Radical copolymerization of methacrylate bearing five-membered cyclic dithiocarbonate moiety and 2-hydroxyethyl methacrylate and its application to networked polymer synthesis

Yukiko Inoue,* Kozo Matsumoto,** and Takeshi Endo*

* Molecular Engineering Institute, Kinki University
(11-6, Kiyanomori, Iizuka-shi, Fukuoka 820-8555, Japan)
** Department of Biological & Environmental Chemistry, Kinki University
(11-6, Kiyanomori, Iizuka-shi, Fukuoka 820-8555, Japan)

Synopsis

Radical copolymerization of 5-(methacryloyloxy)methyl-1,3-oxathiolane-2-thione (DTC) [1] and 2-hydroxyethyl methacrylate (HEMA) [2] were carried out in dimethyl sulfoxide (DMSO) using 2,2'-azobis(isobutyronitrile) (AIBN) as a radical initiator. The copolymerizations proceeded smoothly to give poly(DTC-co-HEMA)s with various compositions in almost quantitatively. Thermal properties of the obtained polymers were evaluated by thermal gravimetric analysis (TGA) and differential scanning calorimetry (DSC). The obtained polymers showed 5 wt% loss temperature ($T_{d5}$) in the range from 163 to 204°C. The polymers obtained here exhibited glass transition temperature ($T_g$) in the range from 63 to 93°C. The copolymer with 4 mol % DTC content could be cross-linked by using 4,7,10-trioxa-1,13-tridecanediamine or poly(ethylene glycol) bis(3-aminopropyl) terminated ($M_n = 1500$) as a cross-linker. The obtained networked polymers were swollen in water exhibiting 165 and 242% swelling ratio, respectively. It was also found that lysine ammonium salt could be used as a crosslinker of the poly(DTC-co-HEMA).

Key-words: 2-hydroxyethyl methacrylate, Five-membered cyclic dithiocarbonate, Diamine, Radical polymerization, Water swellable

1. Introduction

Radical polymerization is one of the most widely used methods in polymer synthesis not only because of its easy polymerization process including purification of monomers, solvents, and other reagents but also because of the high versatility in the applicable monomers.1-3) A number of functional polymers have been prepared by the radical homo- and co-polymerizations. Among these functional polymers, so-called reactive polymers, which can be used for the precursors of various functional polymers, have been of particular interest. We previously reported radical copolymerizations between a methacrylate bearing a five-membered dithiocarbonate moiety and methyl methacrylate derivatives such as methyl methacrylate or $n$-butyl methacrylate.4,5) The obtained copolymers acted as typical reactive polymers, because the five-membered dithiocarbonate can react with amines without any catalysts in mild conditions. In these copolymers, methyl
methacrylate and n-butyl methacrylate moieties played a role just for increasing polymer solubility in various organic solvents without acting as reaction sites.

Poly(2-hydroxyethyl methacrylate), which possess a hydroxyl group in the side chain, has often been used in medical applications such as contact lenses, hydrogels and drug delivery systems due to their moderate hydrophilicity, biocompatibility and less toxicity.\(^6\)-8\)

In this study, we considered that copolymers composed of a methacrylate bearing a five-membered dithiocarbonate moiety and 2-hydroxyethyl methacrylate can be novel attracting functional materials, which may be useful for various applications. Herein, we report the radical copolymerization of methacrylate bearing five-membered dithiocarbonate moiety (DTC) and 2-hydroxyethyl methacrylate (HEMA), evaluation of the thermal properties of the poly(DTC-co-HEMA)s, and further examined formation of networked polymers.

### 2. Experimental

#### 2.1 Materials

Carbon disulfide, diethyl ether, dimethyl sulfoxide (DMSO), glycidyl methacrylate, 2-hydroxyethyl methacrylate (HEMA), methanol, and tetrahydrofuran (THF) were purchased from Wako Pure Chemical Industries, LTD. (Osaka, Japan). L-Lysine, 4,7,10-trioxa-1,13-tridecanediamine and poly(ethylene glycol) bis(3-aminopropyl) terminated (\(M_n = 1500\)) were purchased from Sigma–Aldrich (WI, USA). 2,2’-Azobis(isobutyronitrile) (AIBN) was purchased from Tokyo Chemical Industry Co., LTD. (Tokyo, Japan). N,N-Dimethyl formamide (DMF), DMSO-d\(_6\), ethyl acetate (EtOAc), hexane, and lithium bromide were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan). CdCl\(_2\) was purchased from Acros organics (Geel, Belgium). L-Lysine ammonium salt \([6]\) was prepared by a reported procedure.\(^9\) HEMA was distilled under reduced pressure before use. All reagents were used without further purifications.

