Self-Reinforcing Hydrogels Comprised of Hydrophobic Methyl Methacrylate Macromers Copolymerized with *N,N*-Dimethylacrylamide

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ABSTRACT: Methyl methacrylate macromers were synthesized by a catalytic chain-transfer polymerization, with number-average molecular weight values ranging from 600 to 26,000. These macromers subsequently were copolymerized with dimethyl acrylamide in bulk by γ radiation to yield transparent xerogel materials. The copolymerization was confirmed by NMR analyses and by subsequent aqueous extractions of the resultant copolymers. On swelling in deionized water, hydrogels were formed that had significantly higher Young's moduli than hydrogels based on statistical methyl methacrylate/dimethyl acrylamide copolymers of equivalent composition. If macromers of high molecular weight were used, phase separation occurred, resulting in opaque hydrogel compositions. © 2000 John Wiley & Sons, Inc. J Polym Sci A: Polym Chem 38: 810–817, 2000
Keywords: hydrogel; macromer; catalytic chain transfer; modulus; equilibrium swelling; graft copolymer

INTRODUCTION

Hydrogels have found widespread applications in the biomedical industries, predominantly as contact lenses, wound dressings, and skin contact adhesives. The unique properties of hydrogels stem from the combined properties imbued by the polymeric and aqueous phases. One problem often encountered on optimizing hydrogel formulations for specific end uses is poor mechanical strength, which can restrict the utility of the materials. This is evident in membrane applications where hydrogels have many favorable and attractive properties but their fragility often precludes their adoption. The origin of this problem is quite simple; that is, a significant proportion of the material is water, which does not contribute to the mechanical integrity of the gel. Thus, the mechanical strength of hydrogels generally is improved by the addition of a crosslinking agent or hydrophobic monomer to the copolymer mixture. However, this strategy always results in a concomitant reduction in the equilibrium water content (EWC). Therefore, the final choice of a hydrogel formulation is a compromise between optimizing the hydrophilicity and maintaining the mechanical strength.

One method of achieving an optimal balance between mechanical strength and water content is to formulate a hydrogel composition based on a graft copolymer comprising a hydrophobic macromer and a hydrophilic monomer. Yamashita[1,2] showed that high strength hydrogels are possible with this approach, and he used the term *self-reinforcing gel* to describe the materials he made.

In recent work from this laboratory,[3] it was shown that hydrogels made from a hydrophilic polymer backbone substituted with long perfluoro side chains can display very high oxygen permeability by providing two pathways for oxygen transmission. As with conventional hydrogel materials, the water provides one route via dissolved oxygen. The second route is surmised to be via a cocontinuous fluorine-rich polymeric phase. Thus, hydrogels composed of distinct hydrophilic and hydrophobic regions offer great promise for many applications.

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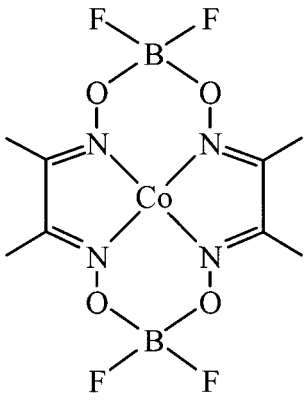
The main disadvantage to the macromer synthetic approach is that macromer production is often via anionic polymerization followed by chain-end modification. Clearly, this is likely to limit the commercial utility of the process and, it also restricts the functionalities that can be targeted. In recent years, major progress has been made in the development of living or controlled radical polymerization methods, and it is evident that these might provide an alternative synthetic route to macromers. In fact, the simplest approach to macromer synthesis may well be catalytic chain-transfer (CCT) polymerization,[4] which yields low molecular weight polymers with virtually 100% vinyl end-group functionality. The limitations to CCT are that polydisperse chains are produced and copolymerization with methacrylates is not viable (addition fragmentation is the preferred mechanism in this case). These restrictions may not be a limitation to the efficacy of the self-reinforcement mechanism in hydrogels. Liu and coworkers[5,6] published articles describing statistical methyl methacrylate/*N,N*-dimethylacrylamide (MMA/DMA) copolymers for use as hydrogels. The aim of the study described in this article was to synthesize a range of hydrophobic macromers with CCT that subsequently would be copolymerized with dimethyl acrylamide to yield novel hydrogel materials.

