

Radical Exchange Reactions of Polymers with Dynamic Covalent Linkages under Various Conditions

蘇, ?

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**Radical Exchange Reactions of Polymers
with Dynamic Covalent Linkages
under Various Conditions**

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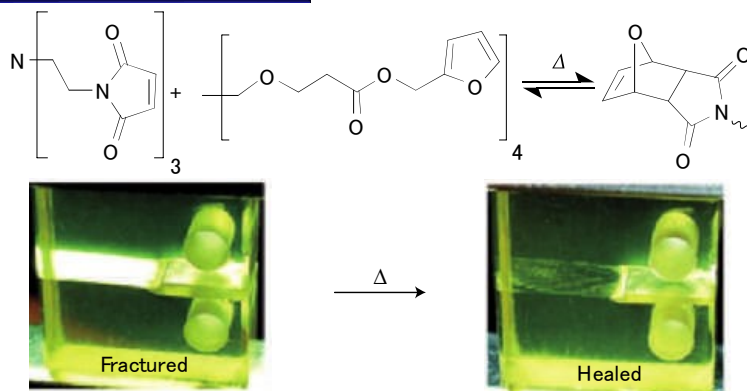
Chapter 1

General Introduction

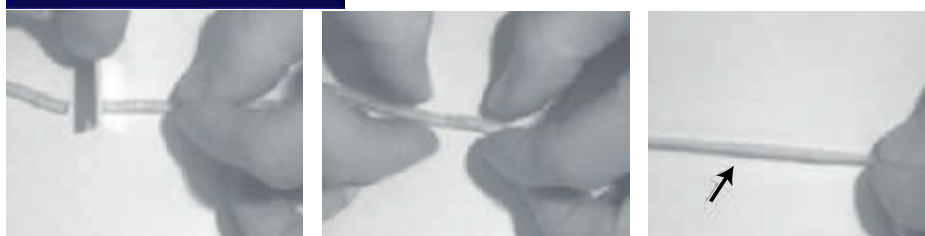
1.1 Introduction

New materials with the ability to reversibly adapt to their environment are continually emerging and their design requires dynamic linkages for the reorganization of the material. For example, some new adaptable and reorganizable materials such as mendable polymers,^{1,2} self-healing polymers,^{3,4} stimuli-responsive polymers,⁵ and reshapable polymers⁶ have been reported using dynamic linkages, as shown in **Figure 1-1**. Dynamic linkages can be classified into non-covalent linkages such as hydrogen bonding and π - π interaction, and covalent linkages.

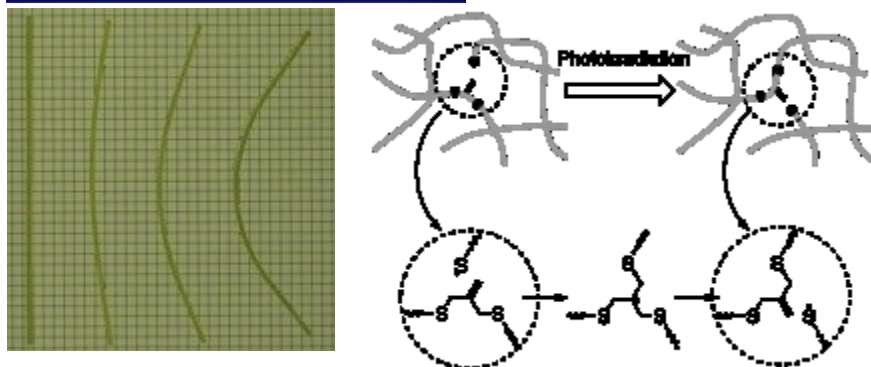
Mendable Polymer



Self-healing Polymer



Stimuli-Responsive Polymer



Reshapable Network Polymer

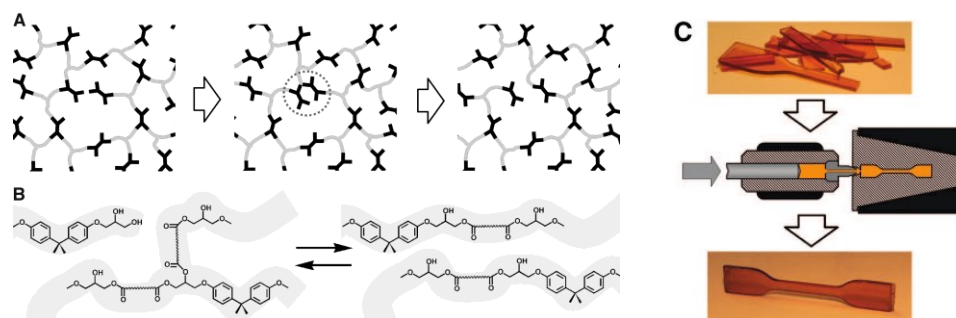


Figure 1-1. Some new adaptable and reorganizable materials using dynamic linkages.

1.2 Dynamic linkages

Dynamic linkages in molecules and their aggregates achieve reversible breaking and combining under equilibrium conditions. The dynamic linkages can be used to include supramolecular interactions and dynamic covalent linkages. They have been used to allow efficient formation of thermodynamically stable products or lead to the creation of dynamic combinatorial libraries.⁷⁻¹⁰

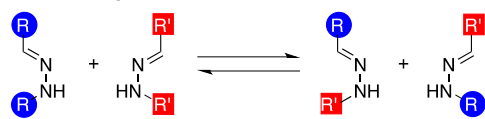
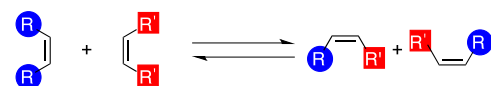
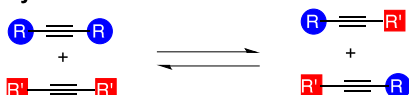
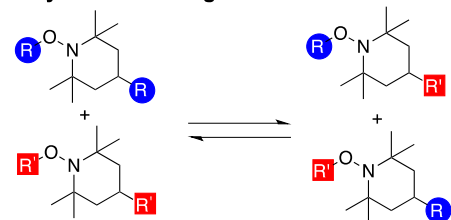
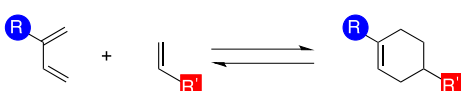
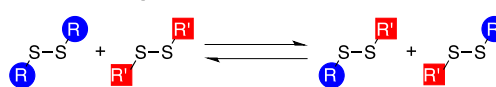
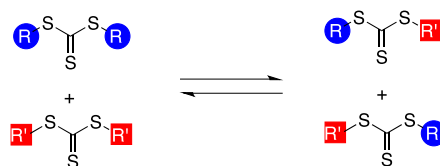
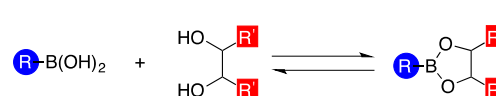
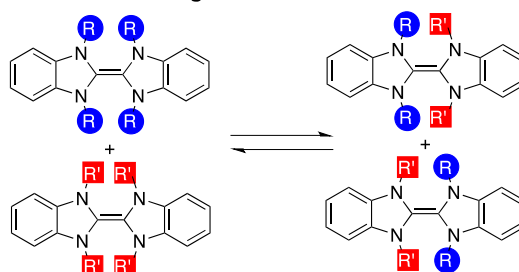
1.2.1 Dynamic processes

Under specific environmental conditions, dynamic processes can be continuous or occur. For example, if dynamic linkages are incorporated into a polymeric architecture, then after reaction polymers will have the potential to show stimuli-responsive properties of dynamic polymers. Also, dynamic linkages under equilibrium conditions can exchange components, and product formation can be influenced by external factors such as temperature, concentration, and so on. On the contrary, without stimuli the dynamic covalent linkages usually cannot show reversibility.

1.2.2 Dynamic non-covalent linkages and covalent linkages

Typical dynamic non-covalent linkages are hydrogen bonding, electrostatic interaction, and π - π interaction. Under continuous equilibrium, dynamic non-covalent linkages are highly susceptible to thermal conditions, solvents, and concentration that can be used to dynamic materials with external stimuli. However, in polymeric systems, the dynamic process can become slow to achieve a virtual fixed state, for example, by kinetically trapping through glass

transition or gelation processes.¹¹ Dynamic covalent linkages are a kind of covalent linkages that can break and reform under the appropriate conditions without irreversible side reactions. The production of robust covalent molecules could be allowed while maintaining a dynamic character that can be accomplished when specific external factors are present. For example, by increasing the concentration of a catalyst, the dynamic linkages can be formed more rapidly, and removal or quenching of the catalyst allows the possibility of kinetically fixing the product. Therefore, when these systems are not under reversible conditions, they behave like traditional covalent molecules whose bonds are not susceptible to concentration or solvent polarity and can be thermally stable. The equilibrium for dynamic covalent linkages can be controlled in a slower process as a result of breaking covalent bonds. Structurally dynamic polymers have made use of dynamic covalent linkages such as C=N exchange,¹²⁻¹⁴ alkene metathesis,¹⁵⁻²⁰ alkyne metathesis,²¹ alkoxyamine exchange,²² Diels-Alder reaction,²³⁻²⁸ disulfide exchange,²⁹⁻³⁴ trithiocarbonate exchange,³⁵⁻³⁷ boronic acid esterification³⁸⁻⁴¹ and carbene dimer exchange,⁴²⁻⁴⁴ as shown in **Scheme 1-1**.