#### 2.2 Characterization

NMR spectra were recorded in deuterated solvents on a JEOL JNM – ECS 400 spectrometer (400 MHz for \(^1\)H). Chemical shifts (\(\delta\)) were reported in ppm relative to residual DMSO proton (2.50 ppm) (using DMSO-d\(_6\)). IR spectra were recorded on a Thermo Scientific Nicolet iS10 spectrometer equipped with a Smart iTR Sampling Accessory. Number-averaged molecular weight (\(M_n\)) and weight-averaged molecular weight (\(M_w\)) were estimated by size exclusion chromatography on a TOSOH HLC 8220GPC system equipped with refractive index and ultra violet (\(\lambda = 254\) nm) detectors, and three consecutive polystyrene gel columns, TSK gels (bead size, exclusion limited molecular weight); super-AW4000 (6 \(\mu\)m, \(>4 \times 10^4\)), super-AW3000 (4 \(\mu\)m, \(>6 \times 10^4\)), and super-AW2500 (4 \(\mu\)m, \(>2 \times 10^5\)). The system was operated at a flow rate of 0.5 mL/min, using a DMF solution of lithium bromide (10 mM) as an eluent at 40°C. Polystyrene standards were employed for calibration. Differential scanning calorimetry (DSC) was carried out with Seiko Instrument Inc. DSC – 6200 using an aluminum pan under a 50 mL/min N\(_2\) flow at a heating rate of 10°C/min. Thermal gravimetric analysis (TGA) was performed with Seiko Instrument TG-DTA 6200 using an alumina pan under a 50 mL/min N\(_2\) flow at a heating rate of 10°C/min.

#### 2.3 Synthesis of 5-(methacryloyloxy)methyl-1,3-oxathiolane-2-thione [1]

5-(Methacryloyloxy)methyl-1,3-oxathiolane-2-thione [1] was prepared by a method reported procedure with some modifications.\(^10\) To a 300mL-round-bottomed flask, which was filled with N\(_2\) gas, were added glycidyl methacrylate (4.0 mL, 30 mmol), carbon disulfide (2.0 mL, 34 mmol), LiBr (0.13 g, 1.5 mmol), and THF (30 mL). The reaction mixture was stirred at room temperature for 16 h. The crude product was purified by silica gel column chromatography using hexane and ethyl acetate as eluents to give cyclic dithiocarbonate [1] in 93 % yield as a yellow liquid. The spectral data were coincident with those reported previously.\(^10\)

#### 2.4 Synthesis of polymer [3] and poly(DTC-co-HEMA) with various compositions.

Typical procedure for synthesis of polymer [3] is as follows. To a 50 mL round-bottomed flask which
was filled with N₂ gas, were added 5-(methacryloyloxy) methyl-1,3-oxathiolane-2-thione ([I], 0.327 g, 1.50 mmol), 2-hydroxyethyl methacrylate ([2], 0.195 g, 1.50 mmol), AIBN (0.015 g, 0.09 mmol) and DMSO (3 mL), and the mixture was stirred at 60°C for 7 h. The product was purified by precipitation in diethyl ether and dried in vacuo to give the desired poly(DTC-co-HEMA)(48:52) ([3], 0.475 g, 2.73 mmol/monomer unit) in 91 % yield. IR (ATR) 3366, 2943, 1722, 1480, 1446, 1386, 1335, 1235, 1183, 1145, 1043, 908, 899, 846, 747 cm⁻¹. ¹H-NMR (DMSO-d₆, 400 MHz) δ 0.61 – 1.09 (6H, br, 2CH₃), 1.66 – 2.06 (4H, br, 2CH₂), 3.47 – 3.75 (3H, br, CH₂ and 1/2 CH₃), 3.79 – 4.04 (3H, br, CH and 1/2 CH₂), 4.09 – 4.44 (2H, br, CH₂), 4.69 – 4.85 (1H, br, OH), 5.51 – 5.66 (1H, br, CH₂). Mₙ = 120000, Mₕ/Mₙ = 3.34 (GPC relative to polystyrene standards). Tₛ = 201°C. T₇ = 81°C.

Poly(DTC-co-HEMA)(4:96):

Poly(DTC-co-HEMA)(4:96) was synthesized by 5-(methacryloyloxy)methyl-1,3-oxathiolane-2-thione ([I], 0.033 g, 0.15 mmol) and 2-hydroxyethyl methacrylate ([2], 0.078 g, 0.60 mmol). IR (ATR) 3391, 2945, 1727, 1444, 1386, 1333, 1233, 1182, 1145, 1043, 908, 878, 844, 746 cm⁻¹. Mₙ = 119, 700, Mₕ/Mₙ = 3.87 (GPC relative to polystyrene standards). Tₛ = 204°C. T₇ = 93°C.