EXPERIMENTAL

Materials

DMA (Aldrich Pty. Ltd., http://www.sigma-aldrich.com) and MMA (Aldrich Pty. Ltd.) both were purified by being passed over a short column of basic alumina to remove the inhibitor. Distilled water was used for all swelling measurements. The CCT agent, bis[(difluoroboryl)dimethylglyoximato]-cobalt(II) (COBF; **I**), was prepared according to the method described by Bakac et al.[7]



(I)

Macromer Preparation

We prepared a stock solution of COBF in toluene by charging COBF (~4 mg) into a dry Schlenk flask and subsequently adding toluene. Conventional Schlenk techniques were used to ensure that an oxygen-free environment was maintained throughout the CCT polymerization procedure.

A solution of MMA (20 mL) in toluene (40 mL) and azobisisobutyronitrile (AIBN) (0.12 g) was purged with nitrogen for 1 h. Subsequently, the COBF solution (6 mL) was added with standard vacuum and syringe techniques. The flask then was placed in an oil bath at 60 °C for 24 h. After completion of the polymerization, the toluene was removed, and molecular weight analysis was performed by gel permeation chromatography (GPC).

Macromers of higher molecular weight [number-average molecular weight (M_n) > ~5,000] were purified further by reprecipitation in diethyl ether. The M_n's of the macromers produced were 26K, 13K, 11K, 10K, 4K, 1.5K, 900, 850, and 550 [i.e., a mixture of dimer, trimer (predominant), tetramer, pentamer, and hexamer].

Copolymerization

Mixtures of DMA and MMA macromers were made up gravimetrically, deoxygenated with nitrogen for 10 min, and irradiated in sealed polypropylene ampoules. As the different copolymerization compositions were designated by weight, this means that the total amount of MMA (repeat unit) remained constant for any given weight percent designation. A consequence of this is that the number of MMA or MMA-macromer double bonds in the monomer mixture decreased as the macromer molecular weight increased. In all cases, the γ-irradiation dose was 1 Mrad, obtained from a ^{60}Co source at the University of New South Wales, the dose rate being 0.01 Mrad/h^{-1} as determined by Fricke dosimetry. The resultant solid rods of xerogel were postcured at 90 °C for 24 h and then lathe-cut to produce thin discs (diameter = 10 mm, thickness = 1 mm) for swelling measurements and cylindrical pellets (diameter = 10 mm, thickness = 20 mm) for mechanical testing. In all cases, conversions were close to 100%, so the final copolymer composition was defined by the original feed composition.

GPC

Molecular weight distributions of the macromers were determined by GPC with a GBC Instru-

Table I. Molecular Weights of the Macromers

Macromer	M_n	M_w	PD
MMA(1)	550	1,800	3.2
MMA(2)	850	1,500	1.8
MMA(3)	900	1,600	1.9
MMA(4)	1,500	3,700	2.4
MMA(5)	4,000	9,000	2.2
MMA(6)	10,000	14,000	1.4
MMA(7)	11,000	21,000	1.9
MMA(8)	13,000	19,000	1.5
MMA(9)	26,000	42,500	1.7

ments (Castle Hill, NSW, Australia) LC1120 HPLC pump, a Shimadzu (http://www.shimadzu.com) SIL-10AD VP autoinjector, a column set consisting of a Polymer Laboratories (http://www.polymerlabs.com) 3.0-μm, bead-sized guard column (50 $\times$ 7.5 mm) followed by three linear Polymer Laboratories (PL) columns (10^5, 10^4, and 10^3), and a Shimadzu RID-10A differential refractive index detector. Tetrahydrofuran (BDH, http://www.bdh.com, HPLC grade) was used as the eluent at 1 mL/min. Calibration of the GPC equipment was effected with narrow poly(methyl methacrylate) standards (Polymer Laboratories; molecular weight range = 200 $-$ 1.6 $\times$ 10^6).

NMR

^{1}H NMR spectra were acquired on two instruments at the University of New South Wales NMR Facility: a Bruker (http://bruker.com) DMX-500 operating at 500.13 MHz for ^{1}H and 125.47 MHz for ^{13}C, and a Bruker ACF-300 operating at 300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C. Both recorded at 298 K. Samples were prepared as solutions in deuterated chloroform ($CDCl_3$).

