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Cationic Amphiphilic Model Networks: Synthesis by Group Transfer Polymerization and Characterization of the Degree of Swelling

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Introduction

Synthetic hydrogels,[1,2] cross-linked hydrophilic synthetic polymers, attract considerable attention due to their applications as actuators, valves, sensors, controlled-release systems for drugs, artificial muscles for robotics, chemical memories, optical shutters, and molecular separation systems.[3] Despite the interesting applications of synthetic hydrogels, their structure is usually poorly controlled: the length of the segments between cross-links in a sample varies widely, and the comonomer distribution in these segments (in the case of copolymer hydrogels) is not uniform. The improvement of hydrogel structure may broaden their application horizon and will also provide a better understanding of the relationship between their structure and properties.

The first efforts to achieve better control over hydrogel structure were undertaken using anionic polymerization which provided segments between cross-links of uniform size.[4] These well-defined gels have been termed model networks. A special type of hydrogels are ionic hydrogels, whose model networks were prepared only recently.[5−7] A subtype of ionic model networks are amphiphilic ionic model networks comprising both ionic hydrophilic and nonionic hydrophobic blocks. Kennedy and co-workers[8] have described the preparation of such networks, which involves two steps: first, the synthesis of a hydrophobic polyisobutylene segment of precise length using "living" cationic polymerization,[9] followed by free-radical polymerization which achieves growth of the ionizable segment and simultaneous cross-linking. Although these networks displayed some new properties, including improved biocompatibility,[10] their structure is not ideal due the free-radical polymerization step which leads to a nonuniform length of the hydrophilic segment.

In an effort to produce amphiphilic ionic model networks of improved structure, we pursued their preparation using a method in which the synthesis of both blocks as well as the cross-linking step was all performed using a "living" polymerization technique. Thus, in this investigation we describe the use of group transfer polymerization (GTP)[11−13] to prepare model networks based on 2-(dimethylamino)ethyl methacrylate (DMAEMA, hydrophilic ionizable unit) and methyl methacrylate (MMA, hydrophobic nonionic unit). The flexibility of GTP allowed the synthesis of three isomeric networks with different architecture of the segments between cross-links. Moreover, the DMAEMA and MMA homopolymer networks were prepared. All networks were characterized in terms of their aqueous degree of swelling as a function of pH, and the effect of chain architecture on the swelling behavior of the amphiphilic networks was investigated.

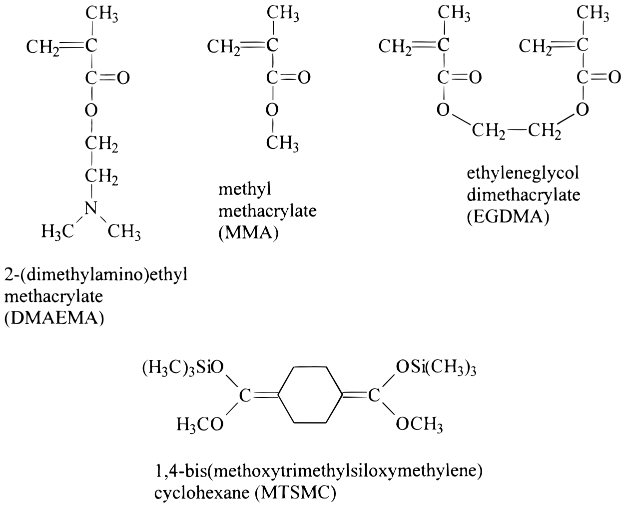

Figure 1. Chemical formulas and names of the monomers, cross-linker, and initiator used in the network preparation.

Results and Discussion

Figure 1 shows the chemical formulas and names of the monomers, DMAEMA and MMA, cross-linker, ethylene glycol dimethacrylate (EGDMA), and bifunctional initiator, 1,4-bis(methoxytrimethylsiloxymethylene)-cyclohexane (MTSMC), used for the network synthesis. While the monomers and the cross-linker are commercially available, the MTSMC initiator was in-house synthesized by the silylation of dimethyl 1,4-cyclohexanedicarboxylate, accomplished in a two-step procedure:[14] the reaction of dimethyl 1,4-cyclohexanedicarboxylate with diisopropylamine and butyllithium in absolute tetrahydrofuran at −78 °C, followed by the reaction of the mixture with trimethylsilyl chloride under the same conditions.

