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Synthesis of α,ω-macrozwitterionic polymers. End group analysis by SEC

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Abstract

A series of macrozwitterionic polymers have been prepared by anionic polymerisation using 2-[(dimethylamino)methyl]phenyl-lithium (DMPLi) as the initiator and 1,3-propanesultone as the terminating agent. Some observations are made on the problems associated with the synthesis of these materials, especially concerning the use of ethereal solvents and the implications these solvents have for the efficiency of the end-functionalisation reaction. Furthermore, we demonstrate that size exclusion chromatography of the sultone-terminated polymer not only allows molecular weight determination but also allows analysis of the yield of the end group functionalisation reaction at molecular weights up to 50,000 g mol^{-1}. At molecular weights of this magnitude, end group analysis by traditional methods such as NMR, IR, elemental analysis and even MALDI-MS would be of limited use. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Macrozwitterionic; End group; Size exclusion chromatography

1. Introduction

The synthesis of macrozwitterionic polymers has attracted much attention in recent years. Antonietti et al. [1] first described the synthesis of polystyrene macrozwitterions by means of anionic polymerisation using 2-[(dimethylamino)methyl]phenyl-lithium (DMPLi) as the initiator and 1,3-propanesultone as the terminating agent, the amine functionality on the initiator residue being subsequently quaternised. The initiator was synthesised in situ by reacting *sec*-BuLi with *N*,*N*-dimethylbenzylamine using toluene/diethyl ether (70/30) as the solvent. Later studies by Schädler and co-workers [2] on the same system demonstrated the benefits of using MALDI-TOF-MS for end group analysis. They found that using toluene as part of the solvent mixture for the in situ synthesis of the initiator resulted in a mixture of initiators, the desired *N*,*N*-dimethylbenzylaminolithium and benzyllithium formed by the deprotonation of toluene by *sec*-BuLi. This problem was overcome by preparing the initiator in advance in cyclohexane/diethyl ether and storing the initiator in tetrahydropyran in a freezer. The same analytical technique was used to confirm the presence of the sulphonic acid end group introduced by the termination reaction between the living polymer and 1,3-propanesultone. However, both papers reported that functionalisation with 1,3-propanesultone is not always quantitative. When polystyrene–polyisoprene macrozwitterions were prepared, the termination reaction between polyisoprenyllithium and 1,3-propanesultone resulted in only ca 70% end group functionalisation.

End group analysis is of paramount importance in the characterisation of telechelic polymers and it is essential that the materials used for subsequent experimental work are quantitatively functionalised. As the molecular weight of the polymer chain increases the relative amount of end group decreases. Traditional techniques such as NMR, IR and elemental analysis that rely on detection of the end group itself, diminish in accuracy and are really only of use on polymers with molecular weights of up to a few thousand g mol^{-1}. MALDI-TOF-MS is also limited to molecular weights of 10,000 g mol^{-1} [2]. Although progress is being made in this field, MALDI-TOF-MS is not yet available to all laboratories.

We have discovered that a mixture of sultone-functionalised and non-functionalised polystyrene elute through size exclusion chromatography (SEC) columns sufficiently far apart to resolve into separate peaks. Not only does this allow us to estimate the yield of the termination reaction but also to show with extreme clarity that any unfunctionalised polymer is completely removed following separation of the mixture by dry column flash chromatography. Whilst SEC does not determine the chemical structure of the end group, and for many end groups the elution behaviour of functionalised and unfunctionalised polymers do not differ,

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it does permit us to analyse the efficiency of the functionalisation reaction for the polymers of interest here to much higher molecular weights than other techniques allow.

2. Experimental section

2.1. Reagents

Benzene (HPLC grade, Aldrich) was washed with concentrated sulphuric acid and then distilled water before drying with calcium hydride (Aldrich). Finally the solvent was degassed by a number of freeze–thaw cycles and stored under vacuum over living polystyryllithium. Cyclohexane (HPLC grade, Aldrich) was dried over calcium hydride. Tetrahydropyran (THP) and diethyl ether (both anhydrous, Aldrich) were dried over sodium wire. Diphenylethylene (DPE) (97%, Aldrich) was distilled under vacuum after stirring with *sec*-Buli. *N*,*N*-dimethylbenzylamine (DMB) (99 + %, Aldrich) and 1,3-propanesultone (98%, Aldrich) were both dried over molecular sieves (4 Å), stirred with calcium hydride and distilled under vacuum before use. Styrene (99 + %, Aldrich) was washed with dilute sodium hydroxide solution and then distilled water (to remove inhibitor), dried over calcium chloride, and then further dried and degassed over calcium hydride. *Sec*-butyllithium (1.3 M in cyclohexane, Aldrich) was used as purchased.

