF and acetone.

The reaction of SBA with either PHEMA or PGMA is shown in Scheme 1a and b, respectively. We adopt the nomenclature used by Bories-Azeau and co-workers to describe the mean degree of esterification, D_{est} [6,39]. Since each GMA residue in PGMA has two hydroxyl groups, the D_{est} for PGMA is half the average number of reacted GMA residues. For example, if D_{est} is 50%, then the mean number of esterified GMA residues is 100% (with each residue containing, on average, one SBA group and one unreacted OH group). Similarly, a D_{est} of 100% for an esterified PGMA homopolymer indicates that each residue contains two SBA groups. The reproducibility was estimated to be ±2% from repeat runs.

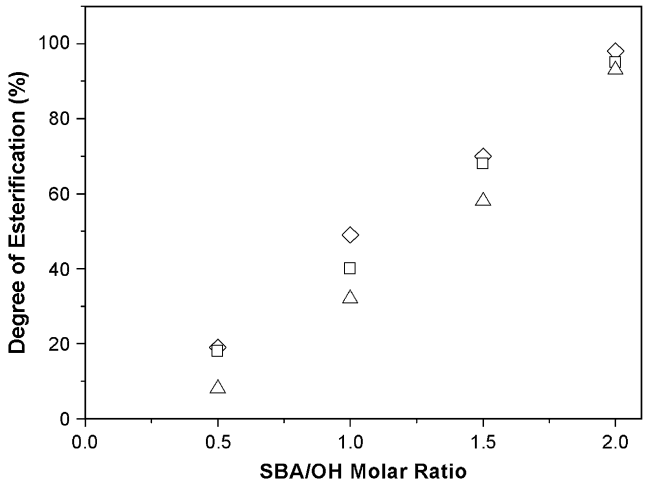


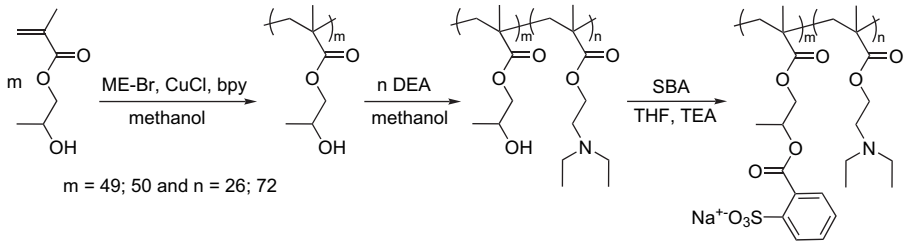
Fig. 1. Degrees of esterification obtained for $PHEMA_{50}$ (◇), $PHPMA_{50}$ (□) and $PGMA_{50}$ (△) using SBA at 20 °C for 64 h at various TEA/OH molar ratios. The initial polymer concentration was 2.5 w/v% in each case.

The data shown in Fig. 1 indicated that the best results were obtained with a SBA/hydroxyl group molar ratio of 2.0 and a TEA/hydroxyl group molar ratio of 2.0. Similar molar ratios were also required by Bories-Azeau et al. [39,40] in order to achieve high degrees of esterification of hydroxy-functional (co)polymers using succinic anhydride. The degrees of esterification obtained for PHEMA and PHPMA decreased as the TEA/hydroxyl group molar ratio was reduced from 2.0 to 1.0 (Scheme 2).

Kinetic studies indicated differing rates of reaction for the three homopolymers. In the early stages of esterification PHPMA is the most reactive precursor, which is due to its high solubility in THF (in contrast, PHEMA is only swollen in THF). However, the rate of esterification of PHPMA is reduced as the anionic character of the product increases, since this leads to precipitation. PGMA has the lowest reactivity, which is presumably related to its lower degree of swelling in acetone compared to PHEMA in THF. Reduced rates of esterification for PGMA could also be due to the increased steric hindrance of the second hydroxy group on the GMA residues, once the first hydroxy group has reacted with SBA. Interestingly, after relatively slow esterification in the first 12 h, the reaction rate increases until the D_{est} begins to approach that achieved for PHPMA and PHEMA after similar reaction times (>40 h). This may be because the partially esterified statistical copolymer is more swollen than the homopolymer precursor.

