Preparation of Mechanically Cross-Linked Polystyrenes

Masataka Kubo,* Naoki Kato, Takahiro Uno, and Takahito Itoh

Department of Chemistry for Materials, Faculty of Engineering, Mie University, Tsu 514-8507, Japan

Received August 14, 2003; Revised Manuscript Received January 8, 2004

ABSTRACT: This paper reports preparation of mechanically cross-linked polystyrenes using cyclic macromonomer as a nonbonding cross-linking agent. Emulsion and thermal self-initiated copolymerizations of styrene with a well-defined cyclic macromonomer based on a cyclic polystyrene were carried out to obtain mechanically cross-linked polystyrenes with high swellability. Mechanically cross-linked chloromethylated polystyrene was prepared by thermal self-initiated terpolymerization of the cyclic macromonomer, styrene, and 4-vinylbenzyl chloride.

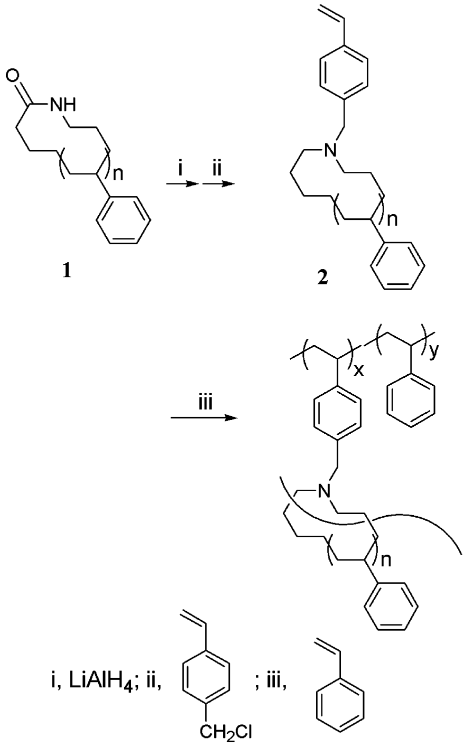
Introduction

New research techniques such as combinatorial chemistry have led to an increasing demand for supported reaction systems.[1] The most frequently used support for solid-phase organic synthesis is based on a cross-linked polystyrene which is usually prepared by radical copolymerization of styrene with divinylbenzene (DVB) as a cross-linking agent.[2] Each polymer chain is tied through covalent bonding to form a three-dimensional structure (chemical cross-linking).

Since the discovery of network formation via in situ self-threading of functionalized macrocycles, a new methodology referred to as a mechanically cross-linking has been developing.[3−5] A mechanically cross-linked vinyl polymer can be obtained by radical copolymerization of a vinyl monomer with a cyclic monomer (cyclic macromonomer) as a nonbonding cross-linking agent. Mechanically cross-linking is achieved by the threading of the ring by a segment of another polymer chain during the copolymerization. This method offers a network polymer with an enhanced swelling property due to the high degrees of freedom in the segmental movement. Zilkha and co-workers reported nonbonding cross-linking agents based on cyclic oligoethylene glycol carrying a polymerizable double bond.[6−9] Tezuka and co-workers prepared a methacrylate-functionalized cyclic poly(tetrahydrofuran), poly(THF), as a cyclic macromonomer for the formation of mechanically cross-linked poly(methyl methacrylate).[10]

We are interested in cyclic polystyrene as a ring moiety for the cyclic macromonomer as nonbonding cross-linking agent. Since polystyrene chain is harder than aliphatic polyether chains, it is expected to form a relatively stiff cavity for easy threading. Recently, we have shown that radical copolymerization of *tert*-butyl acrylate with a well-defined cyclic macromonomer based on a cyclic polystyrene gives a mechanically cross-linked polymer.[11] As part of our efforts to exploit a new series of mechanically cross-linked polymers, we report in this paper our work on the preparation of mechanically cross-linked polystyrene (Scheme 1).

Scheme 1



Experimental Section

Instrumentation. Infrared spectra were recorded on Jasco IR-700 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with JEOL EX-270 nuclear magnetic resonance spectrometer using tetramethylsilane (TMS) as an internal standard. Gel permeation chromatography (GPC) was carried out with a set of Tosoh TSK-gel MultiporeH$_{XL}$-M column using tetrahydrofuran (THF) and standard polystyrenes as an eluent and references, respectively. Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI−TOF MS) was performed using a Kratos Kompact II spectrometer using dithranol and silver trifluoroacetate as a matrix and cationization reagent, respectively. Elemental analysis was performed on Yanaco MT-5 CHN CORDER. The swelling volume was determined after immersion in a solvent at room temperature for 24 h.