EWC

Dimensions of the dry discs and pellets were measured with Vernier calipers, and the weighed samples were equilibrated in deionized water at room temperature, with the times to attain equilibrium being 2 to 4 weeks. During this time, the water was changed at frequent intervals to allow for the removal of water-soluble material from the samples.

The EWC of the hydrogels is defined as

$$\text{EWC} = \frac{m_S - m_0}{m_S} \times 100 \qquad (1)$$

where m_S is the mass of the swollen sample and m_0 is the mass of the dry sample.

This EWC measurement needs to be based on the xerogel weight after sol fraction extraction in the aqueous medium:

$$\%\ \text{sol fraction} = \frac{m_0 - m_E}{m_0} \times 100 \qquad (2)$$

where m_E is the dry mass of the extracted sample.

The volume fraction of the polymer within a hydrogel is given as

$$\phi_2 = \left(\frac{D_0}{D}\right)^3 \qquad (3)$$

Where D and D_0 are the diameters of the hydrogel and xerogel, respectively.

Mechanical Testing

Elastic moduli of the hydrogels were determined by stress (compression) –strain measurements. The compression rig consisted of a micrometer dial gauge capable of measuring displacement accurately to 0.01 mm. A cylindrical block of Teflon was fastened to the lower end of a shaft that was attached to this gauge. The hydrogel sample was submerged in water and placed centrally on an electronic balance. The Teflon compressor was moved into contact with the material, and the mass was recorded as a function of deformation of the sample. The sample was allowed to relax for a least 30 min before retesting. All samples were tested in triplicate.

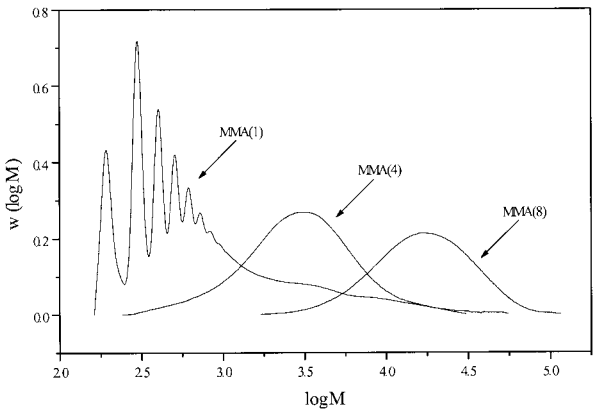


Figure 1. Typical GPC chromatograms for three of the MMA macromers.

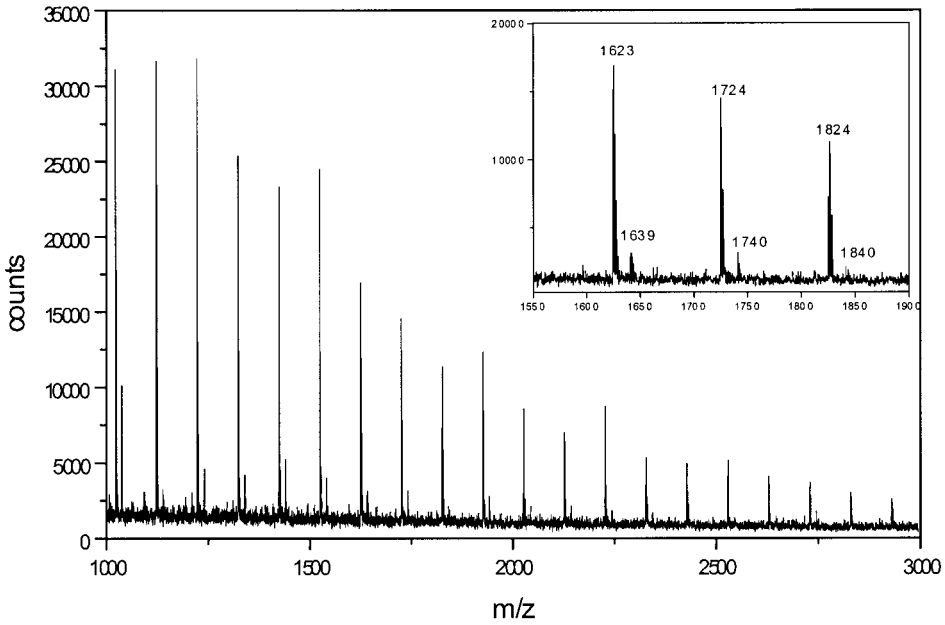
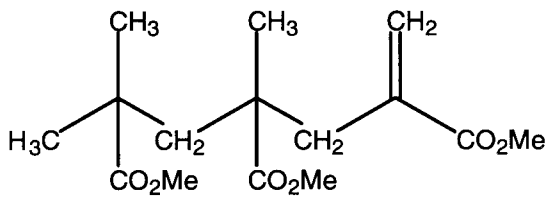