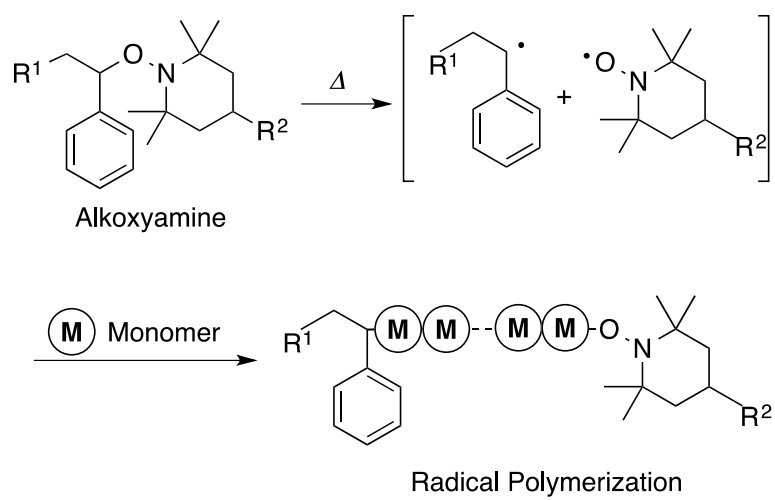
C=N exchange**Alkene metathesis****Alkyne metathesis****Alkoxyamine exchange****Diels-Alder reaction****Disulfide exchange****Trithiocarbonate exchange****Boronic acid esterification****Carbene dimer exchange****Scheme 1-1.** Selected dynamic covalent linkages.

1.2.3 Dynamic polymers

The behavior of dynamic polymer will rest with the nature of the dynamic linkages. It determines to a large extent that stimulus the material will respond and affect the thermodynamic parameters of the response itself. Therefore, this ability to control dynamic linkages in the polymer gives the chemist a molecular method in designing a structurally dynamic polymer. It is different from conventional polymers, the structures and constitutions of polymers with dynamic covalent linkages, dynamic covalent polymers, can be reorganized under appropriate conditions even after polymerization.

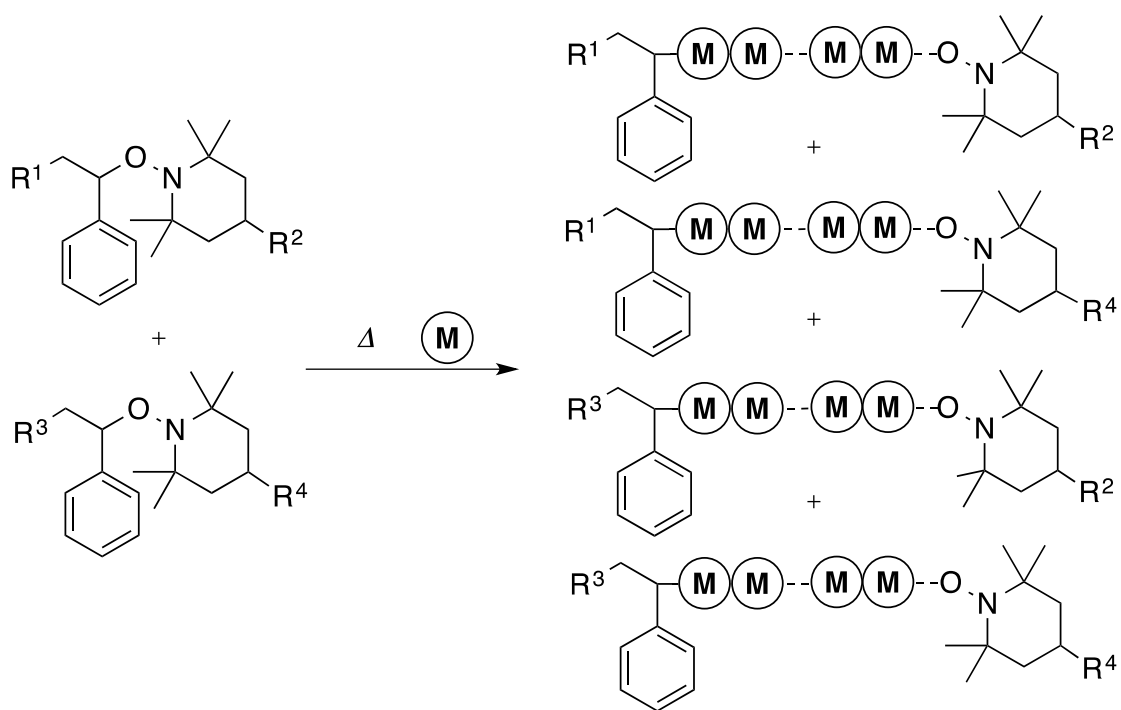
1.3 Alkoxyamines

Since the discovery of nitroxide-mediated radical polymerization^{45,46} using TEMPO, alkoxyamines have been well known as structures of the propagating chain ends in nitroxide-mediated radical polymerization.⁴⁷⁻⁵³ The key step in nitroxide-mediated radical polymerization is the reversible capping of the polymer chain end by a stable nitroxide free radical species.⁵⁴ Another significant advance with nitroxide-mediated radical polymerization was the recognition of an alkoxyamine as a unimolecular initiating agent, providing both the reactive initiating radical and the stable mediating nitroxide radical.⁵⁵ By using the nitroxide-mediated radical polymerization method, monomers such as styrene and acrylate derivatives can be polymerized from alkoxyamine initiators, as shown in **Scheme 1-2**.⁵⁶

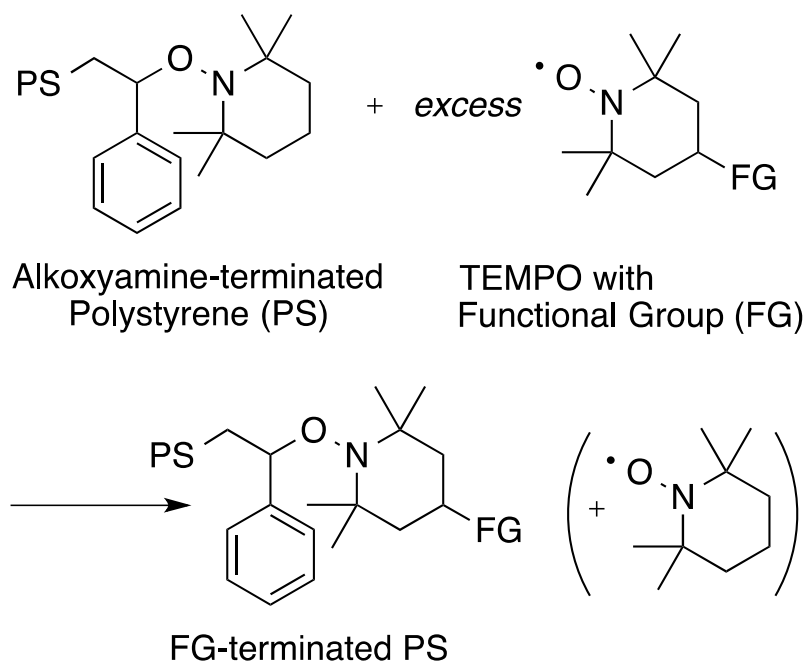


Scheme 1-2. Nitroxide-mediated radical polymerization from alkoxyamine.

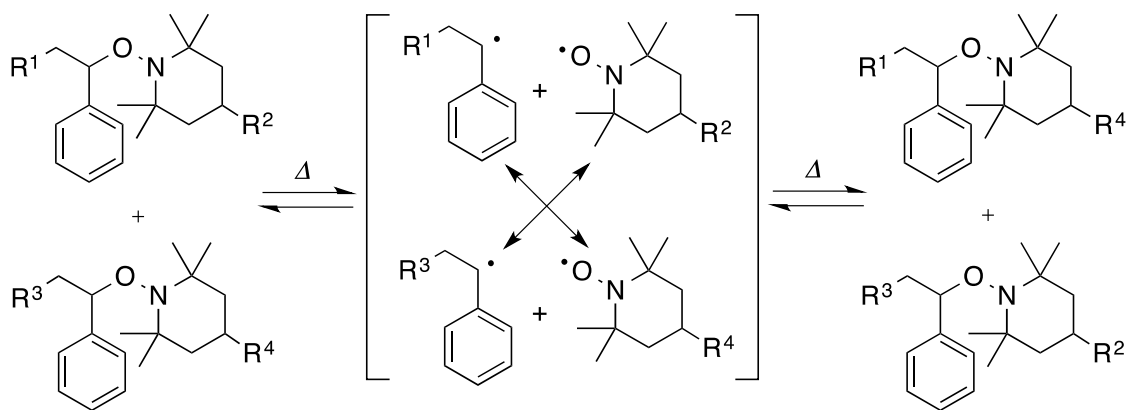
The radical polymerization of styrene with two different unimolecular alkoxyamine initiators, Hawker and co-workers reported that the radical crossover of the mediating nitroxide moieties occurred at the termini of the growing polymer chains during polymerization, as shown in **Scheme 1-3**.⁵⁷ Furthermore, an exchange reaction with an excess amount of other nitroxide derivatives at the terminal group of the polystyrene prepared by nitroxide-mediated radical polymerization was also reported by Turro et al., as shown in **Scheme 1-4**.⁵⁸ These results suggested that alkoxyamine derivatives have the potential to exchange with each other upon heating. Even though there was no monomer in the system, the alkoxyamine derivatives could be expected to scramble, as shown in **Scheme 1-5**, as a result of reversible C–ON bond cleavage and formation upon heating, because the dissociation energy of the C–ON bond in the alkoxyamine is very low.



Scheme 1-3. Radical crossover of the mediating nitroxide moieties occurred at the termini of the termini of the growing polymer chain during nitroxide-mediated radical polymerization.