Materials. The cyclic macromonomer **2** as a nonbonding cross-linking agent was prepared according to the previous method.[11] The molecular weight of **2** was determined by MALDI−TOF MS. Styrene was dried over CaH$_2$ and distilled under reduced pressure. Sodium stearate (Tokyo Kasei Kogyo), potassium persulfate (Nacalai Tesque), and poly(vinyl alcohol) (average M_w ca. 88 000, Kishida Chemicals) were used as received.

---

* To whom correspondence should be addressed: Tel +81-59-231-9411; Fax +81-59-231-9471; e-mail kubo@chem.mie-u.ac.jp.

10.1021/ma030430k CCC: $27.50

Table 1. Emulsion Copolymerizations[a] of 2 with Styrene

		THF-insoluble fraction	THF-soluble fraction	
entry	[**2**]/[St]	yield (%)	yield (%)	$M_n \times 10^{-5}$ [b]
M_n of **2** = 2500 (DP = 22)				
1	1/960	30	62	6.8
2	1/480	37	56	6.6
3	1/320	33	59	6.0
M_n of **2** = 3600 (DP = 32)				
4	1/960	56	38	6.2
5	1/480	47	51	6.0
6	1/320	68	31	5.9
M_n of **2** = 4900 (DP = 45)				
7	1/960	61	34	4.0
8	1/480	64	30	3.8
9	1/320	63	31	3.0
10	0	4	95	7.6

[a] Conditions: St = 1.0 g, $K_2S_2O_8$ = 5 mg, $CH_3(CH_2)_{16}CO_2Na$ = 50 mg, 1% PVAL = 5 mL, temperature = 60 °C, time = 10 h. [b] Determined by GPC.

Table 2. Thermal Self-Initiated Copolymerizations[a] of 2[b] with St

		THF-insoluble fraction	THF-soluble fraction	
entry	[**2**]/[St]	yield (%)	yield (%)	$M_n \times 10^{-5}$ [c]
1	0	0	97	5.8
2	1/1900	82	16	5.0
3	1/960	84	13	4.2
4	1/480	97	2	1.6
5	1/960[d]	0	98	5.6

[a] Conditions: St = 1.0 g, temperature = 80 °C, time = 48 h. [b] M_n of **2** = 4900. [c] Determined by GPC. [d] Cyclic polystyrene **1** was used instead of cyclic macromonomer **2**.

Emulsion Copolymerization. A mixture of styrene (St), cyclic macromonomer **2**, sodium stearate, potassium persulfate, and 1% solution of poly(vinyl alcohol) (PVAL) was placed in a round-bottom glass flask. The system was purged with nitrogen to remove the dissolved air and heated at 60 °C for 10 h with magnetic stirring. The resulting polymer was precipitated into an excess of methanol and washed well with methanol. The obtained polymer was soaked in a large excess of THF for 1 day to extract the unlinked polymers. Then the swollen gel was placed under reduced pressure to remove the solvent to obtain a mechanically cross-linked polystyrene as a white solid.

Thermal Self-Initiated Copolymerization. A mixture of cyclic macromonomer **2** and styrene were placed in an ampule that was degassed completely by the freeze−thaw method and sealed. The ampule was placed in a bath at 80 °C for 48 h with magnetic stirring. Tetrahydrofuran (THF) was added to the reaction mixture, and the swollen gel was recovered. The obtained gel was soaked in a large excess of THF for 1 day to extract the unlinked polymers. Then the swollen gel was placed under reduced pressure to remove the solvent to obtain a mechanically cross-linked polystyrene as a white solid.

Degradation of Mechanically Cross-Linked Polystyrene. A 0.1 g portion of cross-linked polystyrene (obtained from entry 3, Table 2) was introduced into 10 mL of dichloromethane, and the mixture was stirred at room temperature for 3 h. 1-Chloroethyl chloroformate (0.1 g, 0.7 mmol) was added, and the mixture was heated under reflux for 48 h. Then, methanol (2 mL) was added, and the mixture was heated under reflux for 12 h. The reaction mixture was analyzed by GPC.