Figure 2. MALDI analysis showing the molecular weight distribution of poly(methyl methacrylate), MMA(4), generated in a CCT reaction.

RESULTS AND DISCUSSION

Macromer Synthesis

The molecular weight analysis results are given in Table I. The macromers ranged in molecular weight from about 500 to 25,000. Typical GPC chromatograms are shown in Figure 1 for three of the macromers. A matrix-assisted-laser-desorption-ionization (MALDI) mass spectrometry analysis showing the molecular weight distribution of poly(methyl methacrylate) (PMMA) generated in a CCT reaction is given in Figure 2. Each peak mass (m) is consistent with the expression $m = (100.1 \times n) + 23.0$, where n is the degree of polymerization, 100.1 is the mass of the repeat unit, and 23.0 is the mass of the sodium counterion. There are no chains evident with an AIBN initiator fragment (mass = 68). This result is concordant with a polymerization process dominated by CCT.[4] Finally, an NMR analysis of the lowest molecular weight macromer is given in Figure 3(a), clearly showing that the vinyl peaks are consistent with a typical macromer structure (**II**).



Macromer Reactivity

Proof of macromer reactivity in the copolymerization reaction was obtained by ^{1}H NMR. Figure 3 shows three NMR spectra corresponding to (a) the macromer, (b) DMA and (c) a copolymer dissolved in $CDCl_3$. The vinyl peaks are evident in the spectra of 3(a,b) and plainly absent in 3(c). The spectrum of 3(c) also shows the presence of peaks from both the macromer and DMA. Some limited data is available on the reactivity of the macromer double bonds in copolymerization reactions. Cacioli et al.[8] showed that MMA macromers prepared via CCT copolymerized with ethyl acrylate. In more recent work, Abbey et al.[9] estimated reactivity ratios for MMA dimers (made by CCT) with styrene. A number of patents[10–12] also have been published on synthesizing comb and star polymers with macromers produced by CCT via copolymerization with acrylate monomers. In summary, it seems clear from the NMR analysis that copolymerization indeed occurred, a result that is quite consistent with previous studies.

Xerogel and Hydrogel Appearance

All of the xerogel materials were transparent in the dry state and maintained their transparency on swelling with the exception of the copolymers MMA(7), MMA(8), and MMA(9), which displayed an opacity consistent with phase segregation.

