10246 *Macromolecules* **2010**, *43*, 10246–10252
DOI: 10.1021/ma101950f

Macromolecules
ARTICLE

Hydrogels Based on Living Ring-Opening Metathesis Polymerization

Ke Zhang, Jun Cui, Melissa Lackey, and Gregory N. Tew*

Department of Polymer Science and Engineering, University of Massachusetts, Amherst, Massachusetts 01003, United States

Received August 23, 2010; Revised Manuscript Received October 29, 2010

ABSTRACT: Living ring-opening metathesis polymerization (ROMP) of a hydrophilic norbornene monomer (**M4**) was performed successfully in air at room temperature using Grubbs' third generation (G3) catalyst as the initiator. ROMP was then used to copolymerize **M4** with a hydrophilic difunctional norbornene cross-linker to develop a rapid and efficient method for preparing hydrogels. Although intramolecular cyclization was observed under dilute conditions, the critical gelation behavior was found to agree with the mean-field theory of Flory and Stockmayer (FS theory) more consistently than that of conventional free radical polymerization systems. By changing the length of the primary polymer chains, the initial molar ratio between monomer and cross-linker, and the length of the cross-linker, the equilibrium swelling ratio and the corresponding mechanical properties of the resultant hydrogels were manipulated across a broad range.

Introduction

Chemically cross-linked hydrogels are a class of materials of growing interest due to attributes including a stable network structure, a variety of possible functionalities, and numerous potential biomedical applications, such as drug delivery and tissue engineering.[1−4] The copolymerization of a vinyl monomer in the presence of a small amount of a divinyl monomer offers one of the simplest procedures for preparing these polymer networks. Conventional free radical polymerization (FRP) has been used commonly for the copolymerization of vinyl and divinyl monomers[5−14] because of its mild reaction conditions and tolerance to protonic impurities and functional groups. However, because of slow initiation followed by fast chain propagation and termination reactions, FRP can lead to early microgel formation and a heterogeneous final network structure. These structural heterogeneities have a severe impact on the physical properties of the final cross-linked materials. In addition, the critical gelation behavior by FRP proceeds in a highly nonideal fashion, with large discrepancies from the mean-field theory of Flory and Stockmayer (FS theory).[15−20]

To obtain networks with a more homogeneous structure, controlled radical polymerization (CRP) techniques such as atom transfer radical polymerization (ATRP),[21−28] nitroxide-mediated radical polymerization (NMP),[29,30] and reversible addition−fragmentation chain transfer polymerization (RAFT)[31,32] have been utilized. Compared to FRP, two essential features of CRP contribute to the formation of more homogeneous networks. First, fast initiation, relative to propagation, provides the simultaneous appearance and a constant number of primary polymer chains throughout the polymerization. Second, the fast activation/deactivation mechanism of CRP ensures a low concentration of the dynamic active propagating radical, which results in a concurrent propagation and a relatively long "dormant" relaxation time for the growing polymer chains. These features of CRP effectively reduce the probability of cyclization and diminish the early microgel formation, resulting in the critical gelation behavior being described more accurately by the FS theory.

*Corresponding author: Fax +1-413-545-0082; e-mail tew@mail.pse.umass.edu.

On the basis of the transition-metal-catalyzed olefin metathesis reaction, living ring-opening metathesis polymerization (ROMP) has been developed as a powerful technique for the preparation of polyolefins with controlled molecular structure. By optimizing the combination of catalyst and monomer type to provide quantitative and rapid initiation and to diminish chain transfer or premature termination, a variety of well-defined polymers have been synthesized by ROMP, including homopolymers,[33] block copolymers,[34] alternating copolymers,[35] conjugated,[36] telechelic,[37] star,[38] and hyperbranched polymers,[39] and polymer brushes.[40] However, few publications have discussed the preparation of elastic materials with covalent network structures by ROMP. In one report, cross-linked resins were prepared by the copolymerization of monofunctional *N*-alkyldicarboxyimidonorbornene and difunctional bis(*N*-alkylenedicarboxyimidonorbornene) in the bulk state, catalyzed by Grubbs' first generation catalyst.[41,42] The focus, however, concentrated on the optimization of the processing conditions for enhanced mechanical properties of the resulting cross-linked resin, rather than the critical gelation behavior by ROMP.

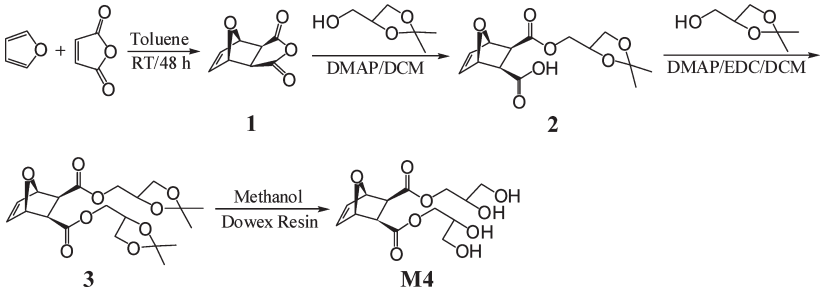
Herein, on the basis of the ROMP technique, we have developed a rapid and simple method for making hydrogels in air at room temperature. In addition to the critical gelation behavior of ROMP network formation, the influence of the primary polymer chain length, the initial molar ratio between the monomer (**M4**) and cross-linker, and the length of the cross-linker on the formation and properties of the resultant hydrogels were also studied.