Mechanically Cross-Linked Chloromethylated Polystyrene. A mixture of cyclic macromonomer **2** (M_n = 4900, 49 mg, 0.01 mmol), styrene (1.0 g, 9.6 mmol), and 4-vinylbenzyl chloride (147 mg, 0.96 mmol) were placed in an ampule that was degassed completely by the freeze−thaw method and sealed. The ampule was placed in a bath at 80 °C for 48 h with magnetic stirring. The mechanically linked polymer was obtained according to the above-mentioned method as a white solid (1.1 g, 92%). Anal.: C, 90.27; H, 6.32; N, 0.02; Cl, 3.16.

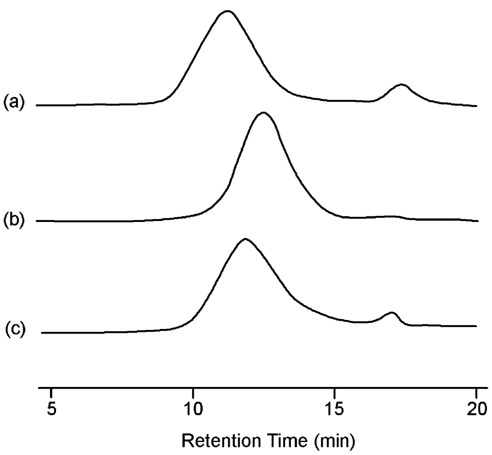


Figure 1. GPC curves of (a) THF-soluble part obtained from entry 5 (Table 1), (b) THF-soluble part obtained from entry 3 (Table 2), and (c) reaction mixture after degradation of the gel obtained from entry 3 (Table 2).

Results and Discussion

Emulsion Copolymerization of Cyclic Macromonomer 2 with Styrene. Our preliminary experiments showed that AIBN-initiated radical copolymerizations of **2** with styrene gave soluble polymers instead of gel.[11] To give a network structure, every chain in the network must have at least one threaded cyclic macromonomer **2**. One approach is to increase macromonomer concentration to introduce enough amounts of cyclic unit into a chain. However, increasing the concentration of the cyclic macromonomer resulted in the decrease of the molecular weight of the resulting polymer, suggesting a chain transfer reaction.

As another approach, we carried out emulsion copolymerizations of **2** with styrene to obtain higher molecular weight polymers. Table 1 summarized the emulsion copolymerization results. The emulsion copolymerizations successfully gave THF-insoluble cross-linked polymers (entries 1−9). A slightly decrease in molecular weight of the soluble fraction was observed with the increase of the macromonomer concentration, indicating chain transfer reactions to **2**. Judging from the molecular weight of the THF-soluble fraction (DP > 2000), sufficient amounts of cyclic macromonomer were seemed to be incorporated into the polymer chain. Varying the ratio [**2**]/[St] had a negligible effect on the yield of THF-insoluble fraction. One possible explanation may be an insufficient supply of the cyclic macromonomer **2** into the micelle where the polymerization occurs. Actually, the GPC curve of the THF-soluble fraction exhibited a small peak due to the unreacted cyclic macromonomer, as shown in Figure 1a. It is apparent that cyclic macromonomer with larger ring is more effective to form cross-linked polymer probably due to the easier threading of larger ring. It is noted there existed some THF-insoluble part even in the absence of cyclic macromonomer (entry 10), indicating a partial cross-linking due to chain transfer reactions to stabilizer (poly(vinyl alcohol)) and/or emulsifier (sodium stearate).

Thermal Self-Initiated Copolymerization of Cyclic Macromonomer 2 with Styrene. Thermal self-initiated copolymerization of cyclic macromonomer **2** with styrene was carried out in order to avoid intrinsic

