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# Synthesis and aqueous solution properties of novel neutral/acidic block copolymers

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**Abstract**

The synthesis of novel acidic diblock copolymers via group transfer polymerisation (GTP) is described. Oligo(ethylene glycol) monomethyl ether monomethacrylate (OEGMA) was copolymerised with either benzyl methacrylate (BzMA) or tetrahydropyranyl methacrylate (THPMA). The BzMA and THPMA act as protected monomers for the methacrylic acid residues, which cannot be polymerised directly using GTP. Provided that the BzMA content of the copolymer is not too high, the benzyl groups can be selectively deprotected by catalytic hydrogenolysis to give the corresponding methacrylic acid copolymers. However, incomplete debenzylation of BzMA-rich copolymers and contamination of the final deprotected copolymers with catalyst residues limited the utility of this synthetic route. On the other hand, THPMA-based copolymers could be deprotected by acidic hydrolysis under mild conditions to give well-defined OEGMA–MAA copolymers. In this case quantitative deprotection was achieved regardless of the block composition and no catalyst contamination problems were encountered. In addition, aqueous GPC confirmed that the narrow molecular weight distributions of the precursor blocks were retained in the final OEGMA–MAA copolymers. Hence, although THPMA is not commercially available, it is preferred to BzMA for the convenient synthesis of OEGMA–MAA block copolymers. Finally, reversible micellisation of selected OEGMA–MAA block copolymers was observed in aqueous media. In the presence of 1 M $K_2CO_3$ the OEGMA chains form the micelle cores, whereas the neutral MAA block forms the micelle core at pH 1. In both cases NMR studies suggest that the micelle cores remain highly hydrated. 

*Keywords*: Group transfer polymerisation; Poly(ethylene oxide); Micellisation

## 1. Introduction

Poly(ethylene oxide) [PEO] is a well-known water-soluble polymer. Block copolymers of PEO with poly(propylene oxide) [PPO] or poly(butylene oxide) [PBO] exhibit both micellisation [1,2] and gelation [3] and have applications both as polymeric surfactants and in drug delivery. Very recently, Bromberg [4,5] has prepared derivatives of these copolymers by carrying out in situ graft polymerisation of monomers such as acrylic acid or acrylamide onto the copolymer backbone via conventional free-radical chemistry. The molecular weight distributions of these terpolymers were relatively broad but interesting thermoreversible gelation behaviour was reported.

Recently there has been considerable interest in 'hydrophilic–hydrophilic' or 'double-hydrophilic' diblock copolymers where one of the blocks is based on ethylene oxide units. For example, two German groups have described the use of commercial poly(ethylene oxide-*block*-methacrylic acid) in order to modify the crystallisation of calcium carbonate in aqueous media [6,7]. Similar block copolymers have been reported to form interesting 'block ionomer complexes' when added to cationic polyelectrolytes such as quaternised poly(4-vinyl pyridine)[8]. In related work, Kataoka's group have demonstrated [9] the formation of 'polyion complex micelles' between mixtures of poly(ethylene glycol-*block*-L-lysine) and poly(ethylene glycol-a,b-aspartic acid). Both groups are investigating drug delivery applications for these new colloidal supramolecular structures [10,11]. In addition, Ulbrich and co-workers have reported [12,13] the formation of colloidal complexes between poly(ethylene oxide)-based neutral-cationic block copolymers and DNA. Thus such copolymers are claimed to be interesting new synthetic (as opposed to viral) vectors for gene therapy applications.

Conventional free radical polymerisation has been recently employed to prepare polydisperse ABA triblock

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copolymers comprising poly(diallyldimethylammonium chloride) and poly(ethylene oxide) via a macro-initiator route [14]. These new copolymers were surface-active (adsorption at the air–water interface apparently occurring via the poly(ethylene oxide) blocks) and proved to be efficient polymeric stabilisers for the synthesis of polystyrene latex particles by emulsion polymerisation.

In an intriguing paper, Topp and co-workers [15] have described the synthesis of poly(ethylene oxide-*block*-*N*-isopropylacrylamide) using ceric ions in aqueous acid at 60°C. The pre-formed poly(ethylene oxide) block is chain-extended on addition of *N*-isopropylacrylamide. Judging by the narrow molecular weight distributions achieved ($M_w/M_n < 1.2$), this polymerisation seems to have significant 'living' character, although this possibility is not explicitly addressed by the authors. It may well be an unusual example of living free-radical polymerisation. In any event, the resulting block copolymers formed micelles reversibly on raising the solution temperature above the cloud point of the poly(*N*-isopropylacrylamide) block. Again, possible drug delivery applications have been suggested [16].

Bijsterbosch et al. reported [17] the synthesis of poly(ethylene oxide-2-methyl-2-oxazoline) diblock and triblock copolymers via living ring-opening cationic polymerisation of the oxazoline monomer using a mono- or bi-functional poly(ethylene oxide) macro-initiator, respectively. The adsorption behaviour (adsorbed amounts and layer thicknesses) of these and related copolymers at the silica–water interface was studied in some detail. We have also reported [18] the use of living cationic polymerisation for the synthesis of new poly(vinyl ether)s containing ethylene oxide residues. These new diblock copolymers exhibit thermoreversible micellisation in aqueous media. Variable temperature proton NMR spectroscopy studies confirmed that the more hydrophilic ethylene oxide-based block formed the solvated micelle corona and the less hydrophilic poly(methyl vinyl ether) block formed the partially dehydrated micelle core. More recently, we utilised the oxyanionic polymerisation chemistry reported by Nagasaki and co-workers [19] in order to prepare a range of PEO–tertiary amine methacrylate diblock copolymers [20]. Depending on the nature of the tertiary amine methacrylate block, these copolymers exhibit reversible temperature-, pH- or salt-induced micellisation.