2.2. Initiator synthesis

The initiator was prepared by reacting freshly distilled DMB, dissolved in a mixture of cyclohexane and diethylether (80% cyclohexane by volume), with a stoichiometrically equivalent amount of *sec*-BuLi. The mixture was stirred at room temperature overnight. The resulting precipitate was filtered, washed with cyclohexane, dissolved in THP and stored in a freezer. The entire reaction including washings and filtrations was carried out under dry nitrogen.

2.3. Polymerisation

The polymerisations were carried out in a mixed solvent of benzene/diethyl ether (80/20 (v/v)) at room temperature. In a typical reaction, approximately 100 ml of the mixed solvent and 15 g of styrene monomer were distilled into a clean dry glass vessel by vacuum transfer. After the addition of solvent and monomer the reaction vessel was brought up to atmospheric pressure with dry nitrogen. The calculated amount of initiator was injected from a gas-tight syringe through a septum. The time allowed for propagation depended upon molecular weights but was kept to an absolute minimum, for molecular weights of 5–10,000 g mol^{-1}, 10–15 min was generally sufficient. For higher molecular weights, 20,000 and 50,000 g mol^{-1}, 30–40 min was allowed for complete propagation. The basicity of the living polystyryllithium chain ends was then reduced by capping with DPE. A ten fold molar excess of DPE was added and although this capping reaction appears complete in a very short time, as indicated by the colour change from orange to deep red, to ensure complete capping the living polymer was stirred with the DPE for 30 min. A small sample of the polymer was then removed from the reaction vessel and terminated with N_2-sparged methanol for molecular weight analysis. The remaining living polymer was functionalised by the addition of 1,3-propanesultone. The polymer was then precipitated in methanol and dried in vacuo.

Thin layer chromatography (TLC) and SEC analysis of the polymer indicated a mixture of two products, the sultone functionalised polymer and a small amount of unfunctionalised polymer. The sultone functionalised polystyrene was separated from any unfunctionalised polymer by dry column flash chromatography (DCFC) [3]. The amino group on the sultone capped polymer was subsequently quaternised by reaction with a large excess of methyl bromide in 75/25 (v/v) THF/nitromethane solution, the mixture was stirred at room temperature for five days. A successful quaternisation process was first proven using polystyrene (less than 5000 g mol^{-1}) initiated with DMPLi but not functionalised with the sultone.

2.4. Dry column flash chromatography/thin layer chromatography

The sultone functionalised polystyrene was separated from any unfunctionalised polymer by dry column flash chromatography (DCFC) [3]. Silica gel 60, 0.040–0.063 mm (Merck) was used as the column packing with a mixture of hexane/THF (60/40 (v/v)) as the eluent. This separates all the unfunctionalised material which is carried through the column with the eluent, from the functionalised polymer which is held back by the polar silica gel. The functionalised polymer was then recovered from the column by changing the eluent to THF/methanol (approx. 50/50 (v/v)).

The DCFC separation process was monitored by thin layer chromatography using silica gel plates and a mixture of hexane/THF 60/40 as the eluent. Under these conditions the functionalised polymer has an R_f value of 0.0 whilst the unfunctionalised polymer elutes with an R_f value of about 0.6. TLC analysis (using hexane/THF 60/40 as eluent) was also used to show that the trial quaternisation was successful. Polystyrene initiated with DMPLi and terminated with methanol, eluted with an R_f value of 0.6. Following quaternisation with methyl bromide TLC indicated a single spot with R_f value of 0.0.