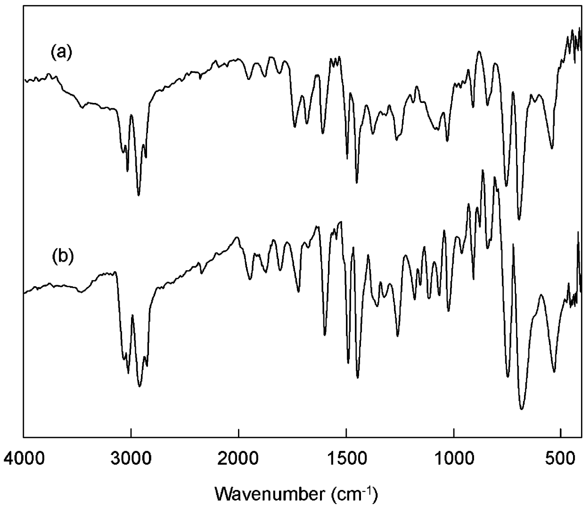


Figure 2. IR spectra of (a) mechanically cross-linked chloromethylated polystyrene and (b) commercial available chloromethylated poly(styrene-*co*-DVB) (1.1 mequiv of Cl/g).

cross-linking due to the added components. Table 2 summarized the thermal self-initiated copolymerization of **2** with styrene. Since only soluble polymer was obtained without cyclic macromonomer **2** (entry 1), the THF-insoluble fraction is considered to be due to the mechanically cross-linking. Further, no gelation took place in the presence of cyclic polystyrene **1** instead of **2** (entry 5), indicating that the existence of the polymerizable double bond is necessary for gel formation. The molecular weight of the THF-soluble fraction decreased with the increase of macromonomer concentration probably due to the chain transfer reaction to the macromonomer. In contrast to the case of emulsion copolymerization, the gel yield was greatly dependent on the macromonomer concentration; i.e., the THF-insoluble fraction increased with the increase of macromonomer concentration. Since the GPC curve of the THF-soluble part no longer exhibits a peak due to the residual macromonomer as shown in Figure 2b, a large amount of pendant cyclic units was incorporated into polystyrene chain to increase the opportunity to be threaded.

A small portion of cross-linked polystyrene (obtained from entry 3, Table 2) was subject to degradation by cleaving the cyclic polystyrene from the chain using 1-chloroethyl chloroformate as a debenzylation agent.[11] The swollen gel gradually dissolved and finally formed a homogeneous clear solution. We analyzed the reaction mixture by GPC, as shown in Figure 1c. The molecular weight of the polymer generated from the network structure was higher than that of the soluble fraction obtained in the preparation of cross-linked polystyrene, suggesting that longer chains are responsible for the network formation. Another reason for the observed high molecular weight may be due to the formation of a rotaxane-type polystyrene product.

Mechanically Cross-Linked Chloromethylated Polystyrene. In the case of our cross-linked polystyrene network both chain and cyclic segments are composed of polystyrene. Thus, the chemical reactivity and stability are expected to be similar to those of conventional chemically cross-linked polystyrene prepared by radical copolymerization of styrene with divinylbenzene. It seemed of great interest to further provide various functional materials based on mechanically cross-linked polystyrene.

Table 3. Swelling Volume (mL/g) of Cross-Linked Polystyrenes

sample	benzene	THF	CH_2Cl_2
1[a]	11	15	20
2[b]	15	23	29
3[c]	13	15	16
4[d]	7.2	5.8	8.2
5[e]	9.4	9.1	9.0

[a] Obtained from entry 8 (Table 1). [b] Obtained from entry 4 (Table 2). [c] Mechanically cross-linked chloromethylated polystyrene obtained in this work. [d] Poly(styrene-*co*-DVB), cross-linked with 2% DVB (200−400 mesh) (Aldrich). [e] 4-Chloromethylpolystyrene resin, cross-linked with 1% DVB (200−400 mesh) (Tokyo Kasei).

Among functional polystyrene resins, chloromethylated polystyrene is the most commonly used for solid-phase peptide synthesis, polymer-bound organic synthesis, and polymer-bound phase-transfer catalysis. Chloromethylated polystyrene can be made by chloromethylation of cross-linked polystyrene under a wide variety of conditions (Lewis acid, solvent, temperature, time). However, it is known that chloromethylation of cross-linked polystyrene is accompanied by intermolecular side-reactions which introduce additional chemical bonding (chemical cross-linking).[12] Thus, we carried out terpolymerization of **2**, styrene, and 4-vinylbenzyl chloride to obtain mechanically cross-linked chloromethylated polystyrene. Figure 2 shows IR spectra of the obtained mechanically cross-linked chloromethylated polystyrene and that of commercial available chloromethylated polystyrene resin (Merriefield resin). Identical absorption spectra are observed for both polymers. Elemental analysis of the obtained polystyrene confirmed substantial incorporation of the chloromethyl functionality.