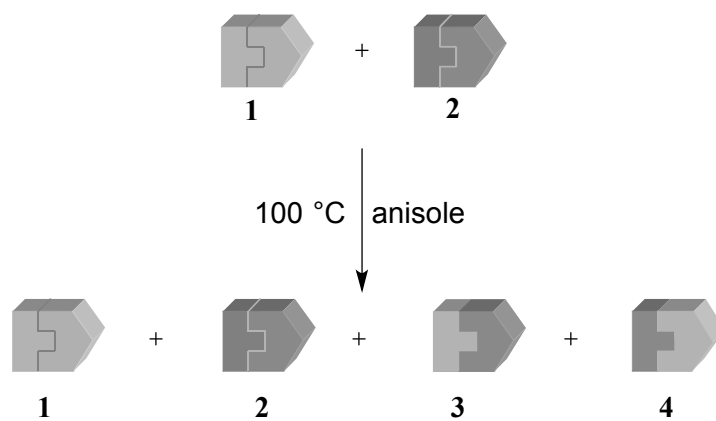
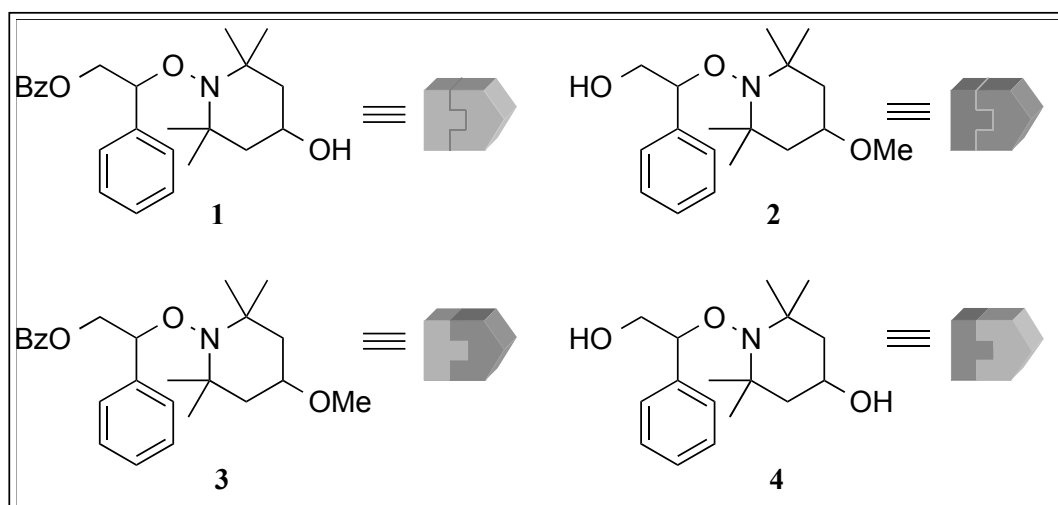


Scheme 1-4. Exchange reaction with an excess amount of other nitroxide derivatives at the terminal group of the polystyrene prepared by nitroxide-mediated radical polymerization.



Scheme 1-5. Radical crossover reaction of alkoxyamine derivatives
in the absence of monomers.

The exchangeability of alkoxyamine units was confirmed by model exchange reactions using low molecular weight alkoxyamines.⁵⁹ The reversible dissociation and formation of the C–ON bond in alkoxyamines were monitored as a crossover reaction between alkoxyamine derivatives. Alkoxyamine derivatives **1–4**, bearing different substituents at both ends, were prepared, and model crossover reactions were carried out, as shown in **Scheme 1-6**.



Scheme 1-6. Model reaction of radical crossover of alkoxyamine derivatives in anisole.

1.4 Cross-linking reaction

Cross-linkings are bonding to that link one polymer chain to another. They can be covalent bonds or ionic bonds. Polymer chains can refer to synthetic polymers. When the term cross-linking is used in the synthetic polymer science field, it usually refers to the use of cross-links to promote a difference in physical properties of the polymers. When polymer chains are linked together by cross-links, they lose some of their ability to move as individual polymer chains. For example, a liquid polymer where the chains are freely flowing can be turned into a solid or gel by cross-linking the chains together.

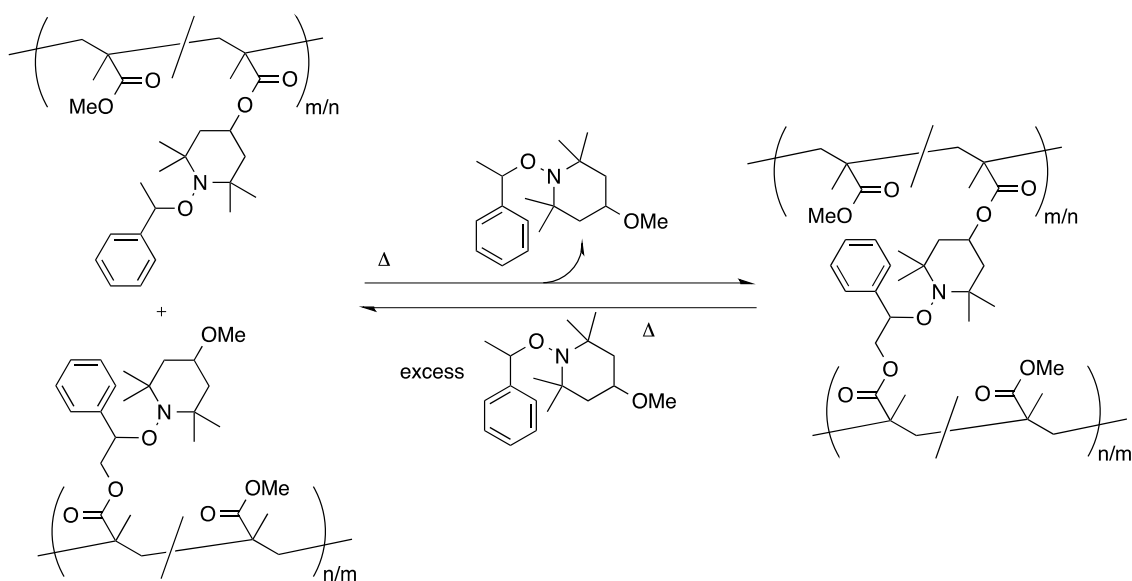
1.4.1 Density of cross-linking reaction

In polymer chemistry, when a synthetic polymer is said to be cross-linked, it usually means that the entire bulk of the polymer has been exposed to the cross-linking method. The resulting modification of mechanical properties depends strongly on the cross-linking density. Low cross-linking densities raise the viscosities of polymer melts. Intermediate cross-linking densities transform gummy polymers into materials that have elastomeric properties and potentially high strengths. Very high cross-linking densities can cause materials to become very rigid or glassy, such as phenol-formaldehyde materials. In the thesis, chapter 2 introduced the cross-linking reaction was carried out in an aqueous system that was typical low cross-linking densities. However, in chapter 3 under bulk condition high cross-linking densities reaction was occurred because the radical exchange reaction was carried out without any solvent at high concentration condition.

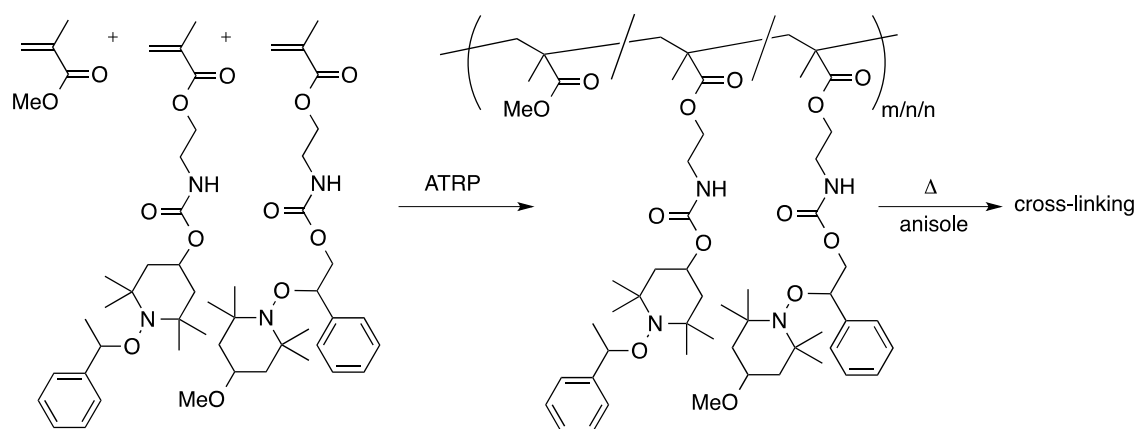
1.4.2 Cross-linking reaction by alkoxyamine unites

Cross-linked polymers have been widely applied in various fields due to their attractive properties, such as adsorption of solvents,⁶⁰ other substances,⁶¹ and their useful functionalities.^{62–65} Because the cross-linking points of typical cross-linked polymers such as poly(styrene-*co*-divinylbenzene)⁶⁶ consist of strong and fixed covalent bonds, it is difficult to change their structures after preparation. Therefore, the crosslinking density and composition of a network polymer are determined in the preparation step. In contrast, dynamic covalent chemistry can impart reorganizability to cross-linked polymers. For example, a thermodynamic covalent cross-linking system based on the radical exchange reaction of alkoxyamine units was constructed. After heating, the solution was transformed into a gel at high concentrations. The crosslinking behavior remarkably depended upon the concentration,⁶⁷ as shown in **Scheme 1-7**.

A smarter system was constructed by using random copolymers of methacrylic esters containing complementarily reactive alkoxyamine units,⁶⁸ as shown in **Scheme 1-8**. The random copolymers of MMA and two types of methacrylic esters with alkoxyamines at different positions were synthesized by the ATRP method. A radical crossover reaction of random copolymer was carried out by heating a degassed anisole solution at 100 °C at various concentrations. At high concentrations, the solution was transformed into a macroscopic gel after heating for several hours, suggesting that the intermolecular crosslinking reaction occurred preferentially under such conditions. At low concentrations, however, no gelation was observed during the reaction. This result suggests that the intramolecular radical crossover reaction occurred preferentially and that the radius of gyration as well as the relative molecular weight of the polymer decreased after the reaction.



Scheme 1-7. Reversible crossover reactions between linear polymethacrylate with complementarily reactive alkoxyamine unites in their side chains.



Scheme 1-8. Cross-linking reaction of linear polymethacrylate with complementarily reactive alkoxyamine unites in the side chains.

1.5 Suggestion and contents

Materials cross-linked by reversible covalent bonds can be expected to possess the same stability as static materials due to covalent connections as well as the reorganizability as with dynamic materials. Dynamic covalent polymer whose structure is stable under normal conditions and is changeable in organic solvent by the cross-link reaction of covalent bonds upon heating were reported²², **Figure 1-2**. However, there is no report on reversible cross-linking and decross-linking reactions of alkoxyamine-containing dynamic covalent polymers in an aqueous system and bulk system. Otherwise, in an aqueous system, water is evidently the most abundant and environmentally benign solvent and has the industrial advantage that it can be used in large amounts without producing hazardous waste. In bulk system, bulk polymeric materials have higher mechanical properties and higher concentration of functional groups than polymer solutions and gels. Also, non-solvent reversible cross-linking systems are environmentally benign.