The model networks of this study were prepared by GTP at room temperature, using tetrahydrofuran (THF) as the solvent and tetrabutylammonium bibenzoate (TBABB)[13] as the polymerization catalyst. The amount of the EGDMA cross-linker used was 8 times the number of moles of the MTSMC initiator, as determined in preliminary investigations in which the synthesis of DMAEMA star homopolymers (with the use of a monofunctional rather than a bifunctional initiator) was optimized.[7] Scheme 1 presents the synthetic procedure used for the preparation of the equimolar amphiphilic model network based on the ABA triblock copolymer with a DMAEMA midblock. This comprises a three-step sequential monomer addition, starting with the preparation of the DMAEMA midblock, followed by the growth of the MMA end blocks, and completed with the incorporation of the dimethacrylate cross-linker. The

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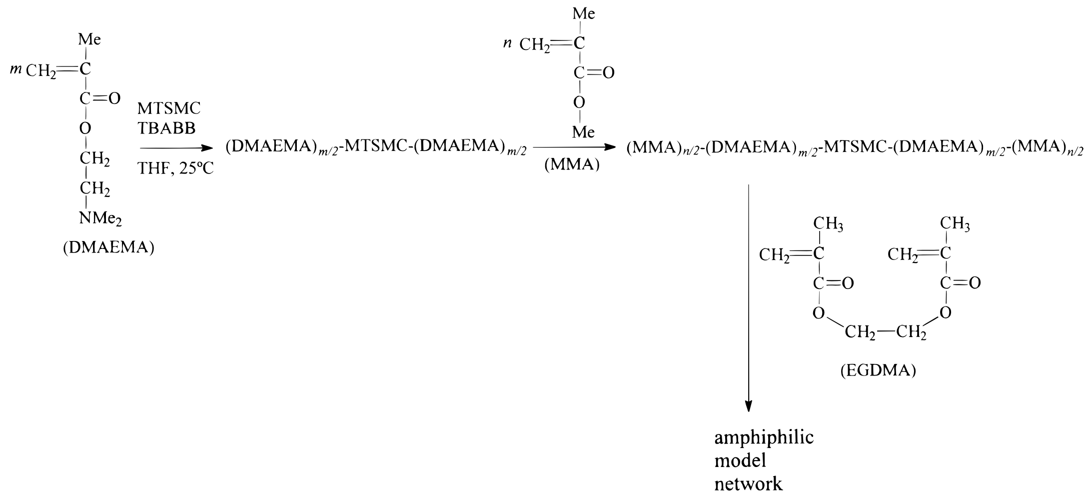
Scheme 1. Synthetic Procedure for the Preparation of the ABA Triblock Copolymer-Based Model Network with a DMAEMA Midblock



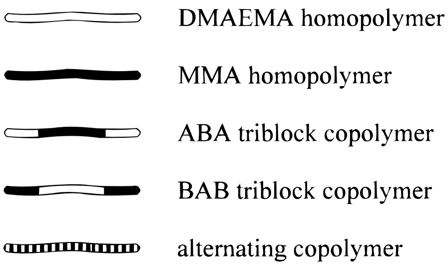


Figure 2. Schematic representation of the linear precursors of the networks. The hydrophilic DMAEMA segments are shown in white and the hydrophobic MMA segments in black.

experimental procedure in the synthesis depicted in Scheme 1 involved the charging of a 15 mL glass vial, kept under dry nitrogen atmosphere, with a small amount of TBABB and 9 mL of freshly distilled THF, followed by the addition of 0.16 mL (0.4 mmol) of MTSMC initiator and the subsequent addition of 1.7 mL (10 mmol) of DMAEMA, under stirring. The polymerization exotherm (19.8−32.6 °C) abated within 5 min, a sample was extracted for gel permeation chromatography (GPC) analysis, and 1.1 mL (10 mmol) of MMA was added. After the completion of the polymerization of this monomer (exotherm 26.2−39.2 °C) and sampling for GPC, 0.60 mL (3.2 mmol) of EGDMA cross-linker was added (exotherm 30.0−36.9 °C) which led to the gelation of the solution within seconds. The BAB triblock copolymer-based network (with an MMA midblock) was also obtained using a similar procedure in which the order of addition of the two comonomers was reversed, whereas the statistical copolymer network was synthesized by the simultaneous addition of the two comonomers. The homopolymer networks were also prepared using an analogous method in which only one monomer was polymerized before cross-linking.

Figure 2 illustrates the various structures of the linear segments between cross-links of the networks prepared in this study. All but one of the networks had segments with degrees of polymerization (DP) between cross-links of 50, and the copolymer networks had an equimolar composition. Linear polymer samples, obtained before cross-linking, were characterized in terms of their molecular weight using GPC in THF (PMMA standards, RI detector, Polymer Laboratories PL Mixed “E” column). These results are presented in Table 1. Narrow molecular weight distributions were obtained in all cases (M_w/M_n < 1.2), and the average molecular weights were close to the theoretical ones. Thus, the homogeneity in the lengths of the segments between cross-links of the networks was confirmed.