2.5. End group analysis

Analysis of the efficiency of the end-group functionalisation reaction was carried out by size exclusion chromatography using a Viscotek 200 apparatus with refractive index, viscosity and light scattering detectors. THF was used as the eluent at a flow rate of 1 ml/min and Plgel 10 μm mixed-B columns (7.5 × 300 mm) were used. The

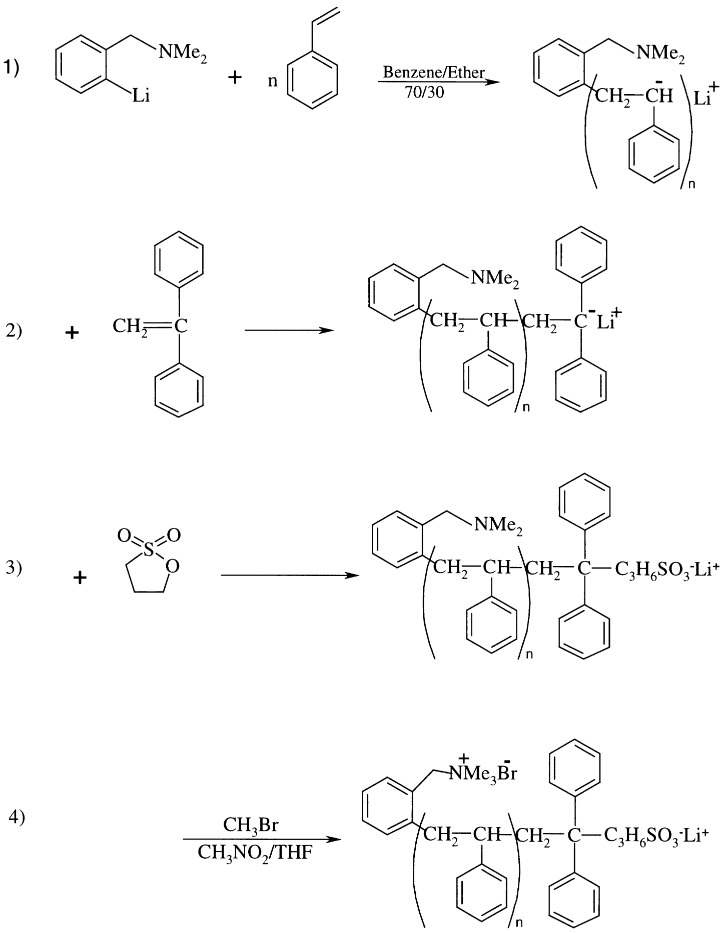

Fig. 1. Reaction scheme for the synthesis of polystyrene macrozwitterions.

sultone functionalised and unfunctionalised polystyrene eluted sufficiently far apart to be resolved into separate peaks. Whilst this effect was not noticeable using the usual set of three columns, the resolution was much better when two extra columns were added. Molecular weights were obtained using the same SEC system under normal running conditions (three columns) with narrow polystyrene standards used as calibrants.

3. Results and discussion

3.1. Synthesis

We essentially follow the synthetic route of Schädler et al. [2] to prepare polystyrene macrozwitterions, using DMPLi as the initiator and 1,3-propanesultone as the terminating agent (see Fig. 1). When using this initiator it is necessary to use a mixed solvent of benzene and ether. In the absence of ether, the rate of initiation is slow with respect to the rate of propagation and consequently the molecular weight distribution broadens. In our experience the polydispersity can be as high as 1.5 in such cases.

A range of molecular weights from 5000–50,000 g mol^{-1} was prepared with reaction times of 15–40 min depending upon the molecular weight. Samples of the polymer were removed for molecular weight analysis before reacting the remainder with a ten-fold excess of DPE for 30–40 min. The polymer was then functionalised by dropwise addition of a THF solution of 1,3-propanesultone. Addition of the sultone was continued until the deep red colour of DPELi had completely disappeared to leave a very pale yellow coloured solution. However, care should be taken not to add an excess of the 1,3-propanesultone since any excess can result in the formation of zwitterions by quaternisation of the amino group on the initiator residue by the sultone [2]. The living polymer was then finally terminated by the addition of nitrogen sparged methanol. Molecular weights by SEC of the polystyrenes prepared in this work are given in Table 1.

Table 1
Molecular weights of DMPLi initiated Polystyrene (unfunctionalised)

Sample	$\bar{M}_w$	$\bar{M}_n$	Pd
PS1	6500	6200	1.06
PS2	10,200	9900	1.03
PS3	21,000	21,500	1.02
PS4	54,300	51,100	1.06

The principal challenge in the synthesis of end-functionalised polymers is to ensure that functionalisation is quantitative. Where quantitative functionalisation is not possible it is essential to be able to detect the degree of functionalisation, to be able to separate functionalised from unfunctionalised material and to be able to show that any separation has been successful.