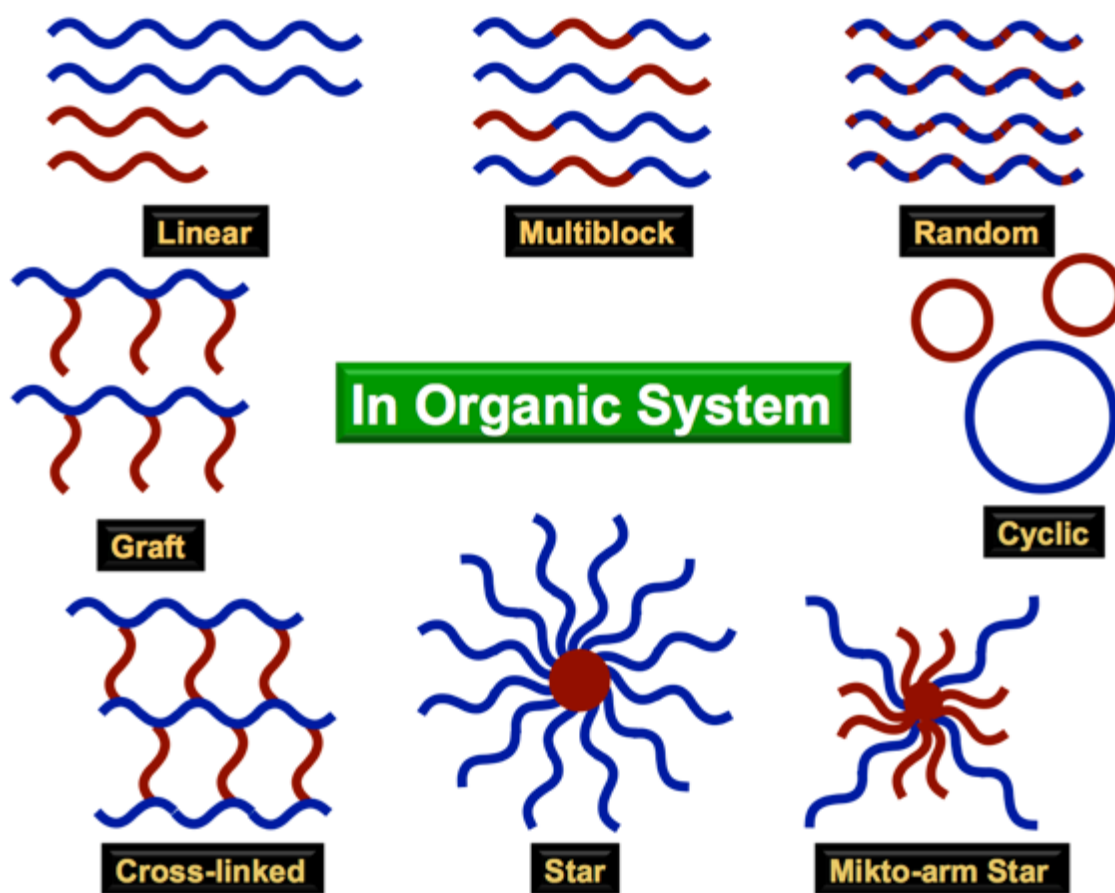


Figure 1-2. Alkoxyamine reactions of polymers.

In this thesis, it is objected to radical exchange reactions of polymers with dynamic covalent linkages under various conditions. Since radical reactions are tolerant of many functional groups and solvents, the present system may be applied to aqueous and bulk conditions, as shown in **Figure 1-3**.

In chapter 2, cross-linking reactions of water-soluble polymers with alkoxyamine units in their side chains were carried out in an aqueous system. Also, de-cross-linking was performed in the presence of excess water-soluble alkoxyamine in an aqueous system.

In chapter 3, cross-linking and de-cross-linking reactions of low glass transition temperatures (T_g) polymers with alkoxyamines were carried out under bulk conditions.

In chapter 4, plasticizer-promoted cross-linking of a dynamic covalent polymer with complementarily reactive alkoxyamine units in the side chain was investigated under bulk conditions.

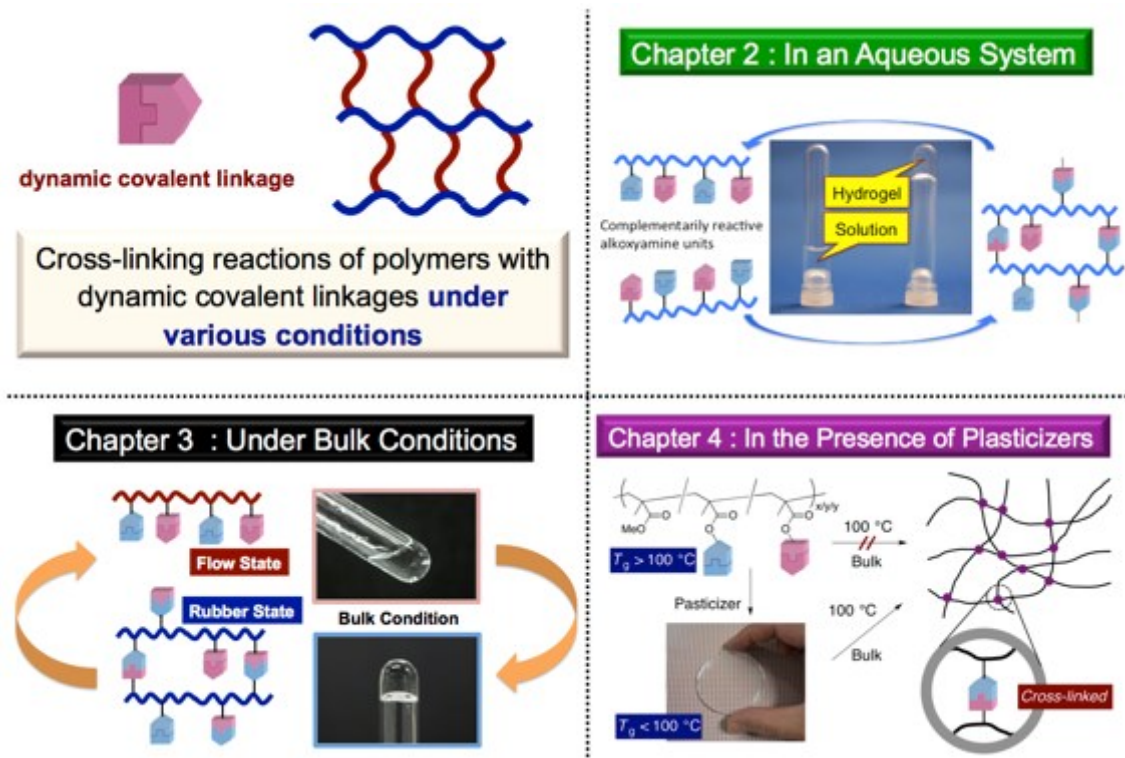


Figure 1-3. Radical exchange reactions of polymers with dynamic covalent linkages under various conditions.

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Chapter 2

Radical Exchange Reactions of Polymers with Dynamic Covalent Linkages in an Aqueous System

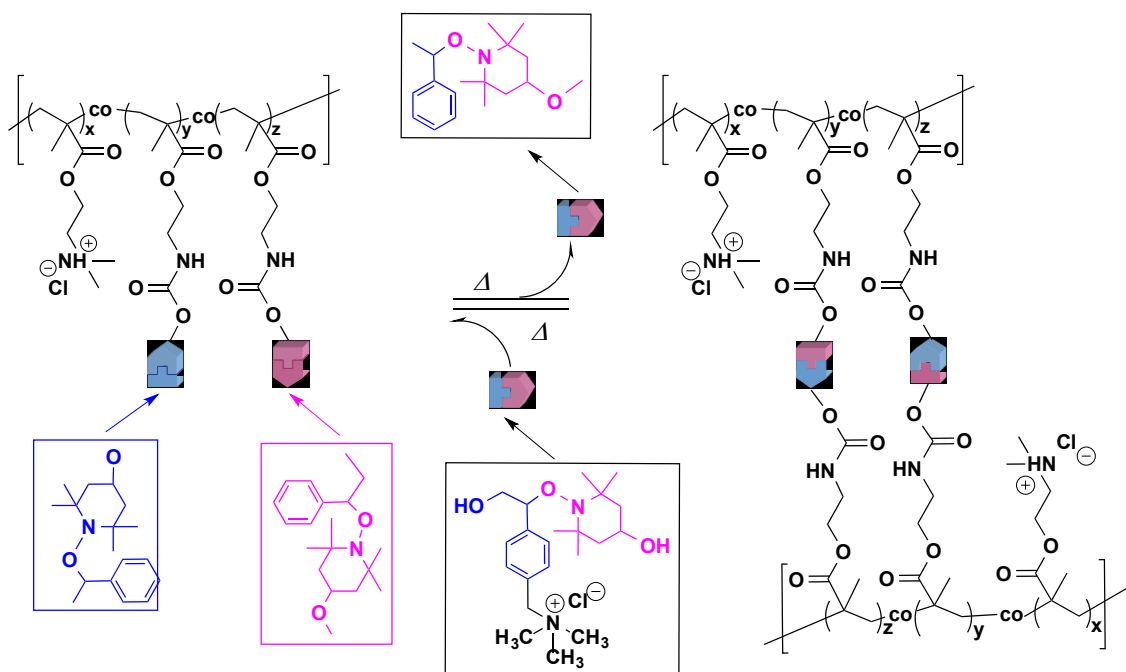
2.1 Introduction

Dynamic covalent chemistry combines the robustness of covalent linkages with the reversibility of non-covalent interactions,^{1–3} which makes it a powerful tool for the synthesis of impressively complex structures under thermodynamic controls.⁴ Reversible covalent exchange reactions such as disulfide exchange,^{2c,d,5} olefin metathesis,⁶ and thermoreversible Diels–Alder reaction⁷ have been utilized for dynamic covalent chemistry and applied to molecular systems, including self-assembly⁸ and structural transformation on environmental change.^{9–13} In response to equilibrium perturbations, such as changes in concentration, temperature, ionic factors, electric or magnetic fields, chemical or biological agents, and mechanical stress, constitutional alterations may result from re-equilibration of the product.^{14–17} Considerable attention has also been attracted in terms of applying dynamic covalent chemistry to developing new polymers such as dynamic covalent polymers,^{2b,14,18–20} which could be considered as reorganizable polymers or stimuli-responsive polymers, consisting of reversible covalent bonds. Formations of multiblock copolymers²¹ and graft copolymers²² from dynamic covalent polymers containing alkoxyamine have been previously reported.