We have recently reported [21] the synthesis of near-monodisperse statistical copolymers based on various oligo(ethylene glycol) monomethyl ether monomethacrylates (OEGMA) and methacrylic acid (MAA) via group transfer polymerisation (GTP). Herein we describe the GTP synthesis of the analogous diblock copolymers by sequential monomer addition. Both benzyl and tetrahydropyranyl esters were evaluated as precursor monomers for the methacrylic acid residues, which required protection prior to polymerisation under GTP conditions. In addition, a preliminary study of the micellisation of selected OEGMA–MAA block copolymers in aqueous media is reported.

## 2. Experimental

### 2.1. General

GTP was used for the synthesis of homopolymers and block copolymers since this ensures predictable molecular weights and narrow molecular weight distributions. All reactions were carried out under dry nitrogen. All chemicals were purchased from Aldrich, unless otherwise stated. All glassware and transfer needles were dried in an oven overnight at 140°C before use. All glassware was assembled hot from the oven, flamed under vacuum and allowed to cool to room temperature. Nitrogen was passed through both silica and $P_2O_5$ drying columns prior to use. All monomers were passed down a basic alumina column to remove the hydroquinone methyl ether inhibitor.

### 2.2. Materials

#### 2.2.1. Solvent

Tetrahydrofuran (THF) (Fisons) was initially dried over sodium wire and refluxed over potassium for three days. This dried THF was stored over 4 Å molecular sieves at room temperature prior to use.

#### 2.2.2. Monomers

OEGMA (Bisomer) was kindly donated by Laporte Specialities, UK ($M_w/M_n = 1.10$ as determined by GPC; proton NMR studies indicated a degree of polymerisation of approximately six EG units). Both OEGMA and BzMA were stirred over a mixture of calcium hydride and bis(dimethylamino)methylsilane (ABCR) and stored at −20°C. The monomers were filtered into a graduated schlenk flask before a second addition of bis(dimethylamino) methylsilane (1.5% of the volume of the monomer) and then stirred for at least 2 h under dry nitrogen prior to use.

THPMA was prepared in-house according to the method of Armstrong et al. [22]. It was stirred over calcium hydride in the presence of 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH) inhibitor, stored at 4°C and distilled under reduced pressure before transfer into the reaction vessel by cannula.

#### 2.2.3. Initiator and catalyst

1-methoxy-1-trimethylsiloxy-2-methyl-1-propane (MTS) was distilled and stored at −5°C in a graduated schlenk flask under dry nitrogen. Tetra-*n*-butyl ammonium bibenzoate (TBABB) was prepared by the method of Dicker et al. [23] and stored under a dry nitrogen atmosphere.

### 2.3. Synthesis of OEGMA homopolymer

To synthesise an OEGMA homopolymer by GTP the solid catalyst (approximately 10 mg, 2 mol % based on

Table 1
Copolymer compositions, number-average molecular weights ($M_n$) and polydispersities ($M_w/M_n$) of OEGMA homopolymers, OEGMA–BzMA and OEGMA–MAA block copolymers

| Sample code | Polymer | OEGMA in feed (mol%) | OEGMA in copolymer (mol%)[a] | $M_n$ (theory) (g mol$^{-1}$) | $M_n$ (experimental) (g mol$^{-1}$)[b] | $\frac{M_w}{M_n}$ [b] | $M_n$ (theory) after deprotection (g mol$^{-1}$)[c] | Degree of deprotection (%)[a] |
|---|---|---|---|---|---|---|---|---|
| VB04 | OEGMA | 100 | 100 | 10 000 | 9100 | 1.09 | – | – |
| VB09 | OEGMA | 100 | 100 | 6100 | 6350 | 1.15 | – | – |
| VB22 | OEGMA–BzMA | 25 | 21 | 10 000 | 12 700 | 1.10 | 8400 | 67 |
| VB15 | OEGMA–BzMA | 50 | 47 | 8650 | 10 000 | 1.15 | 8300 | 100 |
| VB24 | OEGMA–BzMA | 75 | 71 | 10 150 | 10 300 | 1.14 | 9350 | 100 |

[a] As determined by $^1$H NMR spectroscopy.
[b] As determined by GPC (calibrated with poly(methyl methacrylate) standards).
[c] Calculated assuming 100% deprotection.

Table 2
Copolymer compositions, number-average molecular weights ($M_n$) and polydispersities ($M_w/M_n$) of OEGMA–THPMA and OEGMA–MAA block copolymers

| Sample code | Block copolymer | OEGMA content (theory) (mol%) | OEGMA content (NMR) (mol%)[a] | $M_n$ (theory) (g mol$^{-1}$) | $M_n$ (experimental) (g mol$^{-1}$)[b] | $\frac{M_w}{M_n}$ [b] | Degree of deprotection (%)[a] |
|---|---|---|---|---|---|---|---|
| VB58 | OEGMA–THPMA | 20 | 16 | 9950 | 9750 | 1.16 | – |
| VB57 | OEGMA–THPMA | 41 | 41 | 10 000 | 8050 | 1.10 | – |
| VB59 | OEGMA–THPMA | 60 | 64 | 10 600 | 8250 | 1.08 | – |
| MAR | OEGMA–THPMA | 80 | 81 | 10 200 | 13 700 | 1.08 | – |
| VB58D | OEGMA–MAA | – | 16 | 6700c | 11 400d | 1.22d | 100 |
| VB93B | OEGMA–MAA | – | 41 | 6600c | 9200d | 1.19d | 100 |
| VB93A | OEGMA–MAA | – | 64 | 6200c | 7600d | 1.20d | 100 |
| MARI | OEGMA–MAA | – | 81 | 13 000c | 11 450d | 1.26d | 100 |

[a] As determined by $^1$H NMR spectroscopy.
[b] As determined by GPC (calibrated with poly(methyl methacrylate) standards).
[c] Calculated assuming 100% deprotection.
[d] As determined by aqueous GPC (calibrated with poly(ethylene oxide) standards.