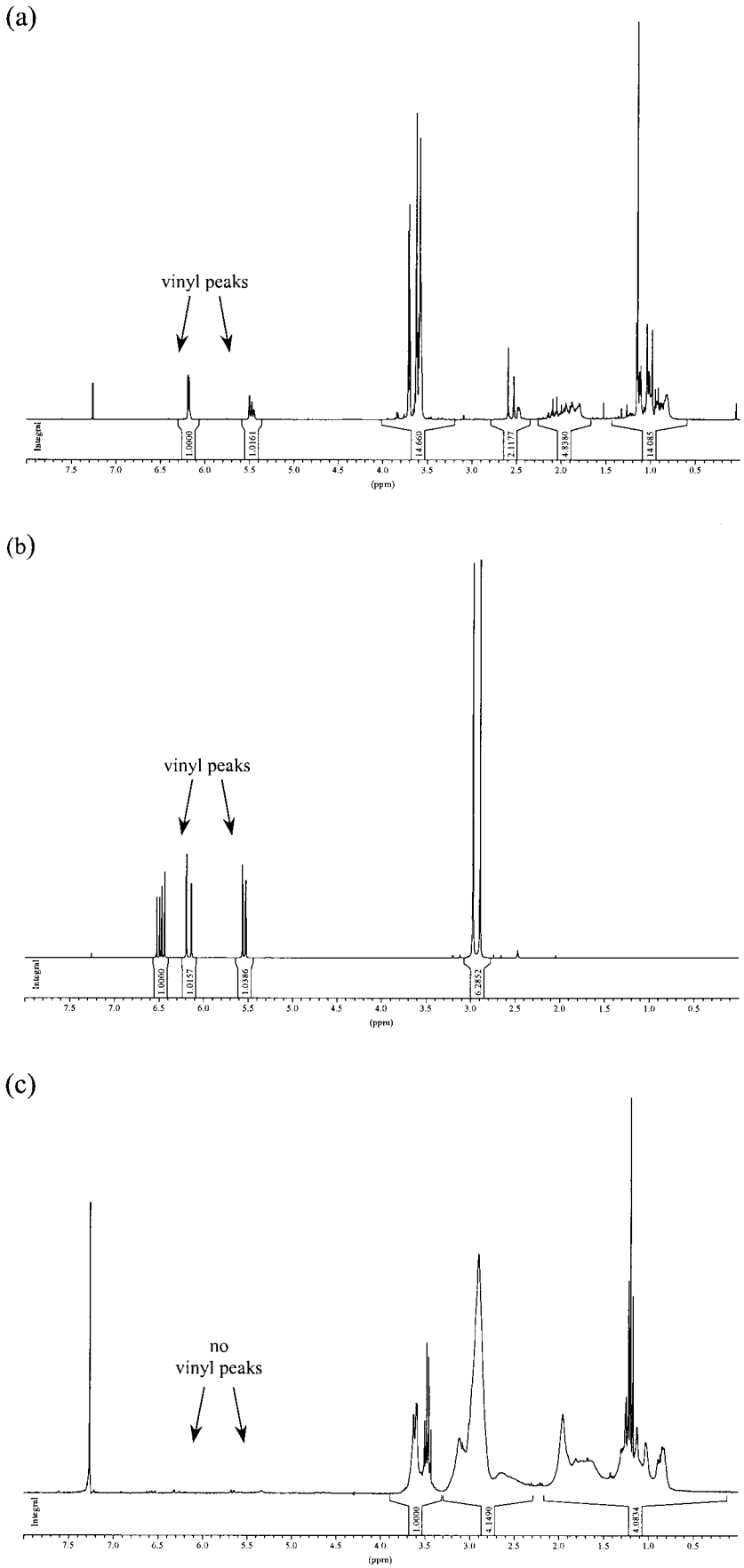


Figure 3. ^{1}H NMR spectra for (a) MMA(1), (b) DMA, and (c) copolymer MMA(1)-30/DMA-70.

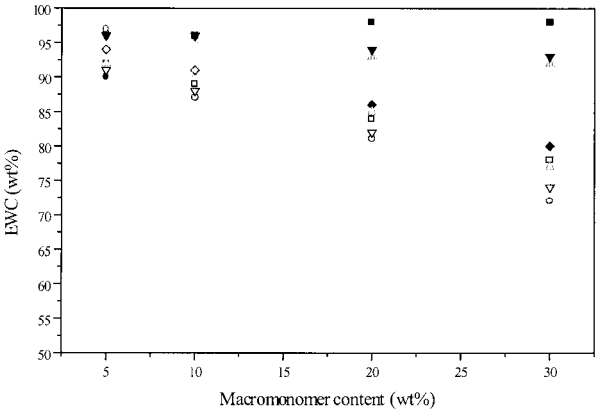


Figure 4. EWC of the materials as a function of total MMA content and macromer chain length. ■ = MMA; ● = MMA(1); ▲ = MMA(2); ▼ = MMA(3); ◆ = MMA(4), □ = MMA(5); ○ = MMA(6); △ = MMA(7); ▽ = MMA(8); ◇ = MMA(9).