Experimental Section

Materials. Maleic anhydride, furan, solketal, 4-(dimethylamino)pyridine (DMAP), *N*-ethyl-*N*′-(3-(dimethylamino)propyl)-carbodiimide hydrochloride (EDC), diethylene glycol, hydroxyl-terminated poly(ethylene glycol) 600 (PEG 600) and 4000 (PEG 4000), triphenylphosphine (Ph_3P), diisopropylazodicarboxylate (DIAD), second generation Grubbs' catalyst, 3-bromopyridine, *N*,*N*-dimethylformamide (DMF), pentane, and methanol were purchased as reagent grade from Aldrich, Acros, Alfa Aesar, or Fisher and used as received. Dowex 50WX2-100 ion-exchange resin (Aldrich) was activated by hydrochloric acid before use. Dichloromethane (DCM) was refluxed over calcium

 Published on Web 12/02/2010

Scheme 1. Synthesis of the Monomer M4



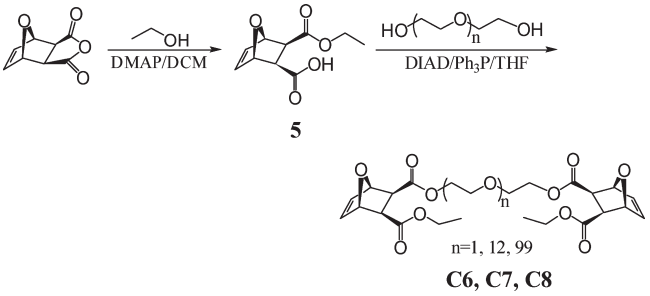
hydride. Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Compound **1**[43] (Scheme 1), compound **5**[44] (Scheme 1), and third generation Grubbs' catalyst (G3) (dichloro-di-(3-bromopyridino)-*N,N'*-dimethylenoimidazolino-Ru=CHPh)[45] were synthesized according to the literature.

Synthesis of Compound 3. Compound **1** (20 g, 0.12 mol) and solketal (35.68 g, 0.27 mol) were dissolved in 180 mL of anhydrous DCM. DMAP (1.47 g, 12 mmol) in 20 mL of anhydrous DCM was added to the solution dropwise. The reaction mixture was stirred at room temperature for 12 h to synthesize compound **2** (Scheme 1). Without purification, the crude mixture was cooled to 0 °C and EDC (26.84 g, 0.14 mol) was added. After 1 h, the reaction mixture was warmed to room temperature and stirred for ~24 h further. Purification processes were followed by washing with 10% sodium bicarbonate aqueous solution (300 mL), saturated $NaHCO_3$ aqueous solution (300 mL), and saturated NaCl aqueous solution (300 mL) successively and then by crystallization from DCM/hexane to provide the white solid product **3** (Scheme 1) with a yield ca. 70%. ^{1}H NMR ($CDCl_3$) δ (ppm): 6.46 (s, 2H, $-CH{=}CH-$), 5.28 (s, 2H, $=CH-CH-$), 4.36−3.70 (m, 10H, $-COO-CH_2-$, $-CH-O-$, $-CH_2-O-$), 2.86 (s, 2H, $-CH-COO-$), 1.43−1.36 (d, 6H, $-CH_3$).

Synthesis of Monomer M4. Compound **3** (10 g, 24 mmol) was dissolved in 30 mL of methanol. Activated 50WX2-100 ion-exchange resin (Aldrich) (10 g) was added to the solution in one pot, and the reaction was stirred at room temperature for about 24 h. After filtration to remove the used ion-exchange resin, the filtrate was concentrated and purified by a silica gel column with ethyl acetate:methanol (5:1, v/v) as eluent. The colorless oil product **M4** (Scheme 1) (1.6 g) was obtained in a yield of 80%. ^{1}H NMR (methanol-d_4) δ (ppm): 6.50 (s, 2H, $-CH{=}CH-$), 5.22 (s, 2H, $=CH-CH-$), 4.25−3.99 (m, 4H, $-COO-CH_2-$), 3.87−3.80 (m, 2H, $-CH-OH$), 3.30−3.32 (m, 4H, $-CH_2-OH$), 2.94 (s, 2H, $-CH-COO-$). ^{13}C NMR (75 MHz, methanol-d_4), δ (ppm): 173.7, 137.8, 82.1, 71.1, 67.4, 64.1.

Synthesis of Cross-Linkers C6, C7, and C8. C6, **C7**, and **C8** (Scheme 2) were prepared from Mitsunobu coupling reactions between compound **5** and diethylene glycol, PEG 600, and PEG 4000, respectively. As an example, compound **5** (5.30 g, 25 mmol), PEG 4000 (20 g, 5 mmol), and Ph_3P (6.56 g, 25 mmol) were dissolved in anhydrous THF (150 mL). DIAD (5.06 g, 25 mmol) was added dropwise by a syringe. The reaction mixture was stirred at room temperature for 24 h. **C6** and **C7** were purified by silica gel columns with ethyl acetate:hexane = 3:1 (v/v) and DCM:methanol = 7:1 (v/v) as eluents, respectively. **C8** was purified by precipitation into a large amount of ethyl ether three times. ^{1}H NMR of **C6** ($CDCl_3$) δ (ppm): 6.45 (s, 4H, $(-CH{=}CH-)_2$), 5.26 (s, 4H, $(=CH-CH-)_4$), 4.35−4.08 (m, 8H, $(-COO-CH_2-)_4$), 3.71−3.65 (t, 4H, $-CH_2-O-CH_2-$), 2.85−2.77 (m, 4H, $(-CH-COO-)_4$), 1.27−1.23 (t, 6H, $(-CH_3)_2$). FAB-MS: m/z 495.2 (M^+), calculated 494.18. ^{1}H NMR of **C7** ($CDCl_3$) δ (ppm): 6.45 (s, 4H, $(-CH{=}CH-)_2$), 5.26 (s, 4H, $(=CH-CH-)_4$), 4.35−4.08 (m, 8H, $(-COO-CH_2-)_4$), 3.71−3.65 (t, 48H, $(-CH_2-O-CH_2-)_{12}$), 2.85−2.77 (m, 4H, $(-CH-COO-)_4$), 1.27−1.23 (t, 6H, $(-CH_3)_2$).