Cross-linking systems have also been prompted by dynamic covalent chemistry. For example, sequence-selective cross-linking of oligoamide in aqueous media to afford the corresponding macrocyclic oligoamide has been reported.²³ In polymer chemistry, reversible covalent bonds have provided covalently cross-linked polymers with particular abilities such as sol–gel transition,^{9,24,25} network structure variation,²⁶ and self-healing properties^{27–31} with no decrease in their high mechanical strengths and stabilities. So far, a reversible cross-linking system in organic solvents using alkoxyamine compounds have been reported, which are

adducts of styryl radicals and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), as reversible covalent bonds. The alkoxyamine compounds are widely known as initiators for living radical polymerizations, reaching equilibrium between the alkoxyamines (dormant species) and radicals (active species) over 60 °C. Additionally, in homolysis, each unit is exchanged by crossover of the radicals to form different alkoxyamine compounds.^{22,32,33} Therefore, the cross-linking reactions occur by the radical exchange of the polymers with alkoxyamine units in their side chains.²⁵

In comparison to polymer reactions in organic solvents, those in aqueous media can be applied as environmentally benign polymeric materials such as coatings and paints. Water is evidently the most abundant and environmentally benign solvent and has the industrial advantage that it can be used in large amounts without producing hazardous waste.³⁴ Because the radical reactions are tolerant of many functional groups and solvents, similar to olefin metathesis polymerization,³⁵ the exchange reaction of alkoxyamine units is a candidate for cross-linking units in aqueous media. In this chapter, reversible cross-linking in aqueous media using water-soluble dynamic covalent polymers with alkoxyamine units is discussed, as represented in **Scheme 2-1**. The cross-linking reactions are traced from the perspective of the amounts of alkoxyamine in the polymer and reaction concentrations. In addition, de-cross-linking reaction is attempted via radical exchange reaction of the cross-linked polymers with hydrophilic alkoxyamine compound.



Scheme 2-1. Cross-linking and de-cross-linking reactions of the water-soluble polymers with alkoxyamine units in the side chain via radical exchange reaction.

2.2 Experimental

2.2.1. Materials

4-Acetyl-TEMPO was synthesized by reference to a previous report.^{27–29} Methacrylic esters with alkoxyamine units (**2-1** and **2-2**) were synthesized as previously reported. 4-Chloromethyl styrene was kindly supplied from AGC Seimi Chemical Co., Ltd., and used without further purification. Benzoyl peroxide (BPO) was purchased from Nacalai Tesque, Inc., and used without further purification. L(+)-ascorbic acid, and 2,2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70) were purchased from Wako Pure Chemical Industries, and used without further purification. Trimethylamine in ethanol solution were purchased from Sigma-Aldrich Co., and used without further purification. 2-(Dimethylamino)ethyl methacrylate (DMAEMA) was purchased from Wako Pure Chemical Industries, and purified by distillation under reduced pressure over calcium hydride.

2.2.2. Measurement

¹H (400 MHz) NMR spectroscopic measurements were carried out at 25 °C with a Bruker AV-400 spectrometer using tetra- methylsilane as an internal standard in chloroform-*d* (CDCl₃) and DMSO-*d*₆. The number-average molecular weights (M_n) and molecular weight distribution of soluble polymers were determined by gel permeation chromatography (GPC) using *N,N*-dimethylformamide (DMF) or water as eluents. DMF-eluent GPC was recorded on a JASCO instrument equipped with a JASCO 2031plus refractive index (RI) detector and two poly (hydroxyethyl methacrylate) gel columns (Shodex OHpak SB804HQ, 0.5 mL min⁻¹). DMF containing 0.01 M LiBr was used as an eluent. A calibration curve was constructed from a

series of well-defined polystyrene standard samples. Aqueous GPC measurement was performed with a Shimadzu high-performance liquid chromatography (HPLC) system connected to three polystyrene gel columns of Tosoh G3000PW_{XL}-CP (pore size 20 nm, bead size 7 μ m) and G5000PW_{XL}-CP (pore size 100 nm, bead size 10 μ m) 2 and equipped with a RI detector (Shimadzu RID-10A) using an acetic acid aqueous solution (500 mM) containing sodium nitrate (200 mM) as an eluent at a rate of 0.6 mL min⁻¹. A calibration curve was constructed from a series of well-defined poly[$\{2\text{-(methacryloyloxy)ethyl}\}$ trimethyl ammonium chloride] standard samples. The dynamic viscoelastic measurements were carried out with a Physica MCR101 rheometer with a parallel circular plate 12 mm and 20 mm in diameter in water (10 wt%) at 25 °C. The storage modulus (G') was evaluated based on the average values of numerous measurements.

2.2.3. Synthesis of poly(DMAEMA-*co*-2-1-*co*-2-2) (2-3).

In a typical run, methacrylic esters with alkoxyamine units **2-1** (0.44 g, 1.0 mmol) and **2-2** (0.46 g, 1.0 mmol), DMAEMA (3.03 mL, 0.018 mol), toluene (3.37 mL), and V-70 (0.308 g, 1.0 mmol) were charged into a glass tube. Then, the atmosphere was replaced by an argon purge using the freeze-pump-thaw process, and the glass tube was immersed into oil bath at 40 °C for 9 h. The product was purified by reprecipitation into hexane, and freeze-drying using benzene to obtain a white solid (**2-3b**) (3.18 g, 85.3% yield). $M_n = 46900$, $M_w/M_n = 2.06$.

2.2.4. Synthesis of water-soluble polymer (2-4).

In a typical run (**2-4b**), polymer **2-3b** (0.50 g) was added in hydrochloric acid (2 N, 1.45 mL)

and stirred for 24 h at room temperature. The solvent was evaporated and the product was freeze-dried to obtain white powder (0.62 g, 93 % yield).

2.2.5. Synthesis of alkoxyamine diester (2-5).

4-acetyl TEMPO (8.94 g, 42.0 mmol) was charged into a 500 mL round-bottom flask, and 4-chloromethyl styrene (150 mL) and BPO (6.17 g, 25.0 mmol) were added. After a nitrogen purge, the mixture was heated at 80 °C for 20 h under the nitrogen atmosphere. Then, L(+)-ascorbic acid was added to reduce acetyl-TEMPO, the product was purified by column chromatography eluting with ethyl acetate/hexane (v/v = 1/20) and dried in vacuo to obtain pale yellow oil of alkoxyamine diester **2-5** (2.2 g, 9 % yield). ¹H NMR (400 MHz, CDCl₃, δ /ppm): 0.74 (s, 3H, CH₃), 1.11 (s, 3H, CH₃), 1.25 (s, 3H, CH₃), 1.41 (s, 3H, CH₃), 1.41-1.85 (m, 4H, CH₂), 3.95 (m, 1H, CH), 4.51 (dd, 1H, CH), 4.64 (dd, 2H, CH₂), 4.83 (dd, H, CH), 5.06 (t, 1H, CH), 7.26-7.93 (m, 5H, aromatic proton).

2.2.6. Synthesis of alkoxyamine diol (2-6).

Alkoxyamine diester **2-5** (1.23 g, 2.51 mmol) and EtOH (150 mL) were charged into a round-bottom flask, sodium hydroxide (1.18 g, 30 mmol) dissolved in water (40 mL) was added into at room temperature. After 6 h, concentrated HCl aq. was added to adjust pH to 7. Then, dichloromethane and NaHCO₃ aqueous solution were added, and the organic layer was washed three times with a NaHCO₃ aqueous solution. The organic layer was collected and dried by magnesium sulfate, and the product was purified by column chromatography eluting with ethyl acetate/hexane (1/1 (v/v)) and dried in vacuo to obtain the colorless oil (0.68 g, 79 % yield). ¹H

NMR (400 MHz, CDCl₃, δ /ppm): 1.21 (s, 3H, CH₃), 1.27 (s, 3H, CH₃), 1.32 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.71-1.98 (m, 4H, CH₂), 3.72 (m, 1H, CH), 4.01 (m, 1H, CH), 4.21 (m, 1H, CH), 4.64 (dd, 2H, CH₂), 5.26 (dd, 1H, CH), 5.32 (dd, 1H, CH), 7.26-7.37 (m, 4H, aromatic proton).

2.2.7. Synthesis of water-soluble alkoxyamine (2-7).

Alkoxyamine diol **2-6** (0.543g, 1.60 mmol) and EtOH (10 mL) were charged into a round-bottom flask, trimethylamine solution (1.91 mL, 1.6 mmol) was added dropwise. After 9 h, the solvent was removed under vacuum, and colorless viscous liquid was obtained (0.53 g, 83 % yield). ¹H NMR (400 MHz, DMSO-*d*₆, δ /ppm): 1.21 (s, 3H, CH₃), 1.27 (s, 3H, CH₃), 1.32 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.71-1.98 (m, 4H, CH₂), 3.29 (s, 3H, CH₃), 3.35 (s, 3H, CH₃), 3.41 (s, 3H, CH₃), 3.72 (m, 1H, CH), 4.01 (m, 1H, CH), 4.21 (m, 1H, CH), 4.59 (dd, 2H, CH₂), 5.26 (dd, 1H, CH), 5.32 (dd, 1H, CH), 7.26-7.37 (m, 4H, aromatic proton).

2.2.8. Cross-linking reaction of poly(DMAEMA-*co*-2-1-*co*-2-2).

In a typical run, water-soluble polymer **2-4b** (100 mg), and water (0.9 mL) were charged into a glass tube, and the solution was degassed by seven freeze-pump-thaw cycles. Then, the glass tube was sealed off under vacuum, and heated at 100 °C. After 24 h, the cross-linked polymers were washed with water, and the mixture of water and THF (3/2 (v/v)) in order, and dried under vacuum for 24 h.