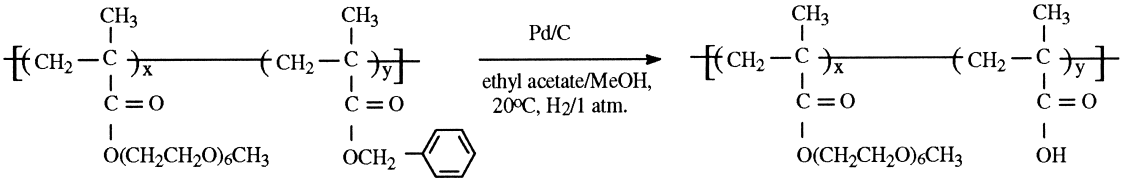


Fig. 1. Reaction scheme illustrating the catalytic hydrogenolysis of OEGMA–BzMA diblock copolymers.

initiator) was added from a side arm under a nitrogen purge into a 250 ml three-necked round bottom flask. THF (100–150 ml) was then transferred into the flask via cannula before the addition of MTS (0.30 ml). This solution was stirred for 15 min and then OEGMA monomer (10 ml) was added dropwise by cannula. A contact thermocouple was attached to the side of the reaction vessel to measure the exotherm during the addition of monomer. The reaction mixture was stirred until the solution temperature returned to ambient (approximately 2 h). Then a 0.5 ml aliquot of the reaction mixture was extracted via syringe for GPC analysis. The reaction was quenched by adding methanol (2 ml) and then the solvent was removed with a rotary evaporator. Finally, the recovered homopolymer was dried in a vacuum oven at room temperature for at least 48 h. This procedure resulted in a high yield (>96%) of homopolymer, with an $M_n$ of ca. 7300 g mol$^{-1}$ by GPC (vs. PMMA standards).

### 2.4. Synthesis of OEGMA–BzMA and OEGMA–THPMA block copolymers

To produce AB diblock copolymer, a 0.5 ml homopolymer aliquot was extracted from the reaction mixture and then the second monomer (either THPMA or BzMA) was added dropwise at about 1 ml min$^{-1}$ via cannula and a second exotherm was recorded. The reaction mixture was stirred at room temperature until the exotherm had abated (approximately 90 min). After a further 0.5 ml aliquot was extracted for GPC analysis, the block copolymer was terminated with methanol and recovered using a rotary evaporator, before drying under vacuum at 20°C for 48 h.

Copolymers of differing compositions were produced by changing the molar ratio of comonomers and different molecular weights were obtained by varying the comonomer/initiator ratio. All copolymerisations gave very high yields (>96%). In all block copolymerisations, the first monomer was OEGMA.

### 2.5. Catalytic hydrogenolysis of the OEGMA–BzMA block copolymers

Debenzylation of the OEGMA–BzMA block copolymer was achieved by catalytic hydrogenolysis. The copolymer (1.5 g) was dissolved in 100 ml of a 1:10 mixture of methanol:ethyl acetate. The Pd/C catalyst (0.375 g) was then added. The solution was stirred under hydrogen (1 atm) at 20°C for seven days. Finally, the solution was filtered to remove solid catalyst residues and the copolymer was recovered using a rotary evaporator, before drying under vacuum for 48 h at 20°C.

### 2.6. Acid hydrolysis of THPMA residues in the OEGMA–THPMA block copolymer

The THPMA-containing copolymers were deprotected by acid hydrolysis in 0.1 M HCl in THF at room temperature. Both the OEGMA–THPMA precursor and the final OEGMA–MAA copolymer were soluble in this reaction medium. In a typical hydrolysis the copolymer (8 g) was dissolved in 300 ml THF and 18 ml of 2 M HCl was added to obtain a solution of 0.1 M HCl in THF. The reaction was stirred at 20°C for 2–3 days before neutralising the excess HCl with KOH and the THF-insoluble salt was removed by filtration. The excess solvent was removed using a rotary evaporator and the copolymer was precipitated into excess *n*-hexane. Finally the copolymer was freeze-dried from water for 48 h.

### 2.7. (Co)polymer characterisation

#### 2.7.1. Gel permeation chromatography

Molecular weights and molecular weight distributions of all the copolymers were determined using two gel permeation chromatography (GPC) instruments. The non-aqueous GPC set-up comprised a Perkin–Elmer LC pump, a refractive index detector, and a PLgel 3 μm Mixed 'E' column (Polymer Labs). Calibration was carried out using a series of

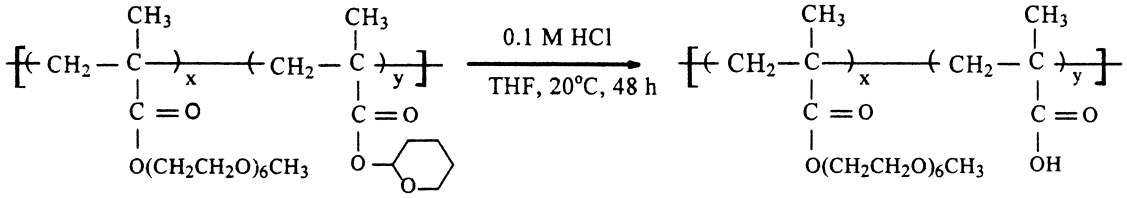


Fig. 2. Reaction scheme illustrating the acid hydrolysis of OEGMA–THPMA diblock copolymers.