Scheme 2. Synthesis of Cross-Linkers C6, C7, and C8



^{1}H NMR of **C8** ($CDCl_3$) δ (ppm): 6.45 (s, 4H, $(-CH{=}CH-)_2$), 5.26 (s, 4H, $(=CH-CH-)_4$), 4.35−4.08 (m, 8H, $(-COO-CH_2-)_4$), 3.71−3.65 (t, 396H, $(-CH_2-O-CH_2-)_{99}$), 2.85−2.77 (m, 4H, $(-CH-COO-)_4$), 1.27−1.23 (t, 6H, $(-CH_3)_2$).

Homopolymerization of M4. A general procedure: **M4** (199.4 mg, 0.6 mmol) was dissolved in 1.0 mL of DMF. After G3 (5.3 mg, 6.0×10^{-3} mmol) in 0.2 mL of DMF was added, the vial was sealed and stirred sufficiently at room temperature ca. 12 h. At timed intervals, samples were withdrawn for measuring the monomer conversion and molecular weight of poly-**M4** by ^{1}H NMR and GPC, respectively.

Preparation of Hydrogels. A general procedure: **M4** (400.5 mg, 1.21 mmol) and **C6** (35.8 mg, 7.24×10^{-2} mmol) were dissolved in 2 mL of DMF in a 6 mL glass vial. After G3 (5.9 mg, 6.67×10^{-3} mmol) in 0.7 mL of DMF was added to the solution and it was stirred sufficiently at room temperature, the mixture was transferred to a homemade Teflon mold with dimensions of 48 × 3 mm ($D \times H$) and covered by a glass plate. Twelve hours later, the resultant gels were washed with large amounts of DMF repeatedly 5 times in 5 days to remove the sol fraction. Then, the same washing procedure was performed using water to remove the DMF and replace it with water. The gel fraction was determined as the weight ratio between the dried gel and the sum of **M4**, **C6**, and G3 used in the synthesis.

Characterization. NMR spectra were recorded on a Bruker DPX300 spectrometer at room temperature.

Gel permeation chromatography (GPC) was performed by a Polymer Laboratories PL-GPC50 instrument with two 5 μm mixed-D columns, a 5 μm guard column, and a Knauer RI detector. DMF with 0.01 M LiBr was used as eluent at a flow rate of 1.0 mL/min. Poly(methyl methacrylate) standards were used for the calibration.

Rheological measurements were performed using a TA Instruments AR2000 stress-controlled rheometer with a parallel plate geometry (40 mm diameter, 1−2.5 mm gap distance depending on the sample) at 25 °C. A solvent trap was used to minimize water evaporation during testing. A stress sweep at a constant frequency of 1 Hz was performed first to determine the linear viscoelastic region for collecting subsequent data. Frequency sweep tests over a range of 0.01−100 Hz were performed at a constant stress (0.1−2.0 Pa, depending on the sample) to measure the elastic modulus (G') and the viscous modulus (G'').

Table 1. Synthesis and Characterization of Poly-M4 by ROMP under Air at Room Temperature

run[a]	feed ratio[b]	conv (%)[c]	M_n[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
1	100:1	99.1	32 900	62 800	1.12
2	200:1	93.5	62 100	141 700	1.15
3	400:1	55.9	74 400	173 000	1.28
4	800:1	33.8	89 900	250 100	1.38

[a] $[\mathbf{M4}]_0$ = 0.5 M in DMF, reaction time = 12 h. [b] Initial molar ratio between **M4** and G3. [c] Calculated from the ^{1}H NMR spectrum. [d] DMF with 0.01 M LiBr was used as the eluent, and poly(methyl methacrylate) standards were used for the calibration.

Results and Discussion

Monomer and Cross-Linker Synthesis. As shown in Scheme 1, a four-step procedure was used to synthesize the monomer, **M4**. In the first step, a Diels−Alder reaction between maleic anhydride and furan was used to prepare **1**. Compound **1** was then reacted with solketal in the presence of catalytic DMAP to obtain **2**, which was used in situ in the third step without purification. By EDC-promoted esterification, **2** reacted with solketal further to produce **3**. Finally, **M4** was obtained by the hydrolysis of **3** in the presence of an acid ion-exchange resin as a catalyst.

To obtain the cross-linkers, the efficient Mitsunobu coupling reaction was utilized (Scheme 2). Using a large excess of **5** (5 times molar excess) for the coupling reaction, three cross-linkers (**C6**, **C7**, and **C8**) were obtained from the three different diols (diethylene glycol, PEG 600, and PEG 4000, respectively) in the presence of Ph_3P and DIAD.

Homopolymer Polymerization of M4. Typically, ROMP is performed under an inert atmosphere (N_2 or Ar) in order to protect the propagating catalyst from oxidative deactivation and obtain well-defined polymer products. However, the involved procedure for removing air is a clear disadvantage for making practical materials in reasonable quantities. To develop a simple preparation method for hydrogels without the protection of an inert gas, it was necessary to study the ROMP of **M4** in air at room temperature to ensure the living conditions.

Table 1 summarizes the synthesis and characterization of Poly-**M4** from ROMP in air at room temperature. The G3 catalyst was chosen as initiator because of its fast rate of propagation, and the monomer concentration was fixed at 0.5 M in DMF. By changing the initial concentration of G3, the molar ratio between **M4** and G3 was varied from 100:1 to 800:1. The monomer conversion was determined by ^{1}H NMR using the area ratio between the signal for double bonds in Poly-**M4** to the sum of those for the unreacted double bonds in **M4** (Figure S1). As shown in Table 1, after a reaction time of 12 h, as the molar ratio between **M4** and G3 was increased, the resulting polymer molecular weight and its distribution increased, but the conversion of **M4** decreased. When the molar ratio was 100:1, the final conversion of **M4** was essentially quantitative, but when it increased to over 200:1, the final conversion decreased significantly, to less than 90%.