Swelling Properties

High-water-content hydrogels were targeted with the aim of improving the mechanical strength while maintaining a high water content. Hydrogels were synthesized based on 5, 10, 20, and 30 wt % of MMA units, utilizing all the macromers listed in Table I. Copolymeric hydrogels based on statistical MMA/DMA copolymers also were synthesized to provide a benchmark with conventional hydrogel materials. The EWC of the materials as a function of total MMA content and macromer chain length is shown in Figure 4. Hydrogels based on statistical copolymers were highly swollen and fragile. The inclusion of macromers did reduce swelling; however, the EWC remained above 70 wt % even with the very high molecular weight macromers. This result is a clear indication that the EWC of the copolymers was dependent not only on the total relative contents of the hydrophobic and hydrophilic components in the gel but also on the chain architecture and subsequent macroscopic morphology of the gel.

With the exception of the statistical copolymers, the sol fractions (water extraction) of these copolymers all fell in the range of 6 to 10 wt %, indicating that most of the DMA effectively was copolymerized. This sol fraction could be reduced further by the addition of a crosslinking agent such as ethylene glycol dimethacrylate (EDMA).

Mechanical Properties

The mechanical properties of the MMA/DMA statistical copolymers were quite poor, with some of the hydrogels failing to hold their form. When the MMA component was included as a macromer, the hydrogels became less fragile, and it was quite clear even visually that the mechanical properties were significantly different in the macromer-based gels.

A step change in the Young's modulus (E) became evident for the hydrogels containing macromers with an M_n greater than 1,500, as can be seen in Figure 5, and this was improved further when the concentration of the macromer was at least 10 wt %. In a control experiment, we synthesized a poly(2-hydroxyethyl methacrylate) hydrogel under identical polymerization conditions and found that the Young's modulus was similar to the more rigid MMA/DMA gels based on the longer macromers in this study. This is a significant result as the water content of these MMA/DMA gels was about 80% higher than that of the PHEMA hydrogel. Thus, it is clear that high strength hydrogels can be synthesized easily by this particular macromer approach and that the polydisperse nature of the macromers does not diminish the self-reinforcing mechanism to any great extent.

Network Parameters

The effective crosslink density (ν_e) was obtained from compression–strain results via

$$\tau = RT\nu_e\phi_2^{1/3}\left(\lambda - \frac{1}{\lambda^2}\right) \tag{4}$$

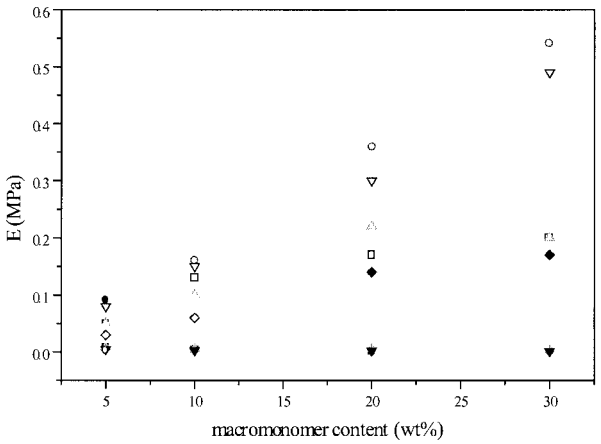


Figure 5. Young's modulus (E) of the materials as a function of total MMA content and macromer chain length. ■ = MMA; ● = MMA(1); ▲ = MMA(2); ▼ = MMA(3); ◆ = MMA(4), □ = MMA(5); ○ = MMA(6); △ = MMA(7); ▽ = MMA(8); ◇ = MMA(9).