SEC analysis supported by TLC indicated the presence of more than one species, i.e. functionalised and unfunctionalised polystyrene. The desired sultone functionalised polymer was separated from the unfunctionalised material by dry column flash chromatography. Whilst this method is time consuming, the materials are completely separated with very little loss of polymer.

The sultone functionalised polymer was then quaternised with methyl bromide.

Successful quaternisation was indicated by TLC analysis of samples of quaternised low molecular weight polystyrene (less than 5000 g mol^{-1}) initiated with DMPLi but not functionalised with 1,3-propanesultone.

3.2. End functionalisation reaction

The termination reaction using 1,3-propanesultone has received much attention. The reaction proceeds by ring opening nucleophilic attack on the sultone by the living anionic end-group, however, several workers [1,2,4,5] have observed that this reaction is sensitive to temperature, solvent and chain end structure and therefore does not always produce quantitative functionalisation. Functionalisation of polystyrene in THF at −78°C yielded only 70% sulphonated polymer. The poor yield was attributed to competing proton abstraction and termination of the polymer by metalation of the 1,3-propanesultone. Yields were improved to greater than 95% by modifying the nucleophilicity of the anionic polystyryllithium end group by reaction with DPE. Schädler et al. [2] reported that attempts to terminate polystyrene–polyisoprene block copolymers with 1,3-propanesultone yielded only 70% of the functionalised polymer even when the polyisoprenyllithium chain end had been capped with DPE. They attributed this to incomplete reaction between polyisoprene and DPE. Though this is possible, it could be avoided by using a greater excess of DPE and allowing sufficient time for the DPE to react. However, other factors probably contribute to the less than quantitative functionalisation.

One factor that will definitely lead to reduced yields of the sulphonated polymer is the introduction of impurities. Whilst rigorous purification of materials reduces the level of impurities to very small amounts, it is practically impossible to avoid the introduction of some impurities when adding, for example, a second batch of monomer, DPE or the 1,3-propanesultone itself. Even if the materials are completely dry the introduction of a small quantity of air can lead to termination via reaction of the living polymer with oxygen or carbon dioxide.

Another probable cause of incomplete functionalisation is the reaction of the propagating species with ethereal solvents, in this case diethyl ether and THP. Organolithium compounds react with ethers [6,7] terminating the living chains in anionic polymerisation. Whilst it is not easy to quantify accurately the extent of this reaction with the solvent, we do know that the order of reactivity of ethers towards alkyllithium compounds is THF > THP > diethyl ether > diisopropyl ether and that the order of reactivity of organolithium compounds towards ethers is tertiary RLi > secondary RLi > primary RLi > phenylLi > methylLi > benzylLi. The range of reactivities is illustrated by the following examples: (a) the half life of *n*-butyllithium in diethylether at room temperature is six days [7]; (b) *n*-butyllithium is completely decomposed in THF at room temperature within 2 h [6]; (c) a 0.14 M solution of *t*-butyllithium in diethyl ether is completely decomposed after 30 min at room temperature [7]. Schädler et al. [2] found that the functionalisation of DPE capped polystyrene by 1,3-propanesultone was close to quantitative but the degree of functionalisation of DPE capped polystyrene–polyisoprene block copolymer was 70%. The propagating species polystyryllithium, is essentially a benzyllithium moiety whereas in the presence of ethers, polyisoprenyllithium is a mixture of species and consists mainly of secondary and tertiary alkyllithium moieties with about 30% primary alkyllithium end groups. All three of these species are more reactive towards ethers than the benzyllithium type end group of polystyrene. Any tertiary alkyllithium groups are particularly likely to react with either diethyl ether or THP. During the 2 h the polyisoprene was given to propagate, it is probable that a significant amount of living polymer was terminated by reaction with the solvent leading to incomplete functionalisation.

Since ethereal solvents are essential to ensure rapid initiation and narrow molecular weight distributions, the time the living polymer is exposed to the ether should be minimised to limit its effect. We found that for low molecular weight polystyrene (up to 10,000 g mol^{-1}) 10–15 min was sufficient time for complete propagation and for higher molecular weights (up to 50,000 g mol^{-1}) 30–40 min was long enough. In the work of Schädler et al. [2] up to 2 h was allowed for the propagation of polyisoprene blocks with molecular weights of 5000–25,000 g mol^{-1}. The larger blocks may require this amount of time but this seems excessive for the polyisoprene block of 5000 g mol^{-1}. Minimising the time for propagation may improve the degree of functionalisation.