Figure 1 shows representative GPC traces of Poly-**M4**, which illustrate the change in molecular weight with reaction time, where the molar ratio between **M4** and G3 was 200:1. In the first hour, the molecular weight of Poly-**M4** increased from 64 300 (at 5 min) to 129 000 (at 1 h), after which it remained constant despite the presence of excess **M4**. The same phenomenon was observed at the higher molar ratios of 400:1 and 800:1 (Figures S2 and S3). Therefore, it appeared that the propagating catalyst at the end of the polymer chains became inactive after 1 h under these reaction conditions, which may be caused by oxidative deactivation. For the lowest molar ratio of 100:1, all of the **M4** was consumed in 1 h (Figure S4). At the same time, as shown in Figure 2, the GPC curves of Poly-**M4** (after a reaction time of 12 h) were symmetrical and monomodal across the whole range of molar ratios studied. Although the PDI increased with the increment of the molar ratio between **M4** and G3, the final PDI in every case was still less than 1.4 (Table 1). As a result, it was concluded that the ROMP of **M4** in air at room temperature, with G3 as the initiator, produced well-defined Poly-**M4** and that a 100:1 molar ratio of **M4** to G3 yielded the best results.

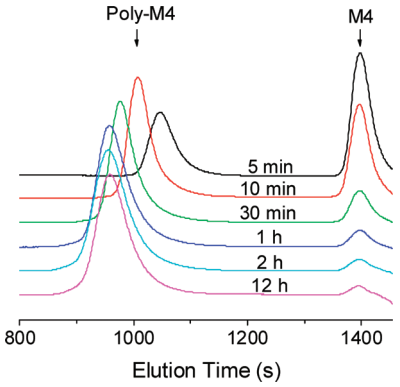


Figure 1. GPC traces of Poly-**M4** from ROMP, $[\mathbf{M4}]_0$ = 0.5 M in DMF, $[\mathbf{M4}]_0/[G3]_0$ = 200:1. DMF with 0.01 M LiBr was the eluent.

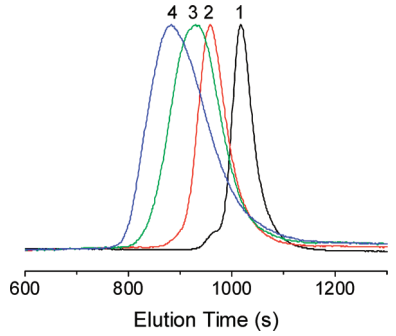


Figure 2. GPC curves of Poly-**M4** from ROMP after reacting for 12 h, $[\mathbf{M4}]_0$ = 0.5 M in DMF. $[\mathbf{M4}]_0/[G3]_0$ equals 100:1, 200:1, 400:1, and 800:1 for curves 1, 2, 3, and 4, respectively. DMF with 0.01 M LiBr was the eluent.

To further prove the living characteristics of ROMP for **M4** at lower molar ratios of **M4** to G3, the polymerization kinetics were studied using ratios less than and equal to 100:1. Figure 3 shows the results of a typical kinetic analysis of ROMP for **M4**, where the molar ratio between **M4** and G3 was 100:1 and the initial **M4** concentration was fixed at 0.125 M in DMF. The semilogarithmic plot of **M4** concentration versus time ($\ln([M]_0/[M])$ vs time) was linear (Figure 3A), indicating **M4** consumption by first-order kinetics and implying a constant concentration of active centers during the polymerization. GPC analyses showed symmetrical unimodal molecular weight distributions (Figure 3B), and M_n increased linearly with conversion (Figure 3C). The PDIs remained low throughout the polymerization (Figure 3C). Similar results were also obtained for the molar ratio between **M4** and G3 of 50:1, as shown in Figure S5. In these cases, the first-order kinetics and linear M_n growth profile both suggested that the living nature of ROMP for **M4** was maintained in air at room temperature.

Preparation and Characterization of Hydrogels. On the basis of the mean-field theory, Flory and Stockmayer developed the classical statistical gelation theory (FS theory) to describe the branching and gelling phenomena of polymers.[15−20]

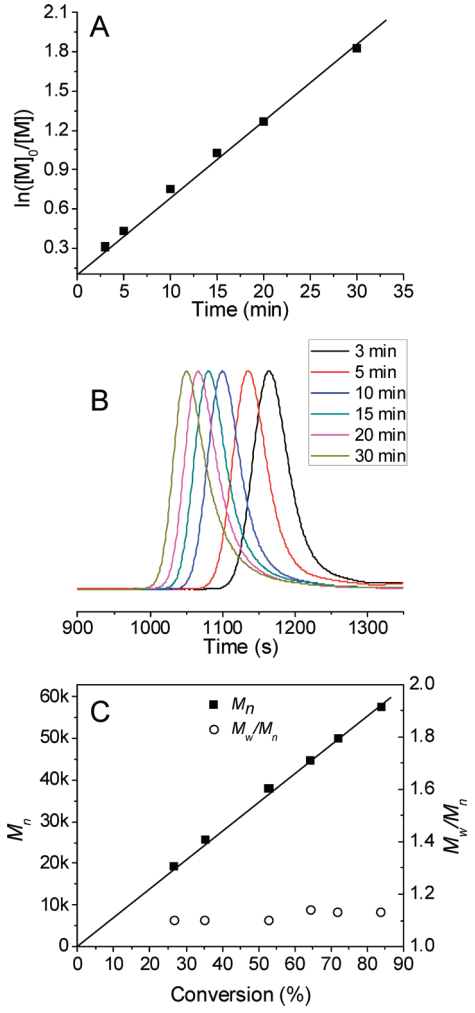


Figure 3. ROMP kinetics for polymerization of **M4** in air at room temperature, $[\mathbf{M4}]_0 = 0.125$ M in DMF, $[\mathbf{M4}]_0/[G3]_0 = 100{:}1$.

For the addition copolymerization of a monovinyl and a divinyl monomer system, with the assumptions of equal reactivity for all vinyl groups and no intramolecular cross-linking, the critical gelation conditions are defined by the equation

$$\frac{1}{\rho_0 \overline{y}_w} = p_c \tag{1}$$

where ρ_0 is the initial fraction of vinyl groups from the difunctional monomer, $\overline{y}_w$ is the weight-average degree of polymerization of the primary chains, and p_c is the extent of polymerization at the gelation point.