The rate of esterification of PHPMA is slower with SBA than that reported with SA under the same conditions [39]. However, essentially complete esterification of PHPMA can be eventually obtained using SBA. The faster rates of esterification observed by Bories-Azeau and co-workers are most likely due to their use of more concentrated polymer solutions (8.3 w/v%, compared to 2.5 w/v% used in this study). The heterogeneous nature of the SBA esterifications suggested that higher homopolymer concentrations may not necessarily be beneficial in the present study. However, selected SBA esterifications conducted at 5.0 w/v% polymer led to a significant increase in the mean D_{est} obtained after 24 h.

The SBA ester linkage proved to be significantly more stable with respect to hydrolysis than that of the SA ester [39]: no spectroscopic evidence for hydrolysis (indicated by the appearance of sharp peaks in the ^{1}H NMR spectra at 7–8 ppm, which corresponds to the liberated 2-sulfobenzoic acid) was observed after 26 h for SBA-esterified PHEMA solutions in D_2O at pH 2, 3, 7, 11 and 12 (the solution pH was adjusted in



Scheme 2. Synthesis of zwitterionic diblock copolymers by esterification of a hydroxy-functional diblock copolymer precursor using SBA. Only the major isomer of HPMA monomer is shown for clarity. Each reaction step was carried out at 20 °C.

each case using either DCl or NaOD). After five days, around 10% of the SBA ester bonds had been hydrolyzed at pH 12, but none of the other solutions displayed any evidence of hydrolysis. SA-esterified PHEMA homopolymer showed similar hydrolytic stability up to approximately pH 11, but at pH 12 this polymer was almost completely hydrolyzed within 16 h [39].

Bories-Azeau et al. [39] reported that higher reaction temperatures unexpectedly *reduced* the degree of esterification of hydroxylated homopolymers using SA in THF. However, in the present work a significant *increase* in the mean degree of SBA esterification [83%, 95% and 75% for PHEMA, PHPMA and PGMA, respectively] was obtained after 8 h reflux using either THF or acetone, compared to esterifications conducted at 20 °C under otherwise identical conditions. This corresponds to more than a sixfold increase in esterification in the case of the PGMA homopolymer. Thus higher reaction temperatures are undoubtedly beneficial for SBA esterification.

GPC curves are shown in Fig. 2 for two hydroxyl-functional homopolymer precursors [$PGMA_{50}$ and $PHPMA_{50}$; analyzed using DMF GPC with poly(methyl methacrylate) standards] and the two corresponding anionic polyelectrolytes obtained after esterification using excess SBA [2SBA:$PGMA_{50}$ and SBA:$PHPMA_{50}$; analyzed using aqueous GPC with poly(sodium 4-styrenesulfonate) standards]. The polydispersities of these two anionic homopolymers are generally similar to those obtained for the corresponding homopolymer precursors (see also Table 1). This indicates that no significant chain scission or cross-linking occurs during derivatization, which is understandable given the mild reaction conditions utilized.

3.2. Esterification of diblock copolymers using SBA

In previous publications [39,40] Bories-Azeau and coworkers reported that esterification of a series of hydroxyalkyl methacrylate/tertiary amine methacrylate diblock copolymers using SA led to new zwitterionic diblock copolymers that exhibited so-called 'schizophrenic' micellar self-assembly in aqueous solution. This behavior was due to the weak polybase/weak polyacid nature of the final diblock copolymers. In contrast, esterification using SBA should lead to novel weak polybase/strong polyacid diblock copolymers, which were hence expected to form only one type of micelle (with polybase cores and polyacid coronas) in aqueous solution.

SBA esterification of $PHPMA_{49}$–$PDEA_{26}$ or $PHPMA_{50}$–$PDEA_{72}$ diblock copolymers (see Table 2) in pyridine proved problematic due to the formation of an insoluble SBA:pyridine complex. Fortunately, replacement of pyridine with a TEA/THF mixture minimized this problem (although an insoluble SBA/TEA complex was formed to a lesser extent). Both the PHPMA and PDEA blocks were initially soluble in THF but the esterified diblock copolymer precipitated from THF as the esterification progressed at 20 °C. Dialysis of the final copolymer solution first against water and then with saturated aqueous NaCl solution successfully removed the excess SBA and TEA salts. Freeze-drying of this purified copolymer