Table 1. Molecular Weights and Polydispersities of the Linear Precursors of the Networks Determined Using Gel Permeation Chromatography

polymer code	polymer formula	theor[a] MW	GPC in THF[b] M_n	M_w/M_n
MS189	$(DMAEMA)_{20}$	3336	4640	1.15
MS190	$(DMAEMA)_{50}$	8046	6870	1.12
MS198	$(MMA)_{50}$	5196	8470	1.09
MS199a	$(DMAEMA)_{25}$	4121	5820	1.11
MS199b	$(MMA)_{12.5}$-*b*-$(DMAEMA)_{25}$-*b*-$(MMA)_{12.5}$	6621	9430	1.09
MS200a	$(MMA)_{25}$	2696	3670	1.12
MS200b	$(DMAEMA)_{12.5}$-*b*-$(MMA)_{25}$-*b*-$(DMAEMA)_{12.5}$	6621	8760	1.11
MS201	(MMA-*co*-DMAEMA)$_{25}$[c]	6621	8650	1.12

[a] Initiator fragment (196 g mol^{-1}) included. [b] PMMA standards, PL mixed “E” column, RI detector. [c] Statistical copolymer.

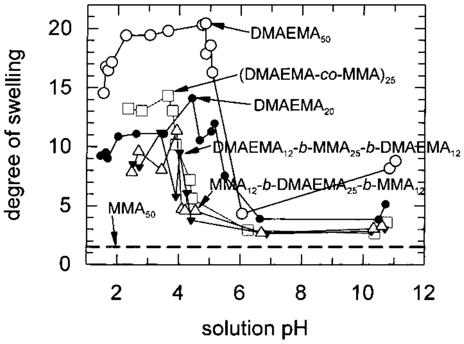


Figure 3. pH dependence of the degree of swelling of the homopolymer and copolymer networks.

Figure 3 shows the aqueous degrees of swelling of all the networks as a function of the solution pH. The degree of swelling is defined as wet network mass divided by dried network mass. Both masses were measured gravimetrically. Dry network samples were obtained by drying overnight in a vacuum oven. All degrees of swelling were determined in triplicate. The average of the measurements is presented in the figure. The size of the error bars is slightly greater than the size of the symbols. Being nonionic and hydrophobic, the MMA-homopolymer-based network remains shrunk over the whole pH range. Its degree of swelling is about 1.5, while we expected it to be 1 (i.e., containing no solvent) due to the insolubility of polyMMA in water. The discrepancy is due to the porous structure of the network, observed visually, which is maintained by the glassy nature of polyMMA (T_g of linear polymer is about 100 °C) and which can preserve some water by entrapment.

Unlike the MMA-homopolymer-based network, the other networks are not porous and more hydrophilic, exhibiting degrees of swelling between 2 and 20. The new component in these networks, DMAEMA, is a hydrophilic weak base, becoming ionized at pH lower than 8.[15−17] Thus, these materials swell under acidic pH conditions due to the osmotic pressure created by the counterions to the protonated tertiary amine monomer repeat units. For pH lower than 2, the degrees of swelling of the networks decreases again, probably due to the increase in the ionic strength conferred by the high hydrochloric acid concentration.[18] The T_g of linear DMAEMA homopolymers is low, at about −10 °C,[19] which explains the absence of porosity in the DMAEMA-containing networks of this study.

The DMAEMA homopolymer network with DP of the segments between cross-links of 50, DMAEMA_{50}, presents the highest degree of swelling of about 20 (pH between 2 and 5). The three equimolar DMAEMA−MMA copolymer networks with a DP of segments between cross-links of also 50 display lower degrees of swelling, due to the presence of the nonionic hydrophobic MMA component. In particular, the degrees of swelling of the two block copolymer networks is about 9, while that of the statistical network is about 13 (pH between 2 and 4). The aqueous degrees of swelling of nonionized and ionized amphiphilic networks prepared by the method of Kennedy[8] were much lower and varied between 1.5 and 3.5.[20−22] It is interesting to note that the maximum degree of swelling of the DMAEMA_{20} network in this study is about 11, intermediate between the values measured for the copolymer gels. The proximity in the degree of swelling of this homopolymer gel with those of the copolymer gels can be attributed to the fact that the greater hydrophilicity of this homopolymer gel, which would favor a higher degree of swelling than that of the amphiphilic gels, is counterbalanced by its low DP between cross-links, which would favor a lower degree of swelling. The lower degrees of swelling of the block copolymer gels than the statistical copolymer gel can be attributed to the microphase separation of the hydrophobic MMA blocks from the aqueous environment in the former types of gel, as shown schematically in Figure 4. This would essentially result in shorter effective lengths between the cross-links in the block copolymer-based networks, leading to lower degrees of swelling. Microphase separation in our networks is anticipated from the findings of Baines and co-workers,[23] who employed light scattering to observe the micellization in aqueous solutions of linear DMAEMA−MMA diblock copolymers prepared by GTP, and from the findings of Süvegh et al.,[24] who performed positron annihilation studies and confirmed the microphase separation of the polyisobutylene segments in DMAEMA−isobutylene model networks prepared by the method of Kennedy mentioned in the Introduction.[8]