3.3. SEC analysis of end functionalisation reaction

As mentioned previously, where quantitative functionalisation is not possible (as in this case) it is essential to be able to detect the degree of functionalisation, to be able to separate functionalised from unfunctionalised material and to be able to show that any separation has been successful. SEC has allowed us to analyse the reaction products of the end functionalisation reaction and to monitor the separation process.

Size exclusion chromatography separates molecules according to their size in solution [8,9]. The columns are packed with porous materials, in this case with beads of divinylbenzene crosslinked polystyrene, containing a distribution of pore sizes. As a sample passes through the column it may penetrate some of the pores, thus spending a fraction of their time within the pores. The small molecules may pass into a wide range of pores whilst larger molecules are able to penetrate far fewer pores, spending less time in the column. Hence larger molecules elute first followed by smaller molecules. In true SEC there is no interaction between the solute and the column packing. However, a mixture of sultone-functionalised and unfunctionalised polystyrene eluted sufficiently differently as to be resolved into separate peaks, presumably due to a weak interaction between the sulphonic acid end group and the column packing. In effect, the SEC columns are separating not only by molecular size but also by chemical composition, rather like HPLC. Interaction of this type between polymers and column packing is not without precedence. Polar solutes such as polyvinylpyridine polymers for example, also show some adsorption onto the column packing resulting in longer than expected elution times [10]. This phenomenon allows us to resolve the end-functionalised polymer from unfunctionalised polymer by simply changing the number of columns, without the need to alter the mobile phase, use a mixed solvent or a solvent gradient, thus removing such problems as reequilibrating columns by long term washing and baseline instability. This method not only allows us to estimate the efficiency of the functionalisation reaction but more importantly to show that following the separation by DCFC the functionalised polymer is not contaminated by any of the unfunctionalised polymer.

Typical analysis of two samples, PS2 and PS4, is included. The phenomenon of peak resolution by SEC columns of a mixture of sultone functionalised and unfunctionalised is demonstrated by Fig. 2a–d which shows PS2 at various stages of the synthetic procedure, before and after separation by DCFC.

Fig. 2a shows the chromatogram of the polystyrene initiated with DMPLi terminated with methanol (unfunctionalised) when eluted through five columns. As expected there is a single peak. Fig. 2b shows the chromatogram of the final product before the separation procedure i.e. polystyrene, capped first with DPE, then 1,3-propanesultone. This has been eluted through only three columns. There appears to be one main peak eluting at about 24.5 ml with a second smaller peak eluting just before the main peak. The main peak gives no indication that there may be a further peak “underneath” when only three columns are used. The smaller peak on the high molecular weight side (lower elution volume) is approximately double the molecular weight of the main peak and is almost certainly the result of living polystyrene coupling together and terminating due to reaction with either carbon dioxide or oxygen. There are also small peaks due to the presence of very low molecular weight impurities, analysis indicates that these have molecular weights in the low hundreds and may be some excess DPE or some residual solvent. Whilst the effect of the sulphonic acid end group was unnoticeable when using our normal set up of three columns (Fig. 2b) the presence of two peaks becomes obvious when two extra columns were added, see Fig. 2c.

Fig. 2c is a chromatogram of the same sample as Fig. 2b but using five columns. The resolution is further improved by reducing the concentration of the polymer solutions (note the difference in the levels of baseline noise between Fig. 2b and the remaining chromatograms, the concentration in 2b being about 4.9 mg/ml whilst the remaining samples were all run at concentrations of less than 1 mg/ml). In Fig. 2c we can see three main peaks. The peak at the lowest retention volume corresponds to the O_2/CO_2 terminated, unfunctionalised polystyrene and the middle peak corresponds to unfunctionalised polystyrene which has not reacted with the 1,3-propanesultone, this middle peak has the exact same elution volume as the methanol terminated polystyrene in Fig. 2a. The main peak is the desired functionalised polymer, the sulphonic acid end group appears to cause a weak interaction with the column packing leading to later elution times. Fig. 2d, is the final product after the unfunctionalised material has been separated from the functionalised material by DCFC. All traces of the two peaks at lower retention volumes in Fig. 2c have gone, leaving only the sultone functionalised polymer. From the areas under the chromatogram in Fig. 2c we estimate that the degree of functionalisation is about 80%. After separation Fig. 2d shows that the remaining material is quantitatively functionalised.