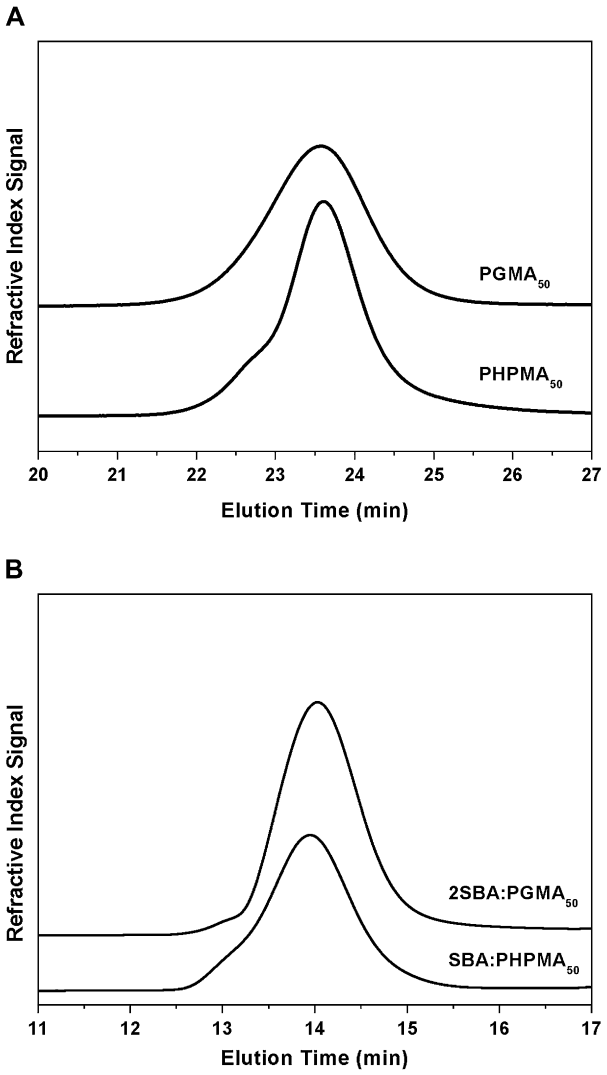


Fig. 2. GPC curves recorded for: (A) $PGMA_{50}$ and $PHPMA_{50}$ homopolymer precursors using DMF eluent and poly(methyl methacrylate) calibration standards; (B) 2SBA:$PGMA_{50}$ and SBA:$PHPMA_{50}$ using a 40/60 v/v mixed eluent comprising methanol and an aqueous solution of 0.20 M $NaNO_3$ + 0.01 M NaH_2PO_4 at pH 7 with poly(sodium 4-styrenesulfonate) standards. In both cases the flow rate was 1.0 mL min^{-1}.

Table 2
Summary of GPC molecular weight data obtained for the homopolymer and diblock copolymer precursors

Copolymer composition[a]	First block[b]		Diblock copolymer	
	M_n	M_w/M_n	M_n	M_w/M_n
$PHPMA_{49}$–$PDEA_{26}$	8400	1.22	10,500	1.24
$PHPMA_{50}$–$PDEA_{72}$	8500	1.20	17,700	1.32
PEO_{45}–$PHPMA_{50}$	3100	1.10	10,600	1.17
PEO_{45}–$PGMA_{50}$	3600[c]	1.05[c]	15,700[c]	1.30[c]

In both cases poly(methyl methacrylate) standards were used for calibration purposes.

[a] Determined by ^1H NMR spectroscopy.

[b] First block is either PEO_{45}–Br or the PHPMA precursor prior to esterification with SBA.

[c] The first three entries were analyzed by THF GPC, whereas the fourth entry required DMF GPC.

solution overnight resulted in isolation of the zwitterionic diblock copolymer. Fig. 3a shows the ^{1}H NMR spectrum of the SBA:PHPMA$_{49}$–PDEA$_{26}$ zwitterionic diblock copolymer in 0.30 M NaCl/D_2O solution at pH 2. The presence of SBA groups in the PHPMA block was indicated by the two aromatic signals at δ 7.2–8.2. Comparison of these integrated signals to those at δ 0.5–2.25 due to the methacrylic backbone (due to both comonomers) indicated that essentially complete esterification of the hydroxyl groups on the PHPMA block had been achieved.