The pH value below which the networks start to swell depends on their composition but is independent of the (copolymer) architecture. Thus, the two DMAEMA homopolymer-based networks start to swell just below pH 6, while all three MMA−DMAEMA copolymer-based networks start to swell below pH 4. The swelling behavior follows closely the hydrogen ion equilibrium of the gels, which was also investigated in this work. More specifically, the hydrogen ion titration curves of the three copolymer gels were superimposable and presented the same effective pK values of 4.4 ± 0.1. This suggests that differences in the ionization behavior of statistical and block copolymers must be small, in agreement with previous experimental work on the hydrogen ion titration of linear copolymer systems.[25] The hydrogen ion titration curves of the two DMAEMA homopolymer gels were also obtained, and an effective pK value of 5.2 was measured for each gel, consistent with the position of the degree of swelling curves of these gels shown in Figure 3. The lower effective pK value of the copolymer gels than that of the homopolymer gels is attributed to the greater hydrophobicity (due to the presence of MMA) of the copolymer gels which leads to the reduction of the dielectric constant, making ionization more difficult and reducing the pK.[18] Siegel and Firestone[26] and Philippova and colleagues[18] have observed a similar dependence of the swelling and titration behavior on the hydrophobic content of their ionic−hydrophobic gels prepared by free-radical polymerization. Linear DMAEMA of degree of polymerization 20 was also titrated in the present study, and an effective pK of 7.1 was determined. The stronger apparent basicity of the linear polymer compared to the corresponding gel can be attributed to counterion partitioning into the gel phase.[18]

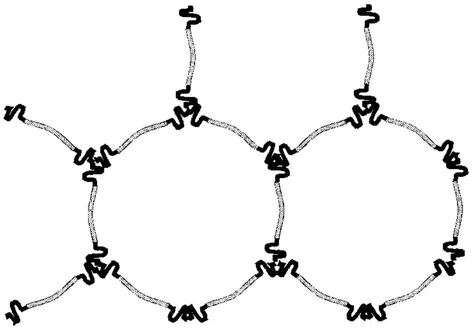


Figure 4. Schematic representation of the microphase separation of the network based on the ABA triblock copolymer with hydrophobic MMA end blocks.

Thus, the three copolymer gels present identical degree of swelling vs pH profiles, closely following their ionization profiles, which are also independent of polymer architecture (statistical vs block). These observations imply that micellization (taking place only within the block copolymer gels) does not affect appreciably the transition pH for gel swelling (although it affects the maximum degree of swelling). We are currently investigating this hypothesis with the use of a molecular thermodynamic model which can predict the degree of swelling as a function of pH of both micellized and nonmicellized gels.

Contrary to our findings, Kokufuta and co-workers[27] observed that the degree of swelling of free radically prepared copolymer gels of acrylic acid and N-isopropylacrylamide at pH 10 (where the acrylic acid units are fully ionized) was greatly affected by the method of network synthesis which determines the comonomer sequence. In this case, however, none of the gels were a model network. Moreover, the observed differences may be due to differences in molecular weights between cross-links and differences in composition, which were not checked after the cross-linking (composition may differ from the stoichiometric one due to incomplete monomer conversion or/and side effects of radiation on the functional groups).

In conclusion, we employed a "living" polymerization technique, GTP, to prepare amphiphilic, ionizable hydrogels with three different architectures: ABA triblock, BAB triblock, and statistical. The pH dependence of swelling of all three isomeric networks was the same, with a substantial increase in the degree of swelling occurring just below pH 4. The higher degree of swelling exhibited by the statistical copolymer-based network compared to that of its triblock counterparts can be attributed to the microphase separation taking place in the latter type of networks. Future work will involve the investigation of the effect of molecular weight and composition of the linear segments on the swelling profile of the networks.

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