2.2.9. De-cross-linking reaction cross-linked poly(DMAEMA-*co*-2-1-*co*-2-2).

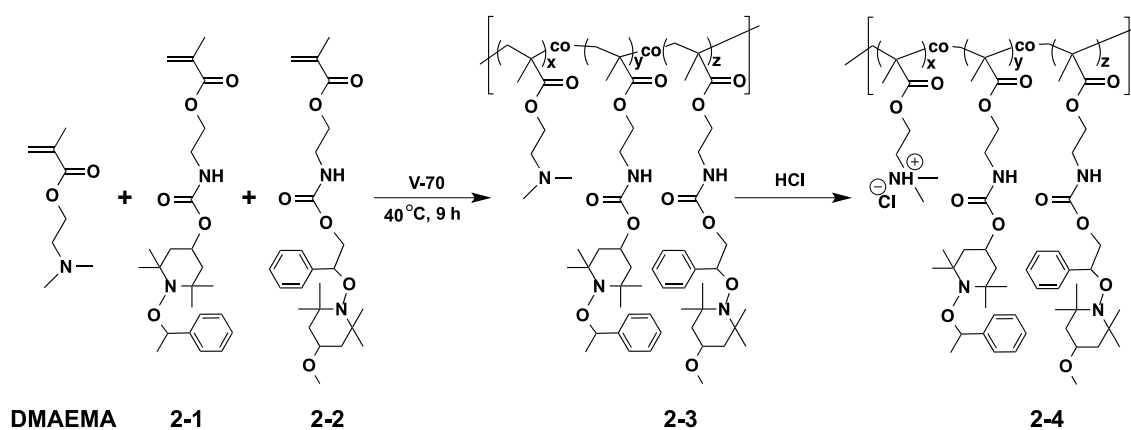
Cross-linked polymer **2-4** (20 mg, 0.0091 mmol), water-soluble alkoxyamine **2-7** (73 mg, 0.18

mmol), and water (0.38 mL) were charged into, and the solution was degassed by seven freeze-pump-thaw cycles. The tube was heated at 100 °C for 24 h.

2.3 Results and Discussion

2.3.1 Design and Synthesis of water-soluble polymer

Water-soluble polymers consisting of both alkoxyamine and hydrophilic side chains were synthesized by two-step synthesis, radical copolymerization of DMAEMA and methacrylic esters with alkoxyamine units (**2-1** and **2-2**), and protonation of dimethylaminoethyl groups by hydrochloric acid, as shown in Scheme 2-2. Poly(DMAEMA-*co*-**2-1**-*co*-**2-2**) (**2-3**) was synthesized by radical copolymerizations of DMAEMA, **2-1** and **2-2** using V-70 as a low-temperature radical polymerization initiator (decomposition half-time: 10 h at 30 °C). The polymerization was carried out at 40 °C, because the alkoxyamine units are stable at this temperature.



Scheme 2-2. Preparation of water-soluble polymer by radical copolymerization of DMAEMA, 2-1, and 2-2, and subsequent protonation of dimethylaminoethyl groups.

As shown in Table **2-1**, four copolymerization experiments with different feed ratio of DMAEMA, **2-1**, and **2-2** were performed. After purification, the composition of each copolymer was estimated by $^1\text{H-NMR}$ measurements (**Figure 2-1**), and M_n and M_w/M_n were evaluated by GPC using DMF as an eluent. In all cases, the compositions of **2-1** and **2-2** in the copolymers, $((y+z)/(x+y+z))$ were very close to the monomer feed ratios of DMAEMA, **2-1** and **2-2**. This result indicated that four types of random copolymers (**2-3a–2-3d**) with different alkoxyamine compositions were successfully obtained by radical copolymerizations of DMAEMA, **2-1** and **2-2**. The molecular weights of the polymers estimated by GPC increased with the ratio of **2-1** and **2-2**, due to the difference in molecular weight between DMAEMA and alkoxyamine-containing monomers.

Table 2-1. Radical copolymerizations of DMAEMA, **2-1**, and **2-2** using V-70 at 40 °C in toluene

Polymer	[DMAEMA] ₀ /[2-1] ₀ /[2-2] ₀	Yield/%	M_n^a	M_w/M_n^a	(y+z)/(x+y+z)/%
2-3a	8 / 1 / 1	95	67 000	2.02	19.3
2-3b	18 / 1 / 1	85	46 900	2.06	9.9
2-3c	38 / 1 / 1	79	45 400	1.86	4.9
2-3d	98 / 1 / 1	76	40 300	2.13	1.6

a) Determined by ¹H-NMR measurements. b) Determined by gel permeation chromatography measurements using DMF as an eluent.

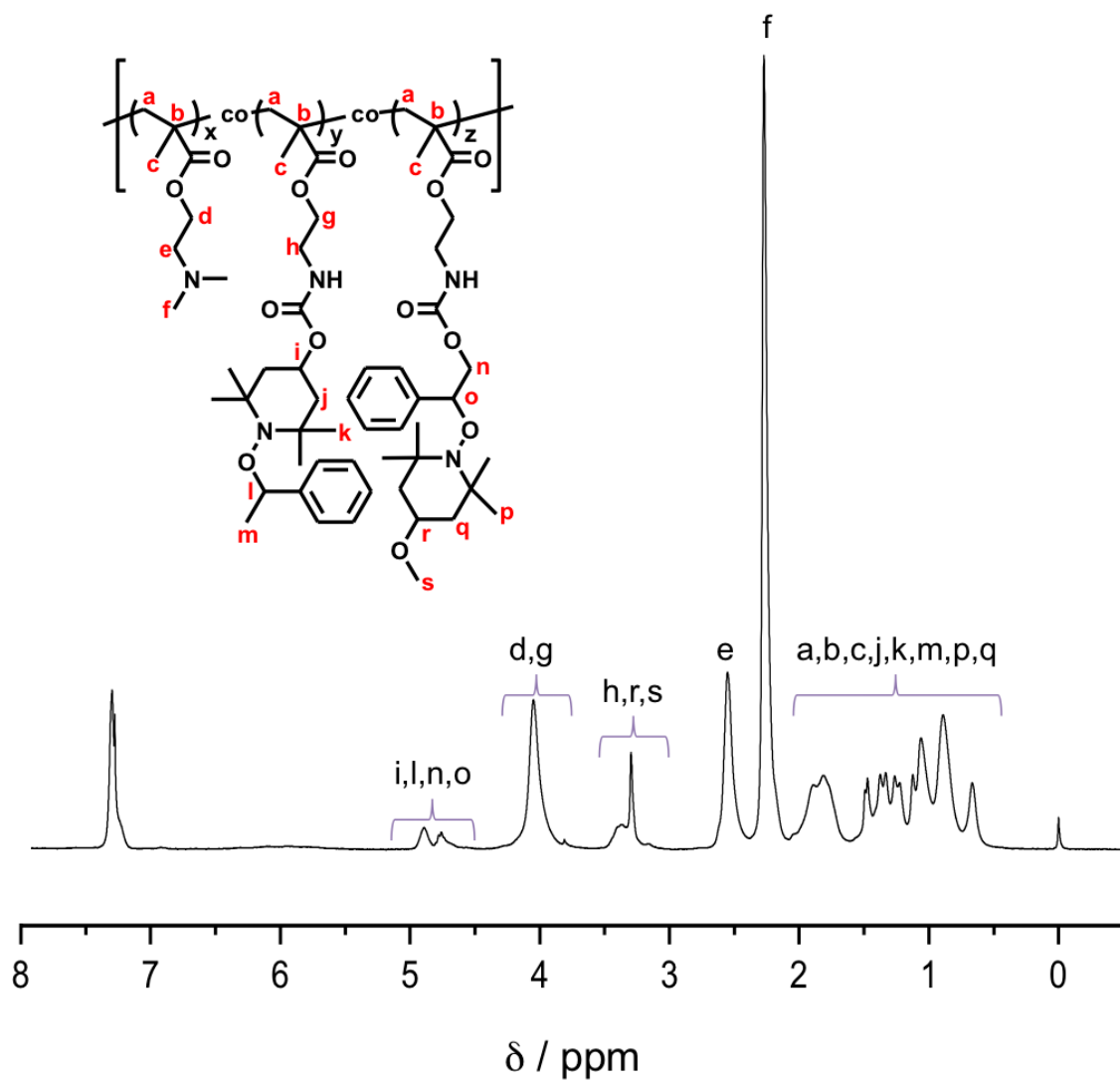


Figure 2-1. ^1H -NMR spectrum of polymer **2-3b** in CDCl_3 .

The dimethylaminoethyl groups in polymers **2-3a–2-3d** were subsequently converted into ammonium groups by treating the polymers with 2 N hydrochloric acid, as shown in **Scheme 2-2**. After the purifications, polymers were dissolved in water. It was confirmed that protonation of the dimethylaminoethyl groups proceeded quantitatively. Furthermore, the molecular weights of the polymers estimated by aqueous GPC increased with the ratio of **2-1** and **2-2**, which results corresponded to the polymer **2-3a–2-3d**. This result means the water-soluble polymers **2-4a–2-4d** were obtained (0.509 g, yield 79% for **2-4a**; 0.620 g, yield 93% for **2-4b**; 0.621 g, yield 91% for **2-4c**; 0.623 g, yield 90% for **2-4d**).

2.3.2 Cross-linking reaction

Since polymers **2-4a–2-4d** have radically exchangeable alkoxyamine units in the side chain, it was expected the cross-linking reaction could proceed even in aqueous media. Aqueous solutions of polymers **2-4a–2-4d** were heated at 100 °C in closed systems under different concentrations. **Figure 2-2** shows the photograph of 10 wt% aqueous solutions of polymer **2-4b** before and after heating for 24 h. The gelation of the system was confirmed after heating without any change in color. At 100 °C, styryl and nitroxide radicals derived from the alkoxyamine units in the side chain generated, and their radical exchanges and formations of different alkoxyamines made cross-linking points form. If the carbon-carbon coupling such as styryl-styryl coupling, takes place, the formation of nitroxide radicals changes the colorless solution into red. Because of the persistent radical effect (PRE),³⁰ carbon-carbon coupling reactions hardly occurred.