DLS studies of 0.10 w/v% solutions of these new zwitterionic diblock copolymers in the presence of 5×10^{-3} M NaCl as a background electrolyte confirmed that relatively small micelle diameters of 16–22 nm were formed at pH 10. The strong polyacid SBA:PHPMA block is pH-insensitive, whereas the PDEA block has a pK_a of 7.3 and is therefore pH-responsive; thus these micelles were expected to comprise hydrophobic PDEA cores and anionic SBA:PHPMA coronas. This structure was supported by ^{1}H NMR studies, since no PDEA signals were observed at pH 10 in D_2O/NaOD, whereas several NMR signals corresponding to the protonated PDEA block (at δ 3.0 and δ 1.1–1.2, see Fig. 3b) were clearly visible at pH 2. The ^{1}H NMR spectrum shown in Fig. 3a was recorded in the presence of 0.30 M NaCl, which was added to screen the electrostatic attractive forces between the cationic PDEA blocks and the anionic SBA:PHPMA blocks. In the absence of any added salt, precipitation was observed, presumably because the isoelectric point for this weak polybase/strong polyacid copolymer is close to pH 2. It is anticipated that, if combined with *cationic* corona micelles described previously [42,43], these new *anionic* corona micelles will be useful for the layer-by-layer construction of multi-layer micelle films [44,45]. Unlike layer-by-layer films constructed using conventional homopolyelectrolytes, these 'mixed micelle' films will have hydrophobic domains (i.e. the PDEA micelle cores) that should allow uptake/release of actives.

PEO$_{45}$–PHPMA$_{50}$ and PEO$_{45}$–PGMA$_{50}$ diblock copolymers with relatively narrow molecular weight distributions were prepared using a poly(ethylene oxide)-based ATRP macro-initiator (Table 2). Monomodal GPC traces of the PEO$_{45}$–Br macro-initiator and the resulting PEO$_{45}$–PGMA$_{50}$ diblock copolymer are shown in Fig. 4. Esterification of both PEO$_{45}$–PHPMA$_{50}$ in THF and PEO$_{45}$–PGMA$_{50}$ in acetone was successfully carried out under similar conditions to those utilized for the PHPMA and PGMA homopolymers. Essentially complete esterification was achieved in both cases, as evidenced by ^{1}H NMR studies (see Fig. 5 for a typical spectrum). These two esterified diblock copolymers are both water-soluble and the PEO$_{45}$–2SBA:PGMA$_{50}$ diblock copolymer has proved to be a particularly interesting crystal habit modifier for calcium carbonate in biomineralization studies conducted by Dr. Meldrum's group at Bristol University, UK.