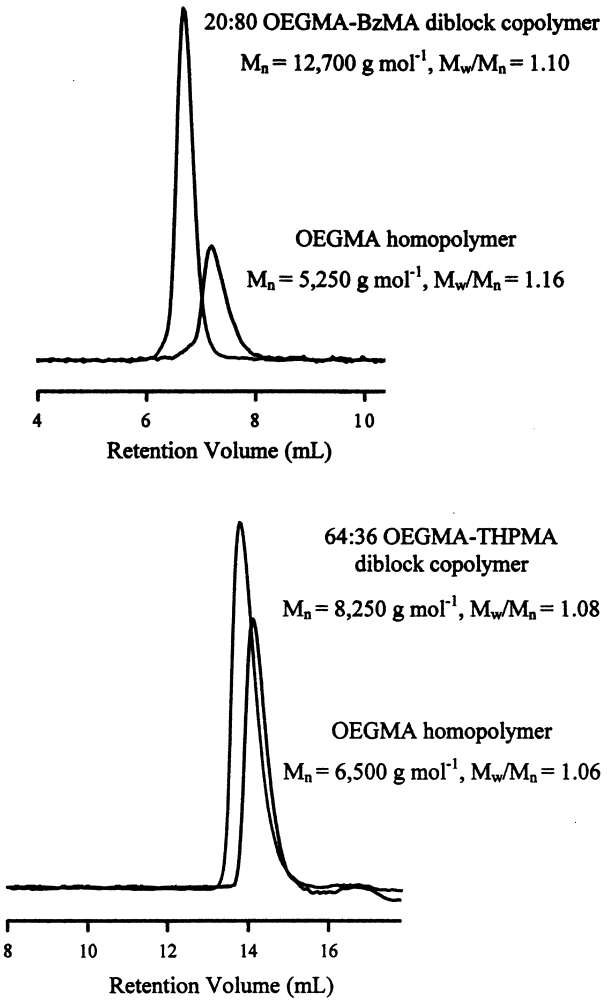


Fig. 3. GPC chromatograms of both OEGMA–BzMA and OEGMA–THPMA diblock copolymers.

poly(methyl methacrylate) (PMMA) standards (Polymer Labs), with $M_n$s ranging from 625 to 29 400. The eluent was HPLC grade THF at a flow rate of 1 ml min$^{-1}$. Aqueous GPC was used to assess molecular weights and molecular weight distributions of the deprotected water-soluble copolymers. This set-up comprised a Polymer Labs HPLC pump, a refractive index detector, and a PL aquagel-OH 40 column (Polymer Labs). Calibration was carried out using a series of poly(ethylene oxide) (PEO) standards (Polymer Labs), with $M_n$s ranging from 620 to 22 800. The eluent was a 0.25 M $NaNO_3$/0.01 M $NaH_2PO_4$ solution in doubly-distilled water at a flow rate of 1 ml min$^{-1}$.

*2.7.2. Nuclear magnetic resonance spectroscopy*

Copolymer compositions were determined using $^1$H NMR spectroscopy by comparing peak integrals assigned to the two comonomer residues. For example, the peak integral of the methoxy protons in the OEGMA residues at $\delta$ 3.2–3.4 was compared to that of the aromatic protons at $\delta$ 7.2–7.4 for benzyl methacrylate-containing copolymers (or to that of the acetal hydrogen of the THPMA ring at $\delta$ 5.8–5.9 for the THPMA-containing copolymers). All $^1$H NMR spectra were recorded using a Bruker 250 MHz instrument, using either $CD_2Cl_2$ or $CDCl_3$ as solvents for the BzMA-containing copolymers and the THPMA-containing copolymers, respectively. The degree of deprotection of the OEGMA–MAA copolymers was assessed from proton NMR spectra recorded in either $d_6$-DMSO or $d_7$-DMF.

*2.7.3. Dynamic light scattering*

The hydrodynamic size of the block copolymers in aqueous solution was measured using a Malvern PCS 4700 spectrometer equipped with a 80 mW argon ion laser operating at 488 nm and a series 7032 Multi-8 Correlator. The measurements were performed at a fixed angle of 90° and data were fitted using both monomodal cumulants analysis and the CONTIN algorithm. All measurements were carried out using 1 w/v% solutions. The solution temperature was controlled to within ±0.1°C.

*2.7.4. Cloud points of OEGMA–MAA block copolymers*

A Perkin–Elmer Lambda 2S UV/VIS spectrometer was used to determine the cloud points of OEGMA–MAA copolymers by turbidimetry.

## 3. Results and discussion

### *3.1. Polymer synthesis and deprotection*

Oligo(ethylene glycol) monomethyl ether monomethacrylate was used to synthesise homopolymers with a methacrylate backbone and oligo(ethylene glycol) side chains. Homopolymerisation gave high yields and low polydispersities. Copolymerisation of the OEGMA with either BzMA or THPMA gave, after deprotection, two series of double-hydrophilic block copolymers (see Tables 1 and 2 and Figs. 1 and 2).