For a controlled living polymerization, at the maximum extent of polymerization ($p = 1$), replacing $\overline{y}_w$ with the number-average degree of polymerization of the primary chains ($\overline{y}_n$) in the above equation yields

$$\mathrm{PDI}\frac{[C]_0}{[I]_0} = \frac{1}{2} \tag{2}$$

where PDI is the polydispersity ($\overline{y}_w/\overline{y}_n$) of the primary chains and $[C]_0$ and $[I]_0$ are the initial concentrations of divinyl cross-linker and initiator, respectively. For the ideal case, where the PDI = 1, the critical gelation point for the controlled living polymerization system is reached when the average number of cross-link units per primary chain is 1/2. Practically, the experimental critical gelation point, measured by different research groups independently, was found to be 2 times larger in CRP systems such as ATRP[25−27] and NMP[30] when high initial concentrations of vinyl groups were used. From eq 2, it is the ratio of $[C]_0/[I]_0$ that determines the critical gelation point as well as the properties of the gels obtained from controlled polymerization systems.

Table 2. Influence of $[G3]_0$ on the Preparation and Properties of ROMP Hydrogels

run[a]	$[G3]_0$ (mM)	$[DBs]_0/[G3]_0$	$[C]_0/[G3]_0$	GF (%)[b]	q[c]	G' (Pa)[d]
C6						
1	10.0	50	2.68	no gel		
2	7.50	67	3.57	38.2	242	47
3	5.00	100	5.36	77.1	11.3	1350
4	2.50	200	10.7	88.0	9.81	1790
5	1.25	400	21.4	74.5	13.1	1100
6	0.63	800	42.9	12.9	151	12
7	0.31	1600	85.8	no gel		
C7						
8	20.0	25	1.34	no gel		
9	15.0	33	1.79	gel		
10	10.0	50	2.68	74.0	13.6	1090
11	7.50	67	3.57	78.2	12.4	2230
12	5.00	100	5.36	88.8	9.59	2600
13	2.50	200	10.7	89.3	8.84	2600
14	1.25	400	21.4	70.4	10.1	1850
15	0.63	800	42.9	18.3	108	110
C8						
16	10.0	50	2.68	89.0	11.0	3750
17	7.50	67	3.57	90.5	10.4	4210
18	5.00	100	5.36	91.3	9.79	4540
19	2.50	200	10.7	91.3	9.59	4580
20	1.25	400	21.4	73.8	12.1	3850
21	0.63	800	42.9	22.9	59.3	200

[a] $[\text{Double bonds}]_0$ ($[DBs]_0$) = 0.5 M, reaction time = 12 h, runs 1−7 use **C6** as the cross-linker, runs 8−15 use **C7** as the cross-linker, and runs 16−21 use **C8** as the cross-linker. [b] Gel fraction (GF) was obtained by the weight ratio of the dried gel to the total weight of **M4**, cross-linker, and G3. [c] Equilibrium swelling ratio (q) in water was defined as the weight ratio of the fully swollen gel to the dried gel. [d] Average shear elastic modulus (G') was measured by shear rheometry from three times measurements, and all of the errors were less than 10%.

As a result, we varied two key parameters in studying our ROMP gelation system: $[G3]_0$, which determines $\overline{y}_w$ (eq 1), and $[C]_0$, which is related to ρ_0 (eq 1). Because the three critical gelation points occurred below $[\mathbf{M4}]_0/[G3]_0 = 100$, it was assumed from the data presented in Table 1 and Figures 3 and S5 that the chains in the gels had narrow PDIs. Therefore, the influence of PDI on the critical gelation point was omitted in this discussion, supposing PDI = 1, as it did not lead to significant deviations when considering the critical gelation behavior of ROMP by FS theory. Furthermore, because a similar approximation was also used in analysis of gelation by ATRP,[25−27] the related results regarding the critical gelation behavior from ROMP can be compared directly.

Using the highly efficient G3 catalyst as initiator, hydrogels were conveniently obtained via ROMP in air at room temperature. Although hydrogels were formed in less than 10 min, the gelation reaction was allowed to proceed for 12 h to provide the largest possible gel fraction (GF). The GF was determined as the weight ratio between the dried gel and the sum of **M4**, cross-linker, and G3 used in the synthesis. The swelling ratio (q) was obtained from the weight ratio between the equilibrium-swollen gel (in water) and the dried gel. The elastic and viscous shear moduli, G' and G'', of the equilibrium swollen gels were measured by parallel plate shear rheometry.

Influence of $[G3]_0$ on the Formation of Hydrogels. To study the influence of $[G3]_0$, the initial concentration of double bonds (from monomer and cross-linker) was maintained at a constant value of 0.5 M, and $[G3]_0$ was fixed at 6 mol % with respect to $[\mathbf{M4}]_0$. Table 2 summarizes the influence of $[G3]_0$

on the formation and properties of the resultant hydrogels. For all three cross-linkers (**C6**, **C7**, and **C8**), there was an optimal $[G3]_0$ of 2.50 mM, corresponding to a $[C]_0/[G3]_0$ ratio of 10.7 and a theoretical $\overline{y}_n$ ca. 200 units. This produced hydrogels with the maximum GF, the minimum q, and the maximum G' (runs 4, 13, and 19, Table 2). At concentrations above and below this optimum value, the GF and G' decreased and the corresponding q increased to the point that hydrogels could not be formed. The **C6** gel system was utilized to further explore these unique phenomena.