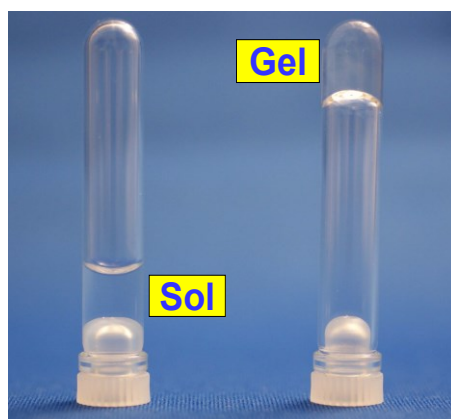


Figure 2-2. Photographs of 10 wt% aqueous solutions of polymer **2-4b** before heating (left) and after heating (right) at 100 °C in a closed system for 24 h.

Dynamic viscoelasticity measurement was performed by using a rheometer with a parallel circular plate in water (10 wt%) at 25 °C. The relationships between storage modulus (G') and angular frequency (ω) of 10 wt% aqueous solutions of polymer **2-4b** before cross-linking, after cross-linking for 12 h and 24 h were measured at 25 °C, as shown in **Figure 2-3**. The storage modulus (G') of before cross-linking reaction suggested that characteristic angular frequency dependence shows typical tendency of linear polymers. As the reaction proceeded, the frequency dependence of storage modulus (G') could almost not be observed and the average of G' was 2.55×10^3 Pa, which suggests that prepared polymer samples have gel characteristics due to their network structure.³¹ These data confirmed that the network structure of the polymer chains was formed after heating.

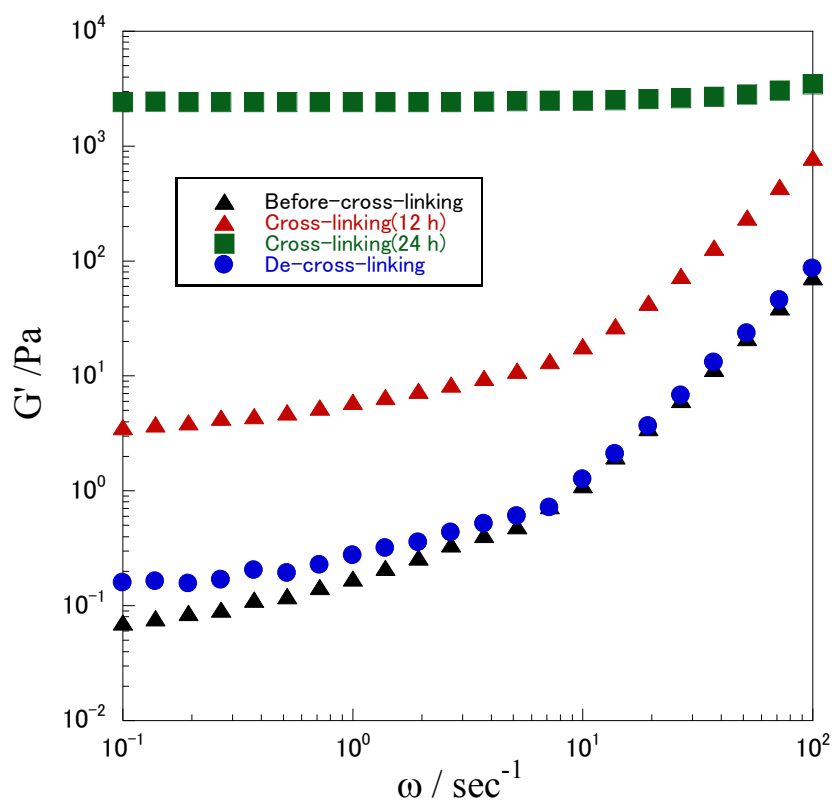


Figure 2-3. Storage modulus (G') vs. angular frequency (ω) of 10 wt% aqueous solutions of polymer **2-4b** before cross-linking, after cross-linking reaction for 12 h and 24 h, and after de-cross-linking at 25 °C.

The cross-linking behavior depended remarkably upon the composition of the copolymers and the polymer concentrations. **Figure 2-4** shows the yield of the gels prepared from **2-4a–2-4d** in various initial polymer concentrations. In the case of **2-4a** and **2-4b**, the gelation of the systems was confirmed particularly in high concentrations, and higher yields of the gel prepared from **2-4a** were obtained in all initial concentrations compared with that for **2-4b**. Furthermore, in both cases, higher yields of the gel were formed with an increase of initial polymer concentration. In the cases of **2-4c** and **2-4d**, however, the gelation of the system was hardly observed, and the yield was almost zero even in high concentrations. This result indicated that the gelation only occurred when increasing the ratio of alkoxyamine units in the side chains, because the network point was composed of alkoxyamine units.

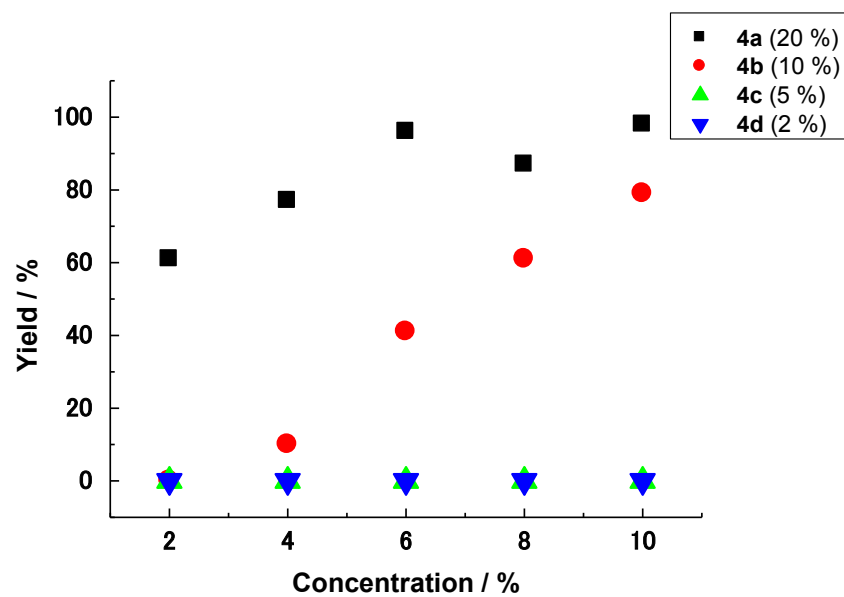


Figure 2-4. Yields of water-insoluble products after heating water-soluble polymers **2-4a–2-4d** in water at 100 °C in closed systems under various concentrations.

A simplified reaction behavior about the cross-linking is discussed from a viewpoint of intramolecular and intermolecular cross-linking reactions. **Figure 2-5** shows GPC curves of the reacted polymers after heating **2-4c** in different concentrations. As mentioned above, the macroscopic gelation of the system was not confirmed after heating **2-4c**. In the case of 1 wt% condition, a peak was observed in lower molecular weight region compared with that for **2-4c** before heating. It is considered that an intramolecular cross-linking reaction proceeded preferentially due to the low concentrations, and hydrodynamic size became lower than that before heating. Meanwhile, under the high concentration conditions, the peaks in higher molecular weight regions were observed. Because of the close distances between polymer chains, intermolecular cross-linking occurred in part, which is not enough for the gelation of the system. As a result, the polymers reacted in the different concentrations have different macromolecular structures by intramolecular and intermolecular cross-linking (**Scheme 2-3**). In other words, this reaction behavior clearly indicated that the cross-linking reactions were caused by the radical exchange reaction between the alkoxyamine units in the side chains. The tendency was clearly observed, however, the quantitative discussion on intra/inter efficiency is not possible in the present system.