The OEGMA content was varied from 20 to 80 mol% while the overall copolymer molecular weight was maintained at ca. 10 000 g mol$^{-1}$ (Tables 1 and 2). The absence of a low molecular weight tail in the GPC trace of the OEGMA block indicated minimal homopolymer contamination (see Fig. 3). The OEGMA-rich copolymers were easily isolated by precipitation into *n*-hexane. However, *n*-hexane was a poor non-solvent for the BzMA- and THPMA-rich copolymers; instead these were recovered by removing excess THF using a rotary evaporator and then drying the resulting viscous solution under vacuum at room temperature. Excellent yields were obtained in all cases. Copolymer molecular weights and molecular weight distributions were determined by GPC and are summarised in Tables 1 and 2. In general, good agreement between the theoretical and GPC molecular weights was observed and polydispersities were low ($M_w/M_n < 1.20$). The copolymer compositions determined by $^1$H NMR spectroscopy (see

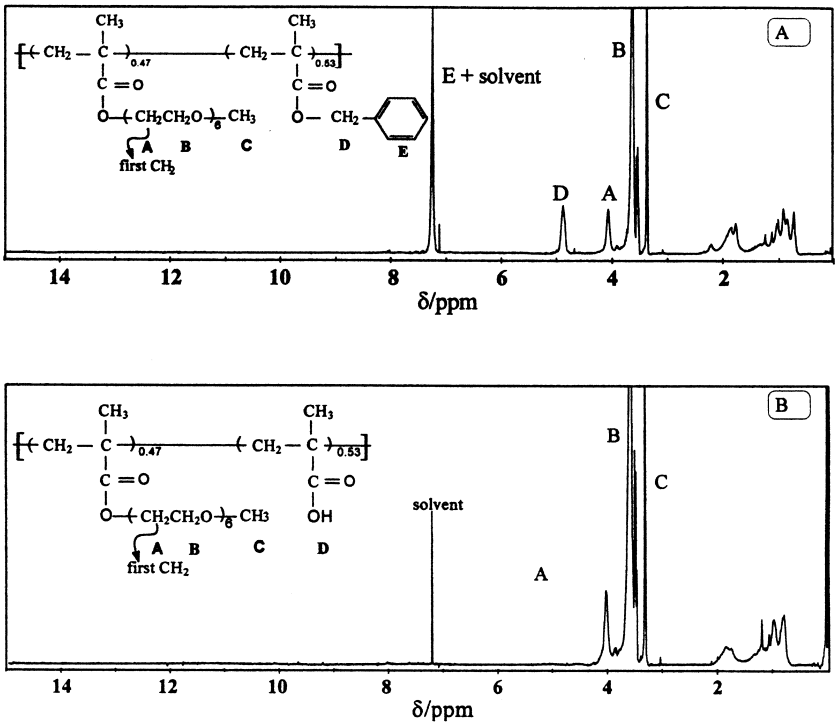


Fig. 4. $^1$H NMR spectra of a OEGMA–*b*–BzMA copolymer, before (upper spectrum) and after (lower spectrum) debenzylation in $CDCl_3$. Note the disappearance of the peaks at $\delta$ 4.9 and 7.3 due to the aromatic and benzyl protons in the lower spectrum.

Tables 1 and 2) were generally in good agreement with the expected values.

Block copolymers were prepared by first polymerising OEGMA, followed by either BzMA or THPMA. This order of monomer addition was selected in view of the broad molecular weight distributions and poor yields encountered by both Lowe [25] and Vamvakaki [26] for the homopolymerisation of THPMA (and, to a lesser extent, BzMA). Surprisingly, these workers reported much better

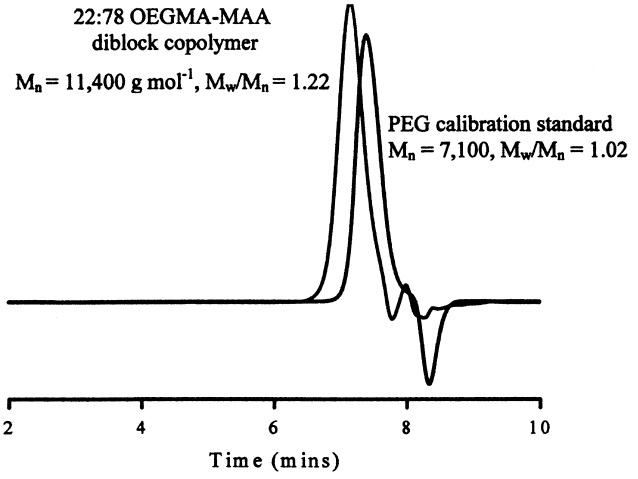


Fig. 5. Aqueous GPC chromatogram of a 22–78 OEGMA–MAA diblock copolymer obtained by acid hydrolysis of the corresponding OEGMA–THPMA precursor.

results for THPMA when it was employed as the second monomer in diblock copolymer syntheses. In contrast, narrow molecular weight distributions and near-quantitative yields were achieved for the homopolymerisation of OEGMA. Thus OEGMA was always employed as the first comonomer in our syntheses.