When a high $[G3]_0$ of 10.0 mM was used, providing a $[C]_0/[G3]_0$ ratio of 2.68 and a corresponding $\overline{y}_n$ ca. 50 units, hydrogels were not obtained even after complete consumption of all double bonds. From eq 2, when $[C]_0$ is constant, there is a maximum $[G3]_0$, corresponding to the lowest $[C]_0/[G3]_0$ and $\overline{y}_n$, at which the critical gelation point is reached. The critical $[C]_0/[I]_0$ ratio of ~3 for this ROMP system was slightly larger than the reported value of 1 for CRP systems with a high concentration of vinyl groups (>4 M). This indicated that intramolecular cyclization occurred under the conditions used for ROMP network formation. However, caution needs to be used in comparing the critical gelation phemomena of ROMP and CRP, since a significantly lower concentration of double bonds (0.5 M) was used in the ROMP reactions. Such low double bond concentrations also caused intramolecular cyclization in ATRP systems. For example, when double bond concentration was ca. 1.0 M, gels could not be obtained in the conditions of $[C]_0/[I]_0$ less than 5.[26] The critical $[C]_0/[I]_0$ ratio of ~3 for the ROMP hydrogels, however, is significantly less than that of FRP systems (10^2-10^3).

Above the critical gelation point, as the $[G3]_0$ decreased until the ratio of $[C]_0/[G3]_0$ reached 10.7 and $\overline{y}_n$ was close to 200 units, the GF increased to the maximum of 88.0%, where the corresponding minimum q and maximum G' were 9.81 and 1790 Pa, respectively. With the decrement of $[G3]_0$, the average number of difunctional monomer units per chain ($[C]_0/[G3]_0$) increased, as did the length of primary chains ($\overline{y}_n$). This increases the probability of intermolecular cross-linking and results in hydrogels with a larger GF, higher cross-linking density, lower q, and higher G'.

When the $[G3]_0$ decreased below the optimum value of 2.5 mM to 0.63 mM and $[C]_0/[G3]_0$ increased to 42.9, the GF and G' decreased to 12.9% and 12 Pa, respectively, and the q increased to 151. A further reduction of $[G3]_0$ to produce a $[C]_0/[G3]_0$ ratio of 85.8 resulted in no hydrogel formation. From Table 1, for the homopolymerization of **M4**, when the molar ratio of monomer to initiator was greater than 200, the final conversion of monomer decreased significantly. As expected, this lower conversion resulted in a decreased GF and cross-linking density in the gels. In addition, the unreacted monomer diluted the propagating polymer chains in the gel precursor solution, enhancing the probability of intramolecular cyclization in the primary polymer chains. This reduced GF and cross-linking density to the point that a network could not be obtained.

Influence of $[C]_0$ *on the Formation of Hydrogels.* To study the influence of $[C]_0$ on ROMP hydrogel formation, the optimal $[G3]_0$ of 2.5 mM was used and the concentration of double bonds was fixed at 0.5 M. Figure 4 shows how changing the initial molar ratio of cross-linker to monomer ($[C]_0/[\mathbf{M4}]_0$) affects the GF (Figure 4A), q (Figure 4B), and G' (Figure 4C) of the resultant hydrogels. Since the q of hydrogels made with **C6** at $[C]_0/[\mathbf{M4}]_0 = 2\%$ was as high as 120, it was not included in Figure 4B. With increasing cross-linker concentration, the GF and G' increased while q decreased, regardless of the length of cross-linker. Such a result is

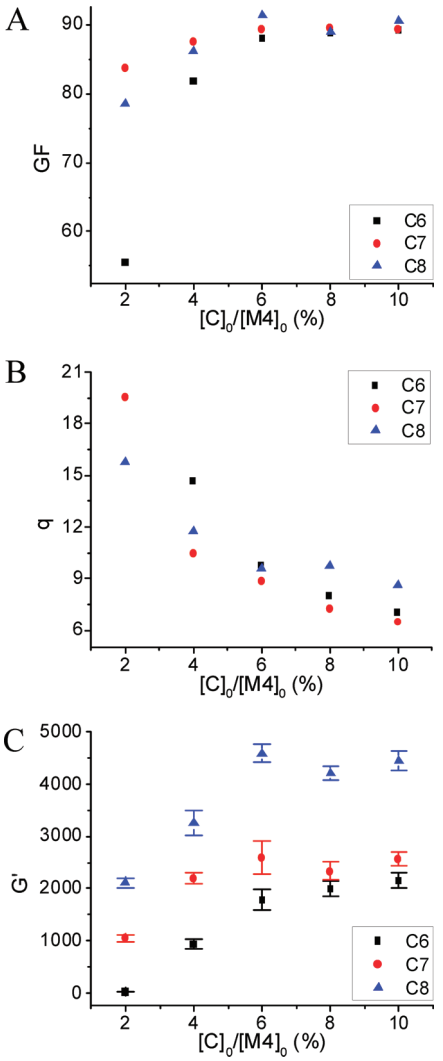


Figure 4. Influence of cross-linker concentration on the gel fraction (GF) (A), swelling ratio (q) (B), and shear elastic modulus (G') (C) of ROMP hydrogels. Squares, circles, and triangles represent **C6**, **C7**, and **C8** as the cross-linker, respectively. $[G3]_0 = 2.5$ mM, and the initial double bond concentration was fixed at 0.5 M.

reasonable, as the average number of difunctional monomer units per chain ($[C]_0/[G3]_0$) increases with $[C]_0$, resulting in hydrogels with a high GF and cross-linking density, which leads to a low q and high G'.

Influence of Cross-Linker Length on Hydrogel Formation. It has been reported that the use of long cross-linkers can efficiently reduce the possibility of intramolecular cyclization,[14,32] which results in the critical gelation behavior being described more accurately by FS theory. From Table 2, when the repeat unit of PEG in the cross-linker increased from 1 (**C6**) (runs 1−7) to 12 (**C7**) (runs 8−15), the ratio of $[C]_0/[G3]_0$ at the critical gelation point decreased from ca. 3 to ca. 1.5, which is closer to the reported critical value of 1 for CRP systems. With the longer cross-linker, the probability of intermolecular cross-linking increased, resulting in hydrogels with a higher cross-linking density and an increased GF along with a lower q and a higher G'. Comparing the two cross-linkers **C6** and **C7**, as shown in Table 2, at the same value of $[C]_0/[G3]_0$, the GF and G' were always higher and the corresponding q was always lower for the **C7** hydrogel system. Furthermore, since a low cross-linker concentration may delay the cross-linking reaction and increase the possibility of intramolecular cross-linking, the effect of cross-linker