The above analysis was carried out on polymer with a molecular weight of circa 10,000 g mol^{-1}. At this molecular weight, end group analysis is extremely inaccurate using traditional techniques such as NMR and elemental analysis. Even MALDI-MS is approaching the limits at which it may be used. However SEC can be used to analyse polymers of this type with molecular weights of up to 50,000 g mol^{-1} and maybe higher (50,000 g mol^{-1} was the highest molecular weight polymer made). Fig. 3 superimposes SEC chromatograms of PS4 before and after the separation procedure.

As with PS2 when the polymer is passed through five columns the crude material resolves into three peaks and it is shown that the separation process has resulted in quantitatively functionalised material.

At molecular weights as high as 50,000 g mol^{-1}, NMR and elemental analysis are inapplicable and, at present this molecular weight is above the range at which MALDI-MS is commonly used.

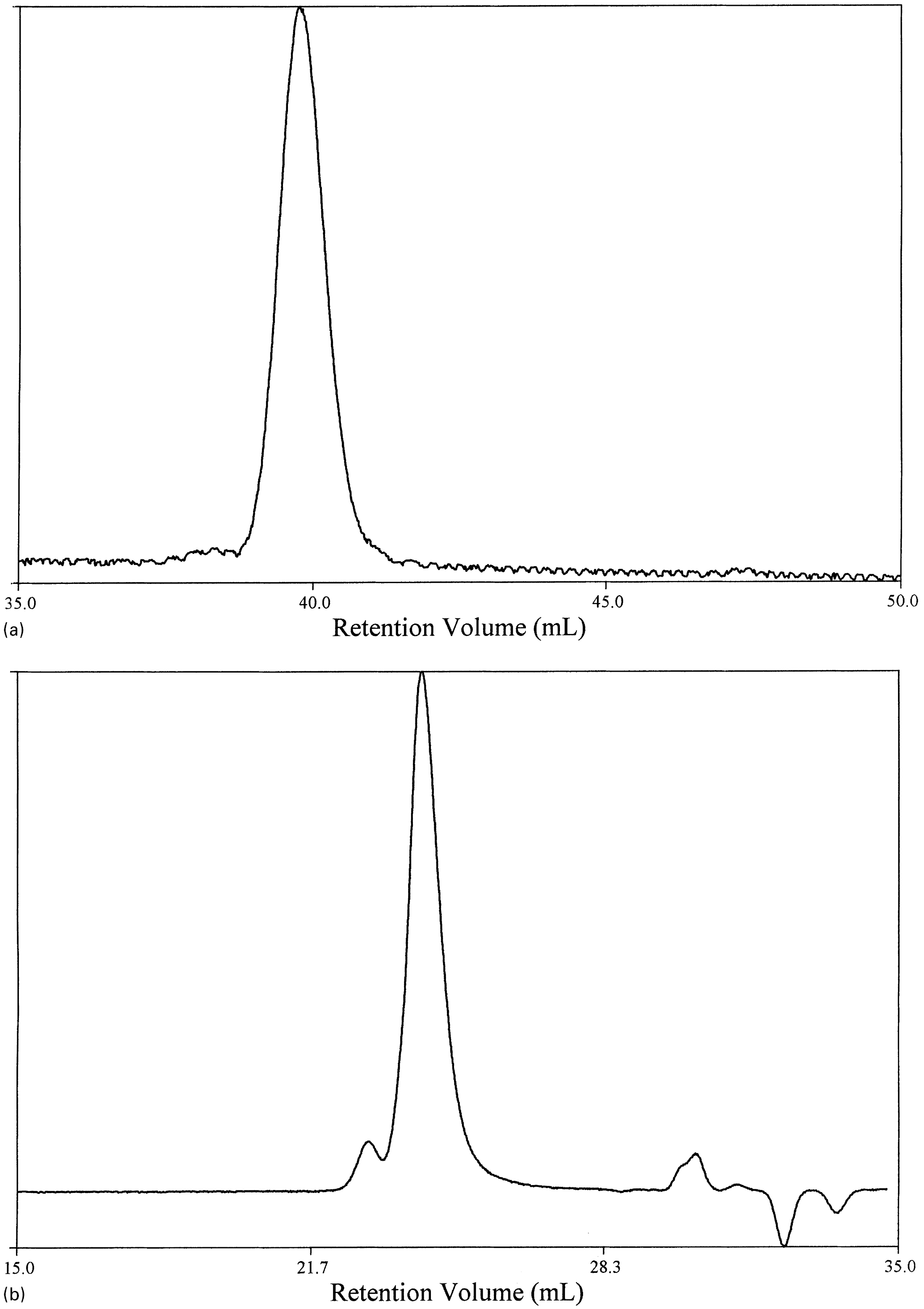

Fig. 2. (a) SEC chromatogram of the methanol terminated polystyrene (PS2) eluted through five columns. (b) SEC chromatogram of PS2 after termination with 1,3-propanesultone but before separation by DCFC, eluted through three columns. (c) As Fig. 1b but eluted through five columns. (d) SEC chromatogram of PS2 after termination with 1,3-propanesultone and separation by DCFC, eluted through five columns.

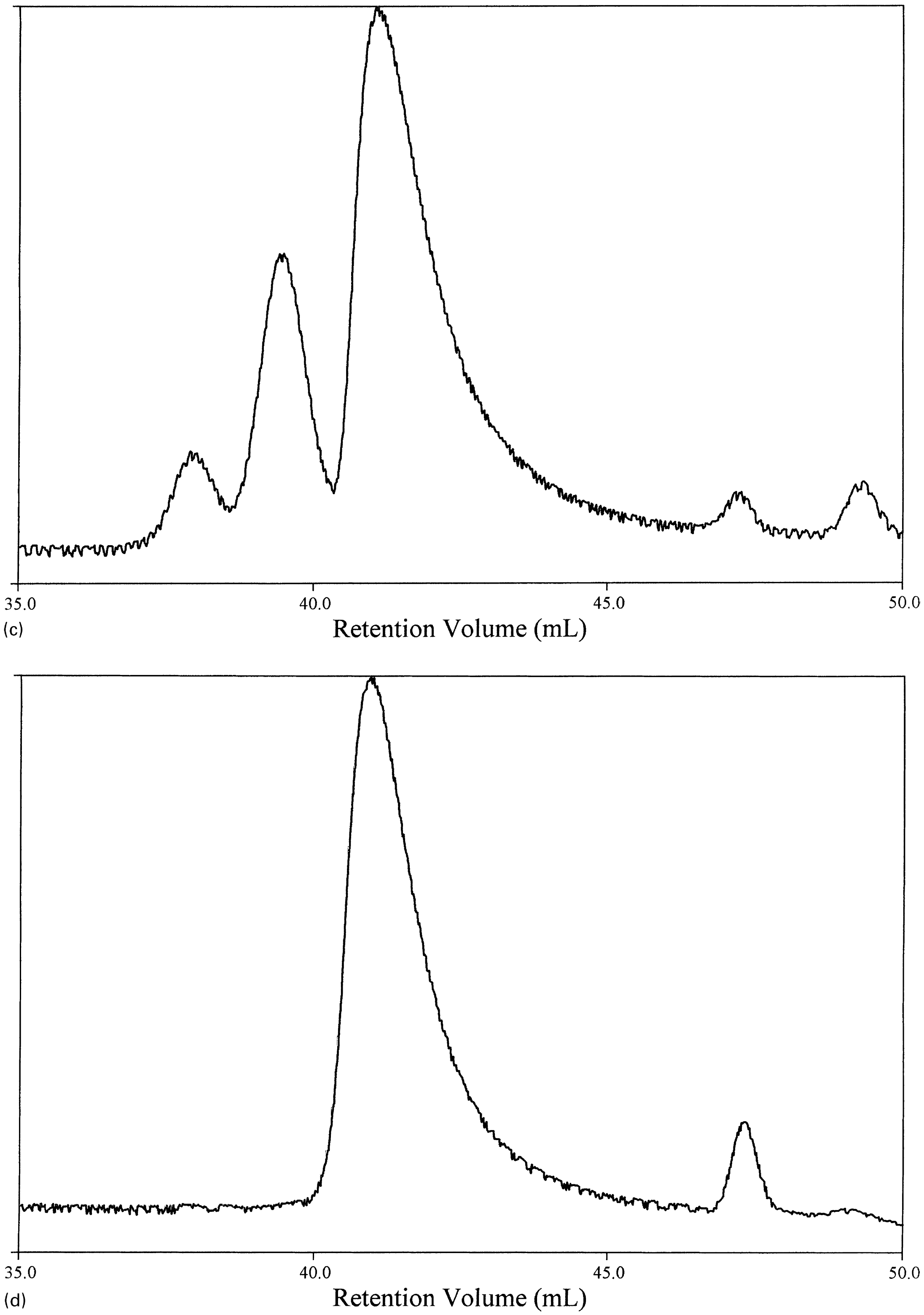

Fig. 2. (*continued*)