The BzMA-containing copolymers were deprotected by catalytic hydrogenolysis (see Table 1). Debenzylation was indicated by the disappearance (or, in some cases, reduction) of the signals due to the aromatic and benzylic protons in the NMR spectra of the precursor copolymers (see Fig. 4a and b). The actual degree of debenzylation was determined by comparing the peak integral of the non-ionised carboxylic acid proton (at $\delta$ 12.5 in either $d_6$-DMSO or $d_7$-DMF) of the deprotected copolymer to that of the terminal $-OCH_3$ protons of the OEGMA residues at $\delta$ 3.2–3.4 (see Fig. 4a). Quantitative debenzylation was only achieved for copolymers containing less than 54 mol% BzMA. At higher BzMA contents (e.g. 79 mol%) deprotection was substantially incomplete (see Table 1). Moreover, in all cases the deprotected copolymers suffered from catalyst contamination. Ultrafiltration using 0.20 μm filters failed to remove these catalyst residues. Similar problems were reported earlier by Forder et al. [24], who suggested that tri(ethylene oxide)-based poly(vinyl ethers) adsorbed irreversibly onto the catalyst particles. Thus reduction of the effective catalyst surface area due to polymer adsorption most likely accounts for the incomplete deprotection. Catalyst contamination was also reported by Vamvakaki

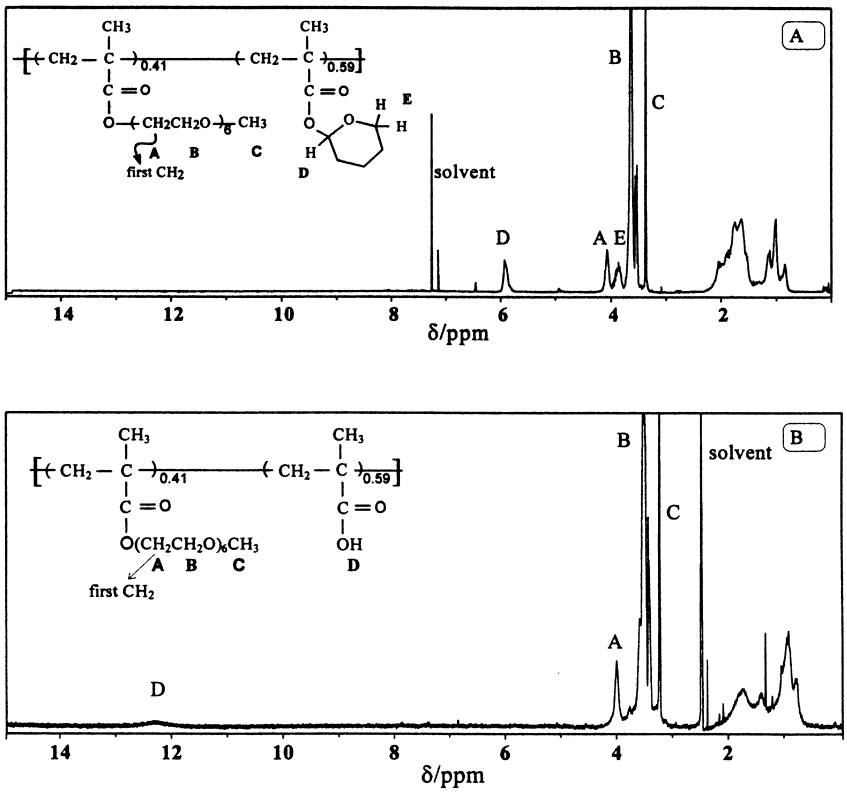


Fig. 6. $^1$H NMR spectra of a 41:59 OEGMA–THPMA copolymer, before (upper spectrum, $CDCl_3$) and after (lower spectrum, $d_6$-DMSO) deprotection. Note the disappearance of the peaks at $\delta$ 3.9 and 5.9 due to the tetrahydropyranyl protons in the lower spectrum.

et al. [21,26] for a series of OEGMA–BzMA *statistical* copolymers. In this latter study debenzylation was incomplete for copolymers containing more than 67 mol% BzMA. If the diblock copolymers prepared in the present study are adsorbed onto the heterogeneous catalyst particles via their OEGMA residues it is perhaps understandable that deprotection of the BzMA residues might be less efficient. This probably explains why incomplete debenzylation is observed at lower proportions of BzMA for the diblock copolymers compared to the analogous statistical copolymers. Even where debenzylation was completely successful, catalyst contamination prevented analysis of the final OEGMA–MAA diblock copolymers by aqueous GPC.

In an earlier study [26] Vamvakaki had experienced difficulties in deprotecting a 10–90 OEGMA–THPMA statistical copolymer in 0.1 M HCl: proton NMR studies confirmed that no reaction occurred in this aqueous medium, probably due to the insolubility of the precursor copolymer. Thus, 0.1 M HCl in THF was used for the deprotection of our OEGMA–THPMA diblock copolymers, which were soluble in this medium. The target OEGMA–MAA copolymers were readily obtained by acid hydrolysis at room temperature (see Table 2). Since a homogeneous acid catalyst was used, no catalyst contamination problems were encountered. Aqueous GPC was used to confirm that the deprotected OEGMA–MAA copolymers retained the narrow molecular weight distributions of the corresponding OEGMA–THPMA precursors (see Fig. 5). Copolymer molecular weights before and after acid hydrolysis are in good agreement, suggesting that no significant chain scission or cross-linking occurred under the mild hydrolysis conditions. The actual degree of deprotection (see Table 2) was determined using $^1$H NMR spectroscopy (see Fig. 6). Quantitative deprotection was routinely achieved, as confirmed by the complete disappearance of the acetal hydrogen signal due to the THPMA residues (observed at $\delta$ 5.8 in either $d_6$-DMSO or $d_7$-DMF in the $^1$H NMR spectra of the precursor copolymers, see Fig. 6A). The peak integral of the signal due to the –COOH proton (at $\delta$ 12.5 in $d_6$-DMSO or $d_7$-DMF) in the deprotected acidic copolymer was compared to that of the $-COOCH_2-$ signal of the OEGMA residues (located at $\delta$ 4.0–4.2; see Fig. 6B). Unlike the