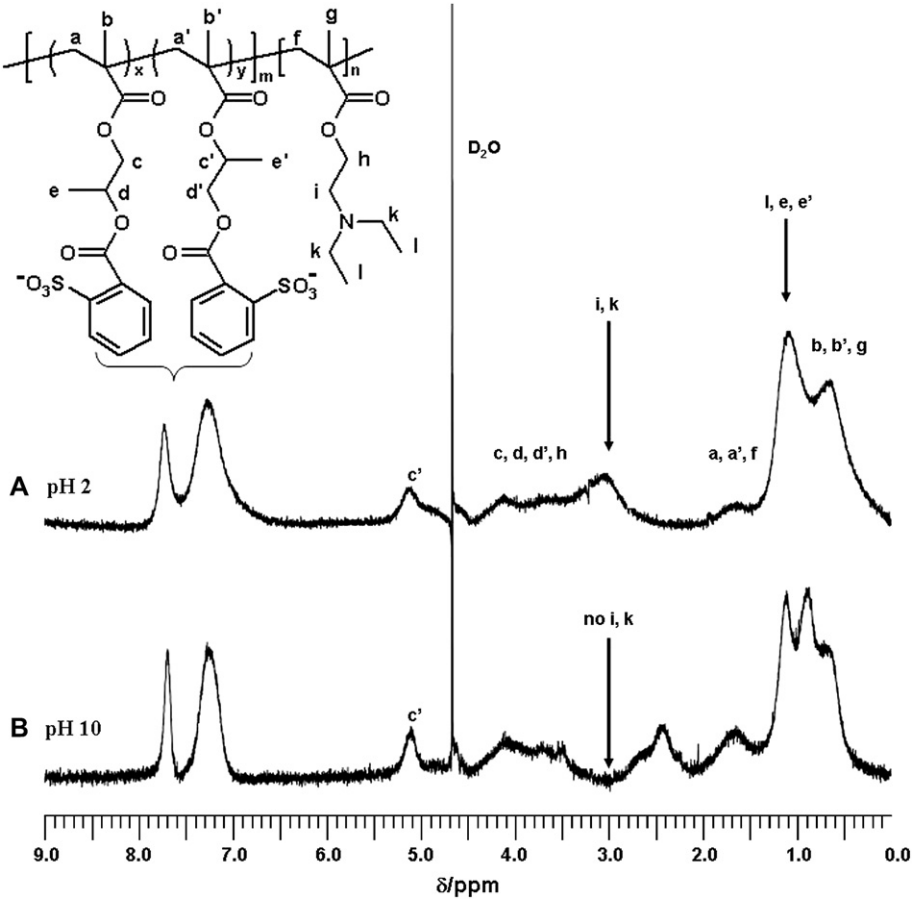


Fig. 3. ^{1}H NMR spectra recorded for SBA:PHPMA$_{49}$–PDEA$_{26}$ in D_2O in the presence of 0.30 M NaCl (A) at pH 2 and (B) at pH 10.

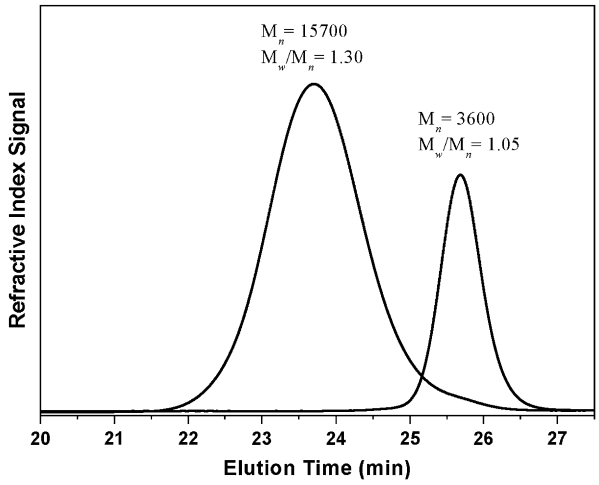
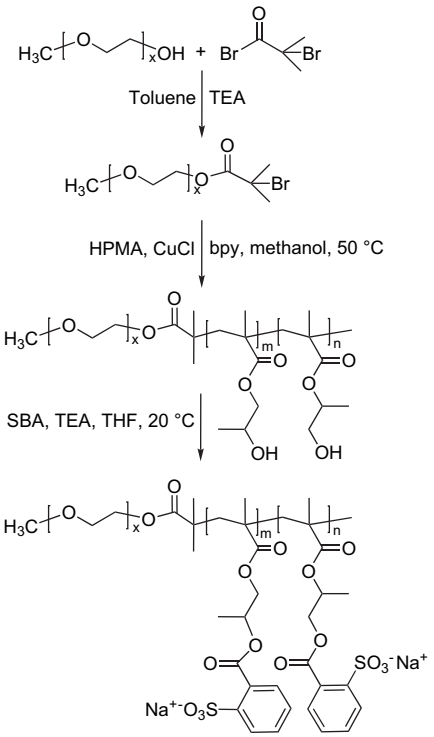


Fig. 4. GPC curves recorded for the PEO_{45}–Br macro-initiator (right) and the PEO_{45}–$PGMA_{50}$ diblock copolymer (left) using DMF eluent and poly(methyl methacrylate) calibration standards.

These results will be reported elsewhere in due course [46] (Scheme 3).



Scheme 3. Synthesis of the PEO_x–Br macro-initiator, PEO_{45}–$PHPMA_{50}$ diblock copolymer precursor and the final PEO_{45}–SBA:$PHPMA_{50}$ anionic diblock copolymer ($x = 45$).

3.3. Polyelectrolyte complex formation between binary mixtures of a PEO_{45}–SBA:$PHPMA_{50}$ diblock copolymer and a PEO_{45}–$PQDMA_{30}$ diblock copolymer in aqueous solution

It is well known that binary mixtures of oppositely-charged *homopolyelectrolytes* can form colloidal complexes in aqueous solution [47]. Recently, there have been various studies of micelle formation between an AB diblock copolymer (in which the A block is electrically neutral and B block is a polyelectrolyte) and a *homopolyelectrolyte* that is of opposite