Swelling Property. The swelling properties of the mechanically cross-linked polystyrenes were evaluated by soaking the sample in different polar and nonpolar solvents such as THF, dichloromethane, and benzene. The volumes of the swollen cross-linked polystyrenes in a selection of solvents are given in Table 3, together with the values of commercial available polystyrene resins. From these data it is clear that the mechanically cross-linked polystyrenes (samples 1−3) exhibited higher swelling volumes than those of chemically cross-linked polystyrenes, probably due to a very low cross-linking level and an easy movement of polymer segment. It was observed that polymer obtained by thermal self-initiated polymerization (sample 2) exhibits higher swellability than that obtained by emulsion polymerization (sample 1). This is reasonably explained by the additional chemical cross-linking during the emulsion polymerization. The swelling volume of sample 3 (chloromethylated polystyrene) was found to be lower than that of sample 2. This is probably due to the quaternization reaction between amine functionality of the cyclic polystyrene and chloromethylsyrene to form additional covalent cross-linking.

In summary, we demonstrated preparation of mechanically cross-linked polystyrene and chloromethylated polystyrene using a cyclic macromonomer as a nonbonding cross-linking agent. To improve the suitability of polystyrene-based supports for solid-phase synthesis, cross-linking agents other than divinylbenzene have been investigated. These include ethylene glycol dimethacrylate,[13] hexane-1,6-diol diacrylate,[14] 1,4-(4-vinylphenoxy)butane,[15] and tetraethylene glycol diacrylate,[16] which lead to supports with higher swellability than Merriefield resin. Introduction of mechanically cross-linking is thought to be one of useful strategy for improving polystyrene-based supports.

Acknowledgment. The authors thank Professor Jacques Roovers at Canadian National Research Council for his valuable comments. This work was partially supported by Shorai Foundation for Science and Technology.

References and Notes

(1) Dörwald, F. Z. *Organic Synthesis on Solid Phase*; Wiley-VCH: Weinheim, Germany, 2000.
(2) Staudinger, H.; Heuer, W.; Husemann, E. *Trans. Faraday Soc.* **1936**, *32*, 323−325.
(3) Gong, C.; Gibson, H. W. *J. Am. Chem. Soc.* **1997**, *119*, 5862−5866.
(4) Gong, C.; Gibson, H. W. *J. Am. Chem. Soc.* **1997**, *119*, 8585−8591.
(5) Gibson, H. W.; Nagvekar, D.; Powell, J.; Gong, C.; Bryant, W. *Tetrahedron* **1997**, *53*, 15197−15207.
(6) Zada, A.; Avny, Y.; Zilkha, A. *Eur. Polym. J.* **1999**, *35*, 1159−1164.
(7) Zada, A.; Avny, Y.; Zilkha, A. *Eur. Polym. J.* **2000**, *36*, 351−357.
(8) Zada, A.; Avny, Y.; Zilkha, A. *Eur. Polym. J.* **2000**, *36*, 359−364.
(9) Zilkha, A. *Eur. Polym. J.* **2001**, *37*, 2145−2146.
(10) Oike, H.; Mouri, T.; Tezuka, Y. *Macromolecules* **2001**, *34*, 6229−6234.
(11) Kubo, M.; Hibino, T.; Tamura, M.; Uno, T.; Itoh, T. *Macromolecules* **2002**, *35*, 5816−5820.
(12) Law, R. V.; Sherrington, D. C.; Snape, C. E.; Ando, I.; Korosu, H. *Ind. Eng. Chem. Res.* **1995**, *35*, 2740−2749.
(13) Sophiamma, P. N.; Sreekumar, K. *Indian J. Chem. Sect. B (Org. Chem.)* **1997**, *36*, 995−999.
(14) Varkey, J. T.; Pillai, V. N. R. *J. Pept. Res.* **1998**, *51*, 49−54.
(15) Toy, P. H.; Janda, K. D. *Tetrahedron Lett.* **1999**, *40*, 6329−6332.
(16) Renil, M.; Pillai, V. N. R. *Tetrahedron Lett.* **1994**, *35*, 3809−3812.

MA030430K