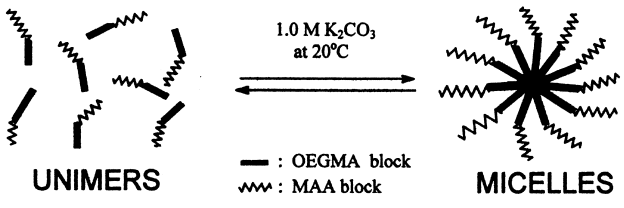


Fig. 7. Schematic representation of micelle formation (OEGMA block in the micelle core) for the OEGMA–MAA block copolymer caused by the addition of $K_2CO_3$.

Table 3
A summary of the copolymer compositions, number-average molecular weights, aqueous solution conditions and micelle diameters of OEGMA–MAA block copolymers

| Sample code | OEGMA content (mol%)[a] | $M_n$ (g mol$^{-1}$)[b] | $K_2CO_3$ concentration (mol l$^{-1}$) | Solution temperature (°C) | Micelle diameter (nm)[c] |
|---|---|---|---|---|---|
| VB58D | 16 | 11 400 | 0.5 | 25 | 2 |
| VB58D | 16 | 11 400 | 1.2 | 25 | 33 |
| VB58D | 16 | 11 400 | 1.2 | 41 | 25 |
| VB93B | 41 | 9200 | 1.2 | 25 | 22 |
| VB93B | 41 | 9200 | 1.2 | 28–38 | Aggregates[d] |
| VB93B | 41 | 9200 | 1.2 | 45 | 15 |
| VB93A | 64 | 7600 | 1.0 | 10 | 10 |
| VB93A | 64 | 7600 | 1.0 | 15–45 | Aggregates[d] |
| VB93A | 64 | 7600 | 1.0 | 55 | 39 |

[a] As determined by $^1$H NMR spectroscopy.
[b] As determined by aqueous GPC (calibrated with poly(ethylene oxide) standards).
[c] As determined by dynamic light scattering.
[d] Diameter greater than 100 nm.

BzMA-based copolymers, quantitative deprotection was achieved for all the copolymers, even for THPMA contents as high as 80 mol%.

### 3.2. Aqueous solution properties of the OEGMA–MAA diblock copolymers

#### 3.2.1. Micelles with OEGMA cores

Control experiments confirmed that the OEGMA homopolymer is insoluble in 1 M $K_2CO_3$. This behaviour was expected since linear PEO is also salted out under these conditions [27]. However, MAA homopolymer remains soluble in 1 M $K_2CO_3$ due to ionisation of the carboxylic acid group. Thus the OEGMA–MAA block copolymers were expected to form micelles in the presence of $K_2CO_3$, with the OEGMA blocks forming the cores and the MAA blocks forming the coronas (see Fig. 7). Dynamic light scattering studies confirmed this hypothesis: the 41:59 OEGMA–MAA block copolymer formed micelles of 22 nm diameter at room temperature (see Table 3).

Table 4
A summary of the aqueous solution conditions and micelle diameters for the study of the 64:36 OEGMA–MAA block copolymer (VB93A, $M_n = 7600$ g mol$^{-1}$) As determined by aqueous GPC (calibrated with poly(ethylene oxide) standards)

| pH | Temperature (°C) | Hydrodynamic diameter (nm)[a] | | | |
|---|---|---|---|---|---|
| | | Cumulants | | CONTIN | |
| | | $d_h$ | Polydispersity | $d_h^{micelle}$ | $d_h^{aggr}$ |
| 1.0 | 20 | 80 | (0.38) | 30 | 120 |
| 1.0 | 40 | 200 | (0.25) | 88 | 250 |
| 1.0 | 50 | 650 | (0.26) | 330 | 900 |
| 1.0 | 60 | 1150 | (0.10) | | 1200 |
| 2.0 | 20 | 80 | (0.37) | 29 | 110 |
| 2.0 | 40 | 90 | (0.36) | 34 | 130 |
| 2.0 | 60 | 1100 | (1.00) | 850 | 1500 |

[a] As determined by DLS.

However, the 64:36 OEGMA–MAA block copolymer formed micelles at 10°C, much larger aggregates (Table 4) (>190 nm) between 25 and 40°C, and smaller well-defined micelles again above 45°C (see Fig. 8A). This behaviour is also confirmed by temperature-dependent turbidimetry studies (see Fig. 8B): the absorption maximum at 32°C indicates the formation of large aggregates which are replaced by smaller micelles at higher temperature (the micelles scatter light less intensely, thus leading to reduced