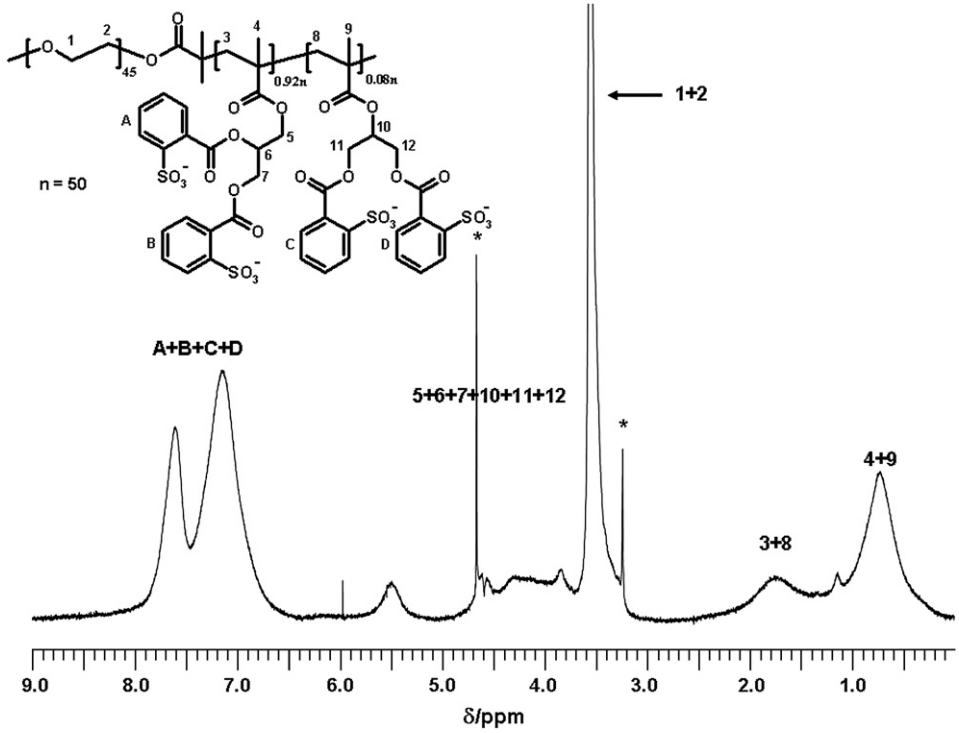


Fig. 5. Assigned ^{1}H NMR spectrum of the PEO_{45}–2SBA:$PGMA_{50}$ diblock copolymer in D_2O.

charge to the B block [48,49]. However, there are relatively few reports of micelle formation between two oppositely-charged *block copolymers* [50,51]. Thus we explored the effect of varying the relative proportions of anionic PEO_{45}–SBA:$PHPMA_{50}$ diblock with a cationic PEO_{45}–$PQDMA_{30}$ diblock [41] in an aqueous solution. DLS studies indicated that well-defined micelles of less than 35 nm were obtained when the cation/anion molar ratio was equal to or exceeded unity (see Fig. 6). An ^{1}H NMR spectrum recorded in D_2O at a cation/anion molar ratio of unity confirmed that micelle formation was due to polyelectrolyte complexation, since all the signals assigned to the methacrylic backbones of both polyelectrolytic blocks were substantially attenuated, leaving only a strong signal due to the PEO chains in the micelle coronas (see Fig. 7).

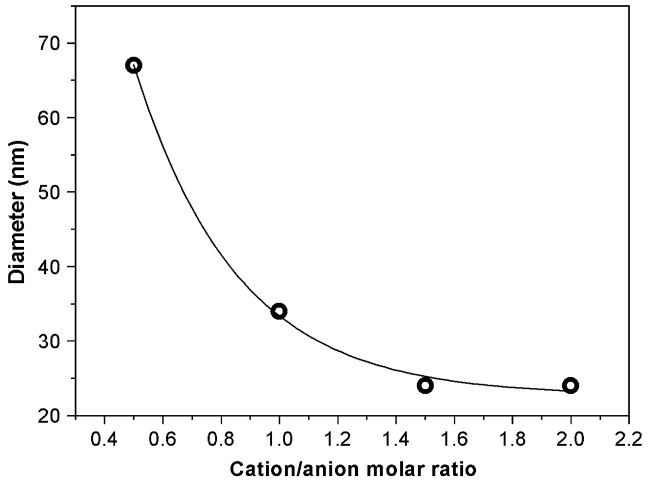


Fig. 6. Change in micelle diameter with increasing cation/anion molar ratio obtained for various mixtures of 1.0 w/v% stock solutions of PEO_{45}–$PQDMA_{30}$ and PEO_{45}–SBA:$PHPMA_{50}$ complex.