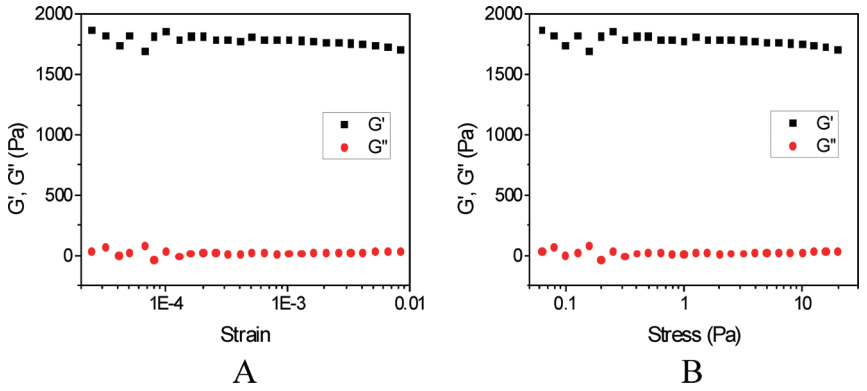


Figure 5. Elastic modulus (G') and viscous modulus (G'') as a function of (A) strain and (B) stress, at a fixed frequency of 1.0 Hz, at 25 °C. The data correspond to the sample listed as run 4 in Table 2.

length on the gel formation and properties should become more obvious with decreasing $[C]_0$. From Figure 4, it is observed that as $[C]_0/[\mathbf{M4}]_0$ ratio was decreased from 10% to 2%, the differences in GF, q, and G' between the **C6** and **C7** systems continuously increased.

However, when the length of the cross-linker increases to match the length of the primary polymer chains, the formation process of the gels is altered, particularly at low cross-linker concentrations (low $[C]_0/[I]_0$). Before the critical gelation point, introducing such a long cross-linker molecule into the propagating polymer chains will abruptly increase the molecular volume of the branched sol molecules. This provides a possibility for gel formation from cross-linking sol molecules at the lower monomer conversion, resulting in a lower GF of obtained gels. Since a longer cross-linker also increased the occurrence of intermolecular cross-linking and resulted in the higher cross-linking density, when there is only a small change in GF, it is possible that the hydrogels with a long cross-linker have both a lower GF and q simultaneously. As a result, when **C8**, with 99 PEG repeat units, was used as a cross-linker, at the low cross-linker concentration ($[C]_0/[\mathbf{M4}]_0$ = 2%), the GF (Figure 4A) and the q (Figure 4B) were both lower than those for the **C7** system. With increasing cross-linker concentration, the higher $[C]_0/[I]_0$ induced early intermolecular cross-linking and efficiently eliminated this influence of cross-linker length on gel formation.

As shown in Figure 4A, at a higher cross-linker concentration, corresponding to $[C]_0/[\mathbf{M4}]_0$ ratios above 6%, the GF of the **C8** system was similar to that of the **C7** system. On the other hand, when $[C]_0/[\mathbf{M4}]_0$ was greater than 6%, the swelling ratios of the **C8** system became larger than those of the **C7** system at the same $[C]_0/[\mathbf{M4}]_0$ (Figure 4B). This is because the weight percent of **C8**, with the long, more hydrophilic PEG chain, surpassed that of **M4** and dominated the composition of the final hydrogels at these points.

Lastly, regarding the influence of cross-linker length on the elastic shear modulus, as demonstrated in Figure 4C, at the same $[C]_0/[M4]_0$, the longer PEG cross-linker always resulted in hydrogels with a higher G' (Figure 4C).

Rheological Behavior of ROMP Hydrogels. The rheological properties of the hydrogels were studied in the equilibrium-swollen state at room temperature (25 °C). Shown in Figure 5 are representative plots of the elastic modulus, G', and the viscous modulus, G'', as a function of strain (Figure 5A) and stress (Figure 5B) at a fixed frequency of 1.0 Hz. The data shown are for the sample listed as run 4 in Table 2. This hydrogel exhibited a linear response across the studied range of applied strain and stress, which is consistent with the properties of covalently cross-linked hydrogels. Figure 6 shows the elastic modulus (G') and viscous modulus (G'') as a function of frequency for the same sample at 25 °C. Both G' and G'' were independent of frequency over a broad range, and G' was significantly larger than G'', which was less than 50 Pa. The values of G' for all of the hydrogel samples are listed in Table 2, and full data are given in Figures S6 and S7. These results indicated that the hydrogels obtained from ROMP were endowed with a stable network structure.

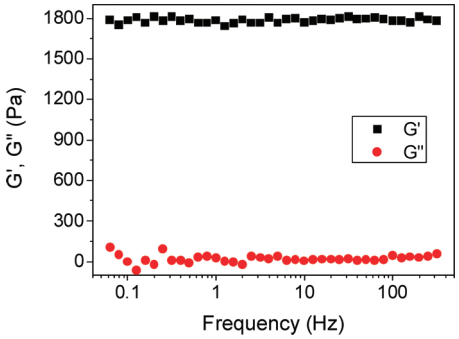


Figure 6. Elastic modulus (G') and viscous modulus (G'') as a function of frequency at 25 °C. The data correspond to the sample listed as run 4 in Table 2.

Conclusion

ROMP of the hydrophilic monomer, **M4**, was performed in air at room temperature using the efficient G3 as the initiator. It was found that the propagating catalyst became inactive after 1 h, and the monomer conversion decreased and the PDI of Poly-**M4** increased slightly with the increment of the initial molar ratio between **M4** and G3. However, under these conditions, the polymerization still displayed living characteristics, especially when a low initial molar ratio of **M4** to G3 was used. Subsequently, by introducing a small amount of a hydrophilic difunctional cross-linker to this ROMP system, a rapid and simple method for preparing hydrogels was developed, which allowed for gel formation in air at room temperature in mere minutes. Because of the living quality of ROMP of **M4**, the critical gelation behavior in this ROMP system followed the FS theory more consistently than that in conventional FRP systems. The optimal molar ratio between double bonds and G3 was determined for this ROMP method, at which the largest gel fraction and elastic modulus and the lowest swelling ratio were obtained concurrently. Furthermore, increasing the cross-linker length proved to be an efficient way to suppress intramolecular cyclization and create hydrogels with improved properties.