4. Conclusions

We have synthesised a series of macrozwitterionic polystyrene polymers essentially following the route of Schädler et al. The principal challenge in the synthesis of end functionalised polymers is to ensure that functionalisation is quantitative. Where this is not possible it is essential to be able to analyse the degree of functionalisation, to be able to

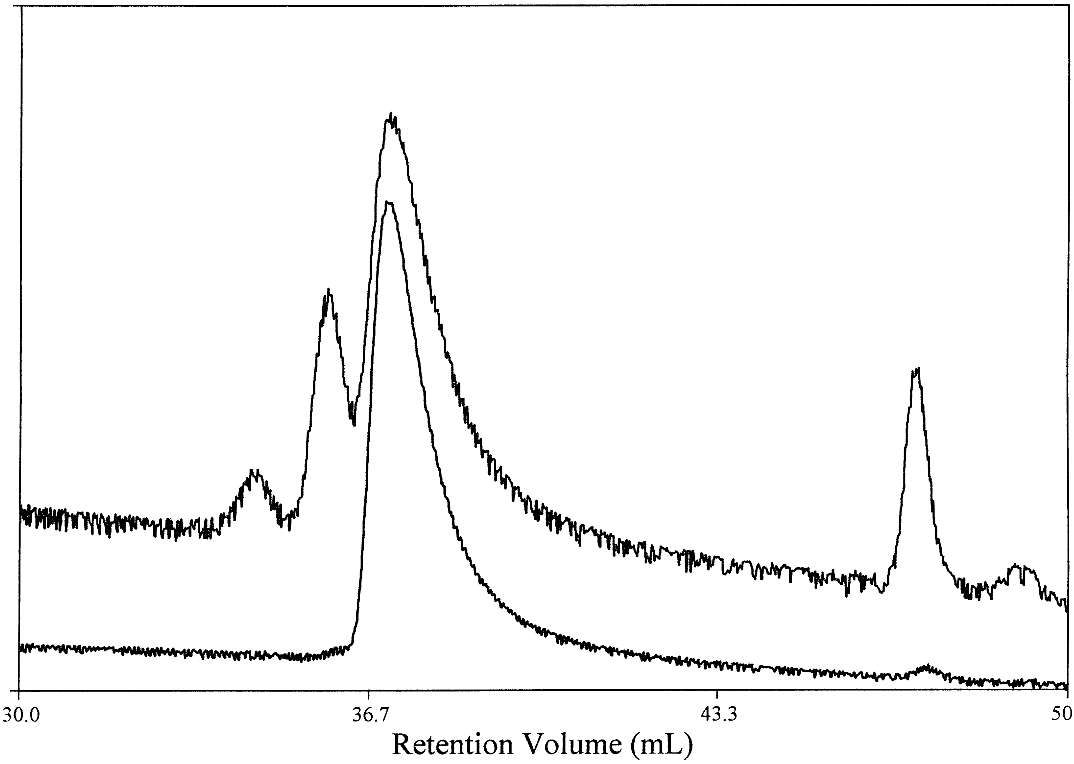

Fig. 3. SEC chromatograms of PS4 before and after separation of functionalised and unfunctionalised polymer by DCFC.

separate functionalised from unfunctionalised material and to be able to show that any separation has been successful.

The problems associated with the synthetic route have been discussed, especially the reasons for incomplete functionalisation of anionic polymers by termination with 1,3-propanesultone. We have shown that, for this particular end group, the use of size exclusion chromatography allows us to analyse not only the degree of functionalisation but also to show that following separation by DCFC, the recovered polymer is quantitatively functionalised. This analysis is possible on polymers with molecular weights as high as 50,000 g mol^{-1}. Traditional techniques such as NMR, IR, elemental analysis and even MALDI-MS would be of little use in end group analysis of polymers of this molecular weight.

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