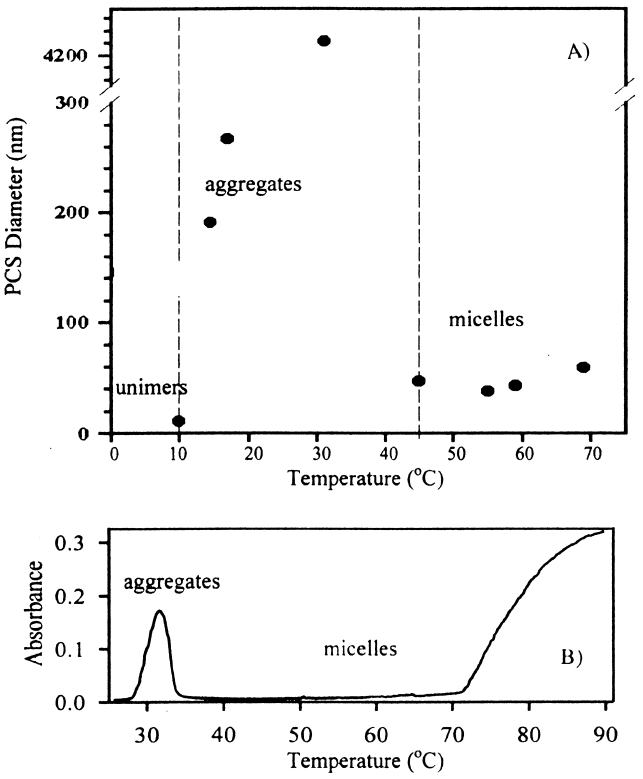


Fig. 8. Aggregation behaviour of a 64:36 OEGMA-MAA block copolymer as a function of temperature in the presence of 1.0 M $K_2CO_3$: (A) dynamic light scattering studies, (B) turbidimetric studies.

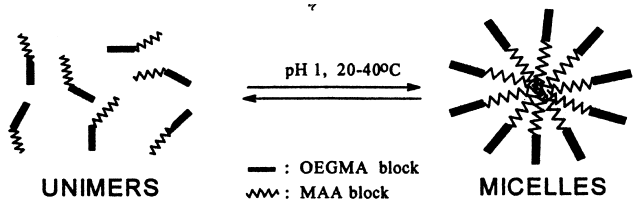


Fig. 9. Schematic representation of the formation of 'reverse micelles' (MMA block in core) by the OEGMA–MAA block copolymer on addition of HCl.

absorption). A cloud-point is observed just above 70°C due to macroscopic precipitation of the block copolymer. This aggregation is reversible: addition of acid to the aqueous copolymer solution leads to micelle dissociation (unimer formation).

*3.2.2. Micelles with MAA cores*

It is well known that MAA homopolymer exhibits a cloud point in aqueous acidic solution at elevated temperatures [31]. Thus the addition of sufficient HCl to a OEGMA–MAA block copolymer solution should allow the formation of 'reverse micelles' comprising neutral MAA cores and OEGMA coronas (see Fig. 9). It was found that relatively acidic solutions (pH 2 or lower) were necessary to suppress ionisation of the MAA residues and hence promote micelle formation. Dynamic light scattering at pH 1 confirmed the existence of micelles of 30 nm diameter even at 20°C, along with some larger aggregates of around 120 nm. At 40–60°C larger aggregates were obtained. A similar trend was obtained at pH 2. Again, micellisation could be easily reversed by adjusting the solution pH: addition of base led to ionisation of the MAA block and dissociation of the aggregates into unimers.

*3.2.3. NMR studies of micellisation*

In several recent studies we have used $^1$H NMR spectroscopy to identify the core-forming block of various micellising AB diblock copolymers in aqueous media [18,20,28,29]. Since polymer chains forming micelle cores are usually less mobile and relatively dehydrated, their NMR signals become less intense and significantly broadened relative to the NMR signals due to chains located in the micelle coronas. This approach was used to verify the first, and so far only, example of an AB diblock copolymer which is capable of forming both micelles (block A in the core) and reverse micelles (block B in the core) in aqueous media [30]. The same NMR technique was applied to the OEGMA–MAA block copolymers of the present study. However, no changes in the NMR spectra were observed for the micelles formed with either OEGMA cores ($K_2CO_3$ in $D_2O$) or MAA cores (DCl in $D_2O$). These negative NMR results strongly suggest that the micelle cores remain extensively hydrated in both cases. This is not unexpected for the OEGMA core micelles, since control experiments indicated that OEGMA homopolymer phase separates from aqueous solution as a 'liquid-like' layer in the presence of $K_2CO_3$. On the other hand, MAA homopolymer phase separated from aqueous solution as a genuine precipitate at pH 1–2, so a corresponding decrease in the NMR signal might have been predicted in this case. In summary, our homopolymer control experiments are certainly consistent with the formation of micelles with OEGMA cores and 'reverse micelles' with MAA cores, but we have been unable to corroborate this hypothesis directly by NMR spectroscopy.

## 4. Conclusions

Two series of well-defined, near-monodisperse block copolymers of oligo(ethylene glycol) monomethyl ether monomethacrylate with either benzyl methacrylate or tetrahydropyranyl methacrylate have been synthesised using GTP. Provided that the BzMA content is not too high (<54 mol%) the benzyl groups can be removed by catalytic hydrogenolysis to obtain the corresponding methacrylic acid copolymers. However, debenzylation was incomplete for BzMA contents above 75 mol% and catalyst contamination of the copolymers also limited the success of this synthetic route. In contrast, the THPMA-based copolymers could be completely deprotected by acidic hydrolysis under mild condition regardless of the block composition and no catalyst contamination problems were encountered. Furthermore, aqueous GPC confirmed the narrow molecular weight distributions of the OEGMA–MAA copolymers. Therefore, although THPMA is not commercially available, it is the preferred monomer for the convenient synthesis of OEGMA–MAA copolymers. Reversible micellisation of selected OEGMA–MAA diblock copolymers was observed in aqueous media. In 1 M $K_2CO_3$ the OEGMA block is believed to form the micelle core, whereas the MAA block forms the core at pH 1 and elevated temperature. In both cases NMR studies indicated no detectable change in solvation for the core-forming block, which suggests that the micelle cores remain highly hydrated.

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