Acknowledgment. Generous support was primarily provided from DMR-0820506 and CMMI-0531171. Partial support was provided from ARO W911NF-09-1-0373 and ONR N00014-10-1-0348. Shared facilities support also comes from DMR-0820506.

Supporting Information Available: Figures S1−S7.This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Kamath, K. R.; Park, K. *Adv. Drug Delivery Rev.* **1993**, *11*, 59.
(2) Hoffman, A. S. *Adv. Drug Delivery Rev.* **2002**, *43*, 3.
(3) Lee, K. Y.; Mooney, D. J. *Chem. Rev.* **2001**, *101*, 1869.
(4) Peppas, N. A.; Hilt, J. Z.; Khademhosseini, A.; Langer, R. *Adv. Mater.* **2006**, *18*, 1345.
(5) Walling, C. *J. Am. Chem. Soc.* **1945**, *67*, 441.
(6) Soper, B.; Haward, R. N.; White, E. F. J. *J. Polym. Sci., Polym. Chem. Ed.* **1972**, *10*, 2545.
(7) Mrkvicková, L.; Kratochvíl, P. *J. Polym. Sci., Polym. Phys. Ed.* **1981**, *19*, 1675.
(8) Bastide, J.; Leibler, L. *Macromolecules* **1988**, *21*, 2647.
(9) Landin, D. T.; Macosko, C. W. *Macromolecules* **1988**, *21*, 846.
(10) Okay, O. *Makromol. Chem.* **1988**, *189*, 2201.
(11) Antonietti, M.; Rosenauer, C. *Macromolecules* **1991**, *24*, 3434.
(12) Dotson, N. A.; Diekmann, T.; Macosko, C. W.; Tirrell, M. *Macromolecules* **1992**, *25*, 4490.
(13) Matsumoto, A. *Adv. Polym. Sci.* **1995**, *123*, 41.
(14) Kannurpatti, A. R.; Anseth, J. W.; Bowman, C. N. *Polymer* **1998**, *39*, 2507.
(15) Flory, P. J. *J. Am. Chem. Soc.* **1941**, *63*, 3083.
(16) Flory, P. J. *J. Am. Chem. Soc.* **1941**, *63*, 3091.
(17) Flory, P. J. *J. Am. Chem. Soc.* **1941**, *63*, 3096.
(18) Stockmayer, W. H. *J. Chem. Phys.* **1943**, *11*, 45.
(19) Stockmayer, W. H. *J. Chem. Phys.* **1944**, *12*, 125.
(20) Flory, P. J. *Principles of Polymer Chemistry*; Cornell University Press: Ithaca, NY, 1953.
(21) Jiang, C. F.; Shen, Y. Q.; Zhu, S. P.; Hunkeler, D. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3780.
(22) Yu, Q.; Zeng, F. Q.; Zhu, S. P. *Macromolecules* **2001**, *34*, 1612.
(23) Wang, A. R.; Zhu, S. P. *Polym. Eng. Sci.* **2005**, *45*, 720.
(24) Tsarevsky, N. V.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3087.
(25) Gao, H. F.; Min, K.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 7763.
(26) Gao, H. F.; Li, W. W.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 2335.
(27) Gao, H. F.; Miasnikova, A.; Matyjaszewski, K. *Macromolecules* **2008**, *41*, 7843.
(28) Li, W. W.; Gao, H. F.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 927.
(29) Ide, N.; Fukuda, T. *Macromolecules* **1997**, *30*, 4268.
(30) Ide, N.; Fukuda, T. *Macromolecules* **1999**, *32*, 95.
(31) Crescenzi, V.; Dentini, M.; Bontempo, D.; Masci, G. *Macromol. Chem. Phys.* **2002**, *203*, 1285.
(32) Yu, Q.; Zhu, Y. S.; Ding, Y. H.; Zhu, S. P. *Macromol. Chem. Phys.* **2008**, *209*, 551.
(33) Lynn, D. M.; Kanaoka, S.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 784.
(34) Murdzek, J. S.; Schrock, R. R. *Macromolecules* **1987**, *20*, 2640.
(35) Choi, T. L.; Rutenberg, I. M.; Grubbs, R. H. *Angwe. Chem., Int. Ed.* **2002**, *41*, 3839.
(36) Sailor, M. J.; Ginsburg, E. J.; Gorman, C. B.; Kumar, A.; Grubbs, R. H.; Lewis, N. S. *Science* **1990**, *249*, 1146.
(37) Bielawski, C. W.; Scherman, O. A.; Grubbs, R. H. *Polymer* **2001**, *42*, 4939.
(38) Bazan, G. C.; Schrock, R. R. *Macromolecules* **1991**, *24*, 817.
(39) Gorodetskaya, I. A.; Choi, T. L.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 12672.
(40) Xia, Y.; Kornfield, J. A.; Grubbs, R. H. *Macromolecules* **2009**, *42*, 3761.
(41) Hine, P. J.; Leejarkpai, T.; Khosravi, E.; Duckett, R. A.; Feast, W. J. *Polymer* **2001**, *42*, 9413.
(42) Khosravi, E. *Macromol. Symp.* **2002**, *183*, 121.
(43) Alfred, S. F.; Lienkamp, K.; Madkour, A. E.; Tew, G. N. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6672.
(44) Lienkamp, K.; Madkour, A. E.; Musante, A.; Nelson, C. F.; Nüsslein, K.; Tew, G. N. *J. Am. Chem. Soc.* **2008**, *130*, 9836.
(45) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angwe. Chem., Int. Ed.* **2002**, *41*, 4035.