Table II. Network Parameters Obtained from the Swelling and Moduli Data

Material	ν_e (mol/m^3)	M_c (kg/mol)	χ
MMA-5/DMA-95	2.85	392.80	0.503
MMA-10/DMA-90	1.67	749.29	0.503
MMA-20/DMA-80	0.66	1715.99	0.502
MMA-30/DMA-70	Hydrogel would not hold its form		
MMA(1)-5/DMA-95	25.31	45.27	0.516
MMA(1)-10/DMA-90	1.42	807.17	0.510
MMA(1)-20/DMA-80	Incomplete polymerization		
MMA(1)-30/DMA-70	Incomplete polymerization		
MMA(2)-5/DMA-95	2.97	384.30	0.506
MMA(2)-10/DMA-90	1.62	701.74	0.511
MMA(2)-20/DMA-80	1.50	742.33	0.522
MMA(2)-30/DMA-70	0.67	1700.51	0.529
MMA(3)-5/DMA-95	1.82	626.18	0.505
MMA(3)-10/DMA-90	1.00	1136.30	0.511
MMA(3)-20/DMA-80	0.79	1446.92	0.519
MMA(3)-30/DMA-70	0.35	3256.23	0.525
MMA(4)-5/DMA-95	8.57	133.29	0.509
MMA(4)-10/DMA-90	16.00	71.17	0.516
MMA(4)-20/DMA-80	32.81	34.90	0.542
MMA(4)-30/DMA-70	32.88	34.88	0.574
MMA(5)-5/DMA-95	14.93	75.92	0.512
MMA(5)-10/DMA-90	31.92	34.47	0.529
MMA(5)-20/DMA-80	36.12	31.54	0.559
MMA(5)-30/DMA-70	37.99	29.92	0.593
MMA(6)-5/DMA-95	1.31	867.27	0.502
MMA(6)-10/DMA-90	40.41	28.09	0.532
MMA(6)-20/DMA-80	80.22	14.15	0.556
MMA(6)-30/DMA-70	107.20	10.59	0.615
MMA(7)-5/DMA-95	14.62	77.50	0.512
MMA(7)-10/DMA-90	27.37	41.62	0.522
MMA(7)-20/DMA-80	50.23	22.67	0.549
MMA(7)-30/DMA-70	39.49	28.67	0.590
MMA(8)-5/DMA-95	22.33	50.85	0.517
MMA(8)-10/DMA-90	35.99	31.67	0.533
MMA(8)-20/DMA-80	66.01	17.40	0.563
MMA(8)-30/DMA-70	95.93	12.09	0.605
MMA(9)-5/DMA-95	8.56	132.09	0.512
MMA(9)-10/DMA-90	17.00	66.64	0.523
MMA(9)-20/DMA-80	Macromer would not dissolve in DMA		
MMA(9)-30/DMA-70	Macromer would not dissolve in DMA		

where τ is the force/cross-sectional area, R is the gas constant, T is the absolute temperature, λ is the ratio of the deformed to nondeformed lengths of the swollen pellet, and ν_e is the effective crosslink density (mol/m^3).

Values of the polymer–water interaction parameter (χ) were calculated from the following expression valid at the swelling equilibrium:

$$\ln(1 - \phi_2) + \phi_2 + \chi\phi_2^2 + \nu_e V_1(\phi_2^{1/3} - 2\phi_2 f^{-1}) = 0 \quad (5)$$

Where f is the crosslinking functionality of the crosslinking agent and V_1 is the molar volume of water (dm^3/mol).

From the values of ν_e, the molar mass per crosslink (M_c) was calculated via

$$M_c = \rho/\nu_e \quad (6)$$

The network parameters obtained by the combination of the swelling and compression modulus data are given in Table II. Because no crosslinking agent was added, the theoretical crosslink density was zero. The crosslinking can be explained in two ways. First, γ radiation is known to induce crosslinking in acrylates, and DMA might have crosslinked in the γ source. More importantly, the MMA macromers aggregated to form physical crosslinks by hydrophobic interactions. This hydrophobic crosslinking clearly was enhanced in these graft copolymers in comparison to the statistical copolymers containing equivalent MMA concentrations. In contact lens applications, the challenge is to induce this hydrophilic–hydrophobic segregation without causing excessive phase separation resulting in opacity. In this study, copolymers containing macromers with an M_n greater than 10,000 became cloudy/white on swelling.

It may be possible to offset the phase separation via macromers containing a group compatible with the hydrophilic component of the gel (e.g., an H-bonding site), thus enabling higher molecular weight macromers to be used without causing opacity. This would optimize the compromise between mechanical property enhancement and homogeneity. In this regard, CCT is a very versatile synthetic route as it is tolerant of many useful functionalities.

CONCLUSIONS

This study indicated that self-reinforcing hydrogels can be synthesized easily via macromers made by CCT polymerization. The judi-

cious selection of comonomers enables high-modulus, clear xerogel compositions to be made in bulk, suitable for machining to lens materials.

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