2.5 Synthesis of networked polymers

2.5.1 Synthesis of networked polymers [5a] and [5b]

[5a]:

Typical procedure for synthesis of networked polymer [5a] is as follows. In a 20 mL round-bottomed flask, poly(DTC-co-HEMA)(4:96) (0.066 g, 0.5 mmol/monomer unit) was dissolved in DMF (0.45 mL). 4,7,10-Trioxa-1,13-tridecanediamine ([4a], 0.003 g, 0.012 mmol) was added to the solution as a crosslinker, and the mixture was stirred for a while. Then the solution turned to a gel. The product was washed with diethyl ether and methanol. Drying the residue in vacuo gave the desired networked polymer [5a] in quantitative yield. Obtained polymer was immersed in water for 48 h. Swelling ratio was determined by a ratio of the swollen polymer weight to the dry polymer weight. IR (ATR) 3358, 2931, 2870, 1721, 1660, 1557, 1483, 1447, 1386, 1244, 1149, 1080, 1023, 945, 903, 851, 747 cm⁻¹. Tₛ = 169°C. Swelling ratio: 165 %

[5b]:

The networked polymer [5b] was synthesized by using poly(ethylene glycol) bis(3-aminopropyl) terminated (Mₙ = 1500) as a crosslinker instead of 4,7,10-trioxa-1,13-tridecanediamine. IR (ATR) 3414, 2876, 1721, 1450, 1386, 1350, 1244, 1148, 1072, 1022, 943, 899, 846, 747 cm⁻¹. Tₛ = 280°C. Swelling ratio: 242 %.

2.5.2 Synthesis of networked polymer [7]

In a 20 mL round-bottomed flask, poly(DTC-co-HEMA) (20 : 80) (0.044 g, 0.1 mmol/monomer unit) was dissolved in DMF (0.3 mL). A solution of L-lysine ammonium salt ([6], 0.019 g, 0.05 mmol) in DMF (0.1 mL) was added to the solutions as a crosslinker and the mixture was stirred for a while. Then the reaction mixture turned to a gel form. The product was purified by washing the gel with diethyl ether and methanol and dried in vacuo to obtain the desired networked polymer [7] in quantitative yield. IR (ATR) 3305, 2934, 2873, 1721, 1660, 1446, 1384, 1253, 1149, 1077, 1024, 946, 901, 846, 746, 659 cm⁻¹. Tₛ = 135°C.
3. Results and discussion

We examined copolymerization of 5-(methacryloyloxy)methyl-1,3-oxathiolane-2-thione \([1]\) and HEMA \([2]\) (DTC : HEMA = 1:1) in DMSO at 70°C for 7 h using AIBN as a radical initiator (Scheme 1). By this reaction condition, the desired copolymer \([3]\) was obtained in 93% yield. Copolymer composition was determined by \(^1\)H-NMR analysis of the obtained polymer. The \(^1\)H-NMR spectrum of the obtained polymer is shown in Fig. 1. The integral ratio of CH proton \(d\) from DTC unit at 5.51-5.66 ppm to the OH proton \(h\) from HEMA unit at 4.69-4.85 ppm was used for the determination. This reaction proceeded smoothly to give the corresponding copolymer with almost the same copolymer composition to the initial monomer feed ratio. The FT-IR spectrum of the obtained polymer \([3]\) is shown in Fig. 2. A strong absorption at 1183 cm\(^{-1}\) attributed to the C=S stretching of the five membered cyclic dithiocarbonate structure and an absorption at 1722 cm\(^{-1}\) attributed to the C=O stretching of the methacrylate part were clearly observed. A weak absorption at 3366 cm\(^{-1}\) attributed to the OH stretching of the HEMA structure was also observed.

The obtained polymer \([3]\) was soluble in DMF and DMSO but insoluble in THF and Methanol. These results clearly indicated that the desired polymer \([3]\) was obtained.

Fig. 1 \(^1\)H-NMR spectrum of obtained copolymer \([3]\) (in DMSO-d\(_6\)).

Fig. 2 FT-IR spectrum of copolymer \([3]\).

Scheme 1 Radical copolymerization of DTC \([1]\) and HEMA \([2]\).
Furthermore, thermal phase transition behavior and thermal stability were analyzed by DSC and TGA. Glass transition temperature (T_g) was observed at 81℃ and 5 wt % decomposition temperature (T_d5) was observed at 201℃.

Next, copolymerization with various monomer compositions were examined. The results of the copolymerizations are summarized in **Table 1**. All copolymerization proceeded smoothly to give the corresponding copolymers in excellent yield with almost the same composition as the monomer feed ratios (entry 1 – 4). The obtained polymers have high molecular weight over 119700. The molecular weight distribution of the polymer became slightly larger when the feed ratio of DTC increased. This maybe because a subtle cross-linking occurred at the DTC unit, which could not be detected by 1H-NMR spectroscopy.  