4. Conclusions

Although conducted under heterogeneous conditions, esterification of several examples of hydroxy-functional homopolymers with excess 2-sulfobenzoic acid cyclic anhydride provides a facile route to near-monodisperse strong polyacids. Moreover, this approach does not involve protecting group chemistry, requires only mild reaction conditions, and is relatively atom-efficient. New examples of well-defined strong acid-containing diblock copolymers can also be prepared by this method. Some of these examples include zwitterionic diblock copolymers that form micelles with *anionic* coronas at around neutral pH; these self-assemblies may be useful for the construction of multi-layer micelle films when used in conjunction with *cationic* corona micelles. In addition, ^{1}H NMR and DLS studies confirmed that an *anionic* PEO-based diblock copolymer formed various colloidal polyelectrolyte complexes with a *cationic* PEO-based diblock copolymer in an aqueous solution. Finally, selected strong acid-based diblock copolymers are proving to be interesting crystal habit modifiers for fundamental studies of biomineralization processes. These latter data will be reported elsewhere in due course.

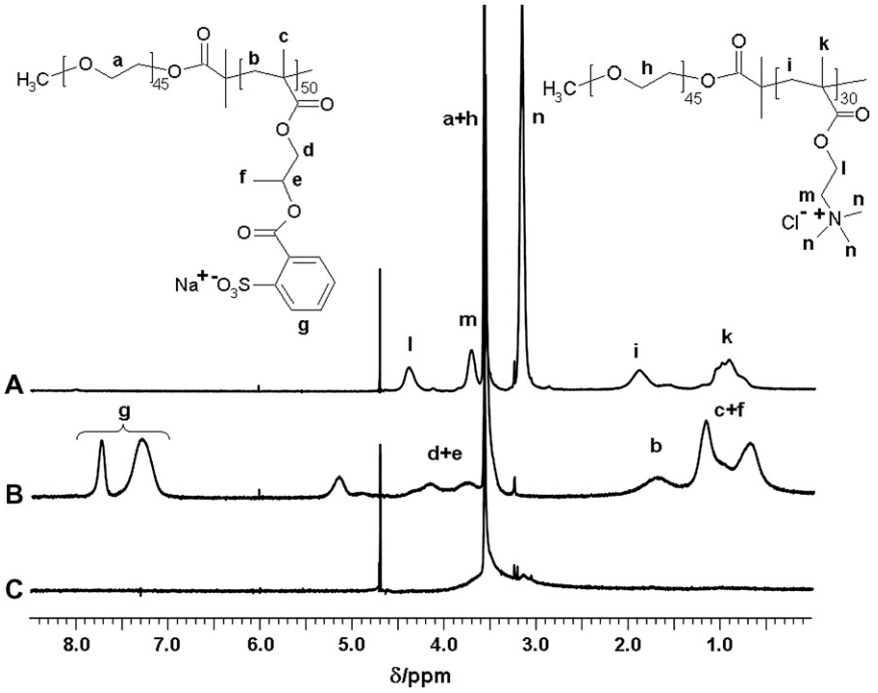


Fig. 7. ^{1}H NMR spectra in D_2O obtained for: (a) PEO_{45}–$PQDMA_{30}$ diblock copolymer, (b) PEO_{45}–SBA:$PHPMA_{50}$ diblock copolymer and (c) a binary mixture of these two diblock copolymers at a 1:1 cation/anion molar ratio. Note the attenuation of all the NMR signals in spectrum (c) except for those due to the PEO block. This provides good evidence for polyelectrolyte complexation, as expected.

Acknowledgments

EPSRC is gratefully acknowledged for a post-doctoral fellowship for C.D.V. [GR/S60419]. P.D.I. thanks EPSRC and Avecia for a PhD CASE studentship. S.P.A. is the recipient of a five-year Royal Society-Wolfson Research Merit Award. We thank Dr. F. Ganachaud for first alerting us to the commercial availability of the SBA reagent. Dr. Y. Li is thanked for the synthesis of the PEO_{45}–$PQDMA_{30}$ diblock copolymer.

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