Thermal phase transition behavior and thermal stability were analyzed by DSC and TGA. DSC and TGA curves are shown in **Fig. 3** and **Fig. 4**. The T_g values of poly(DTC-co-HEMA)s decreased with the increase of the composition of the soft HEMA unit (Fig. 3). The T_g values of the copolymers depend on those of DTC homopolymer (115℃) and HEMA homopolymer (73℃). T_d5 values of the copolymers were observed in lower temperature region (163 to 204℃). These low thermal stability of the copolymers may be due to the occurrence of side reactions between DTC and/or HEMA at around 150℃.

It is well-known that five-membered dithiocarbonate can readily react with various amines without any catalysts at room temperature to give the corresponding thiourethanes. Here, 4,7,10-trioxo-1,13-tridecanediame [4a] and poly(ethylene glycol) bis(3-aminopropyl) terminated [4b] were selected as a cross-linker and their reactions with the obtained polymer were examined (**Scheme 2**). Copolymer poly(DTC-co-HEMA)(4:96) was dissolved in DMF. Addition of diamine [4a] or [4b] to the solution caused instant gelation, which clearly indicated the formation of cross-linked polymers, respectively. A quite small amount of DTC moiety (4 mol %) was enough

**Table 1** Copolymerization of DTC [1] with HEMA [2].

<table>
<thead>
<tr>
<th>Entry</th>
<th>Feed ratio</th>
<th>Composition</th>
<th>Yield (%)</th>
<th>M_n</th>
<th>M_w/M_n</th>
<th>T_g (℃)</th>
<th>T_d5 (℃)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DTC</td>
<td>HEMA</td>
<td>DTC</td>
<td>HEMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>95</td>
<td>4</td>
<td>96</td>
<td>99</td>
<td>120,200</td>
<td>2.37</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>80</td>
<td>20</td>
<td>80</td>
<td>92</td>
<td>135,100</td>
<td>2.95</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>50</td>
<td>48</td>
<td>52</td>
<td>91</td>
<td>120,000</td>
<td>3.34</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>20</td>
<td>78</td>
<td>22</td>
<td>93</td>
<td>119,700</td>
<td>3.87</td>
</tr>
</tbody>
</table>

*a Reaction conditions: DTC [1], HEMA [2] and AIBN (0.03 mmoI) in DMSO (3 mL), at 60℃, for 7 h, under N2.

*b Determined by 1H-NMR.

*c Isolated by precipitation in diethyl ether.

*d Estimated by GPC based on polystyrene standards, eluted by THF.

*e Determined by DSC.

*f Determined by TGA.
to complete the gelation. The cross-linked polymers were isolated by consecutive precipitations in diethyl ether and methanol followed by drying in vacuo. The FT-IR spectrum of the obtained polymer \([5a]\) is shown in Fig. 3. A strong absorption at 1660 cm\(^{-1}\) attributed to the N–C=S stretching of the thiourethane structure was clearly observed along with the absorption at 1772 cm\(^{-1}\) attributed to the C=S stretching of the starting dithiocarbonate. A weak absorption at 3358 cm\(^{-1}\) attributed to the OH stretching of the HEMA structure was also observed. These results suggest that the dithiocarbonate moiety partially reacted with the amine with keeping hydroxyl group of HEMA unit unchanged. Cross-linked polymer \([5a]\) and \([5b]\) were swellable in water. It is generally-known that polyHEMA is insoluble in water but has moderate hydrophilicity. To evaluate the hydrophilicity of the cross-linked polymers, swelling ratio in water \([100 \times (\text{weight of swollen polymer} - \text{weight of dry polymer} / \text{weight of dry polymer})]\) was examined. Swelling ratios of the cross-linked copolymers \([5a]\) and \([5b]\) were 165 and 242 %, respectively. We consider that the swelling ratio of \([5b]\) was higher than that of \([5a]\) because \([5b]\) had longer hydrophilic cross-linker in the polymer networks.

We further tried to use amino acid and its derivative as cross-linkers. When L-lysine was used as a cross-linker, crosslinking did not proceed well due to the low solubility in organic solvent of L-lysine. On the other hand, when L-lysine ammonium salt \([6]\) was used as a cross-linker, the reaction solution gelled immediately. We consider that free amino groups in L-lysine ammonium salt dissolved well in DMF and smoothly reacted with the DTC moieties in the copolymers to provide networked polymer (Scheme 3).

**4. Conclusion**

In this study, we studied radical copolymerization of methacrylate derivative having five-membered cyclic dithiocarbonate and HEMA in DMSO using AIBN as a radical initiator. Copolymerization was proceeded smoothly to give the corresponding copolymers with
various compositions in high yield. We confirmed that the copolymer having even low content of the DTC moiety could react with diamines to give the cross-linked polymers. Further investigations on applications to functional materials are currently in progress.

References

Fig. 5 FT-IR spectrum of obtained polymer [5a].