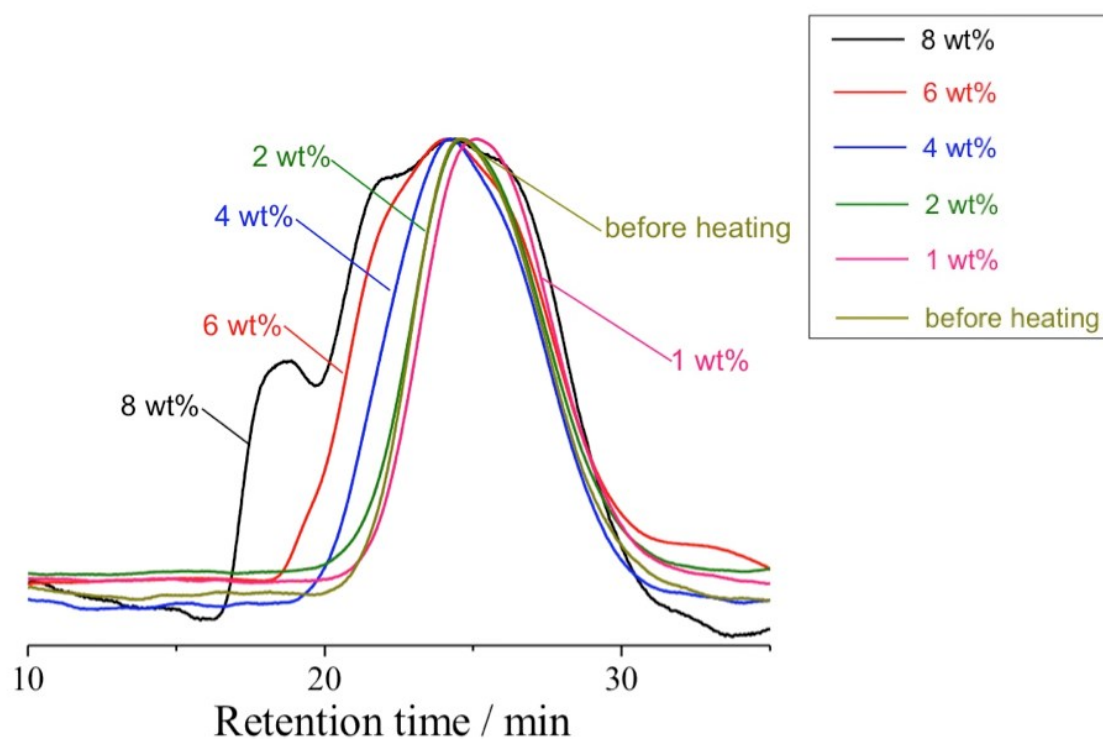
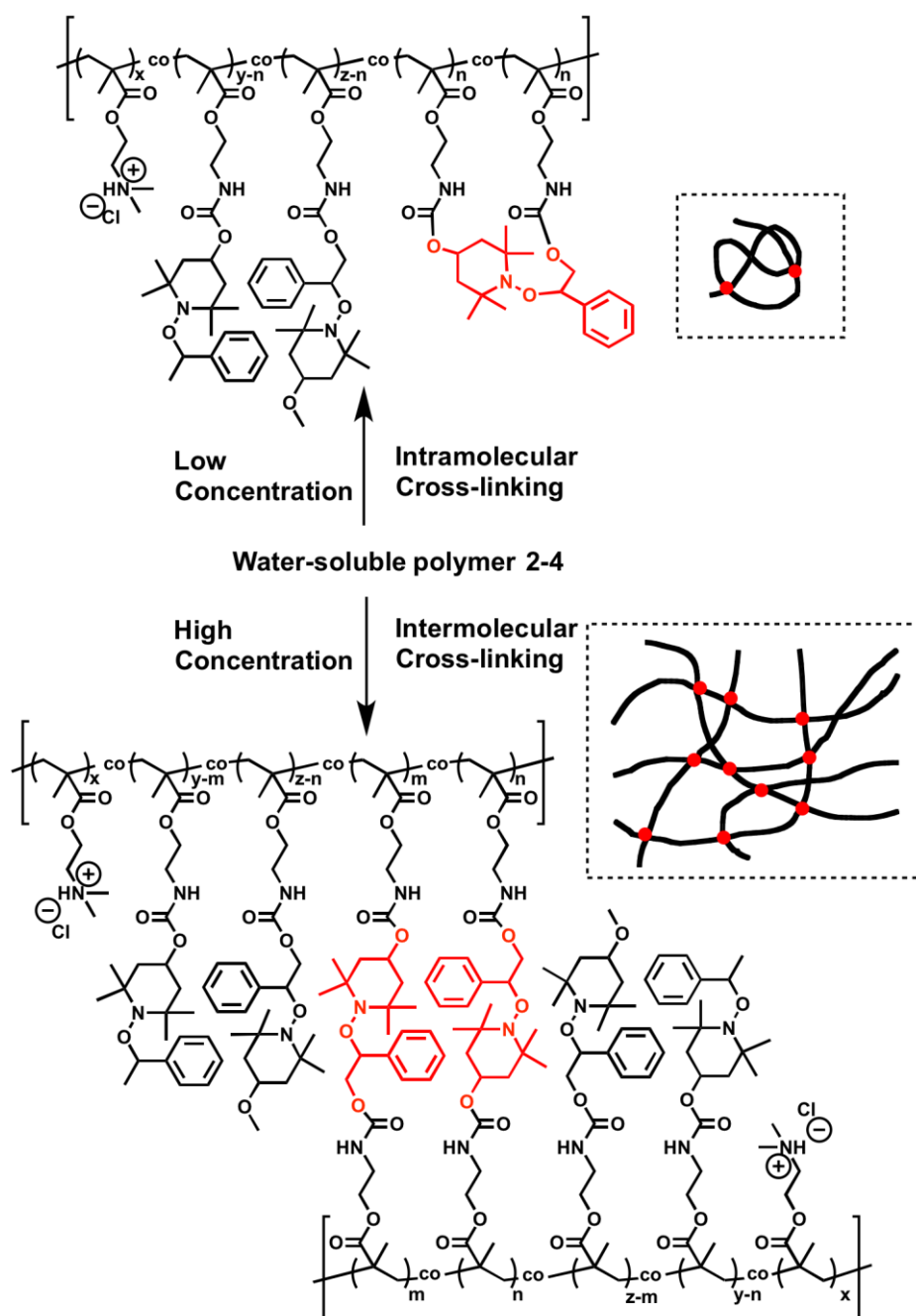


Figure 2-5. GPC curves of the reacted polymers before and after heating aqueous solution of **2-4c** (8 wt%, 6 wt%, 4 wt%, 2 wt%, and 1 wt% concentrations) at 100 °C in closed systems for 24 h.



Scheme 2-3. Intramolecular and intermolecular cross-linking reactions of polymer 2-4.

2.3.2 De-Cross-Linking Reaction

The gels cross-linked by reversible covalent bonds have potential for the reverse de-cross-linking reaction that could turn macroscopic gels into solutions. Here, water-soluble alkoxyamine **2-7** was designed as a de-cross-linking agent and was prepared according to **Scheme 2-4**. Although water-soluble alkoxyamines attached by PEG were reported,³² they tended to form aggregates under heating condition. The de-cross-linking reaction was carried out by heating the cross-linked polymer swollen in water with an excess amount of **2-7** (20 equiv/alkoxyamine unit) at 100 °C in a closed system for 24 h. After heating, the gel turned into solution. This result proves that the cross-linking points and **2-7** were thermally dissociated, and radical exchange reaction proceeded between the generated radicals. As a result, de-cross-linking reaction proceeded.

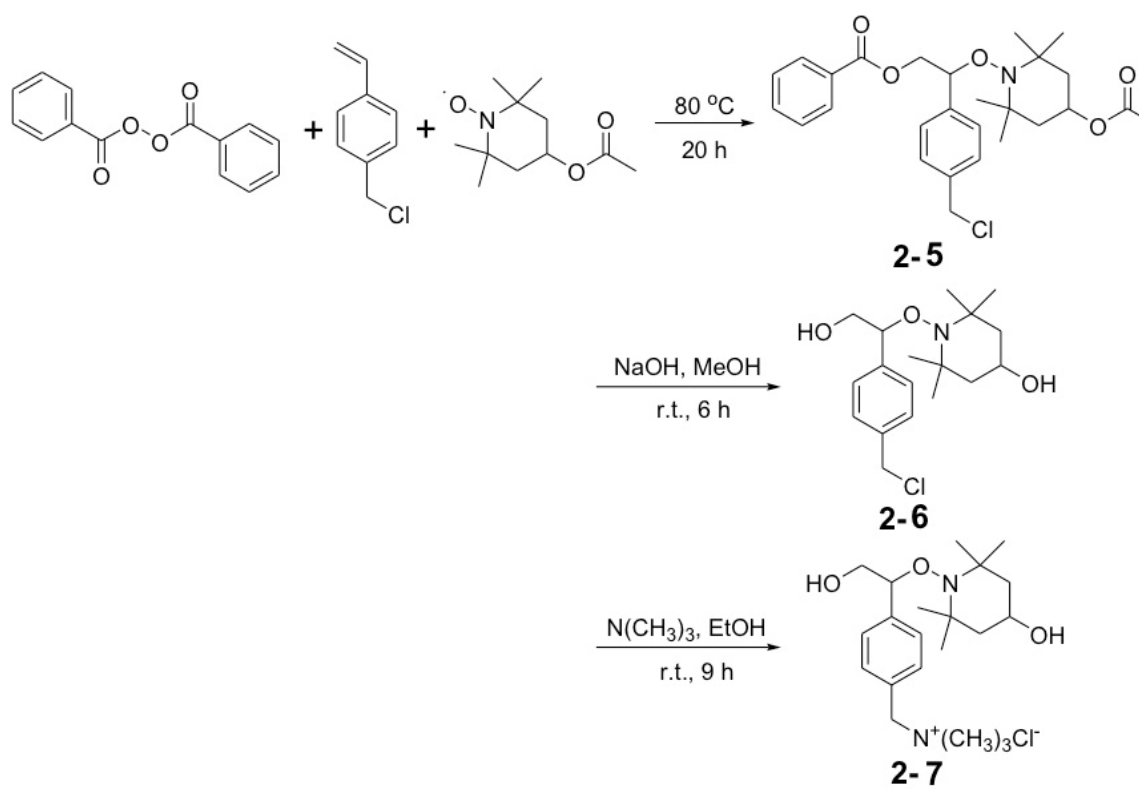
Scheme 2-4. Preparation of water-soluble alkoxyamine **2-7**.

Figure 2-6 shows aqueous GPC curves of polymer **2-4b** and the de-cross-linked polymer, which was generated by treating with the gel prepared from **2-4b** with water-soluble alkoxyamine. Before cross-linking, the M_n of polymer **2-4b** was 39700, which was determined by aqueous GPC system. After de-cross-linking reaction of the gel prepared from **2-4b**, the M_n of the decross-linked polymer was 66000, indicating that most of polymer chains were de-cross-linked.

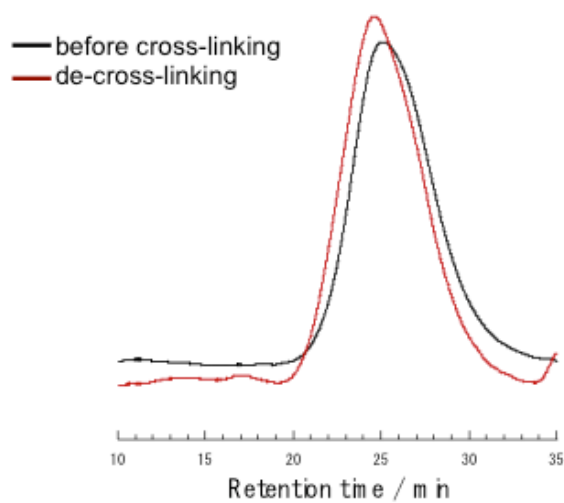


Figure 2-6. GPC curves of polymer **2-4b** ($M_n = 39700$, $M_w/M_n = 3.04$) and de-cross-linked polymer by treating with the gel prepared from **2-4b** with water-soluble alkoxyamine ($M_n = 66000$, $M_w/M_n = 2.38$).

Dynamic viscoelasticity measurement also supported the progress of de-cross-linking reactions. The relationships between storage modulus (G') and angular frequency (ω) of 10 wt% aqueous solutions of polymer **2-4b** before cross-linking and after de-cross-linking of the gel prepared from **2-4b** was shown in **Figure 2-3**. The plots for the two samples are very similar, meaning that the network structure was broken down by treating with the gel prepared from **2-4b** with water-soluble alkoxyamine.

2.4 Conclusion

Reversible cross-linking reactions of alkoxyamine-containing dynamic covalent polymers in aqueous system have been demonstrated. Water-soluble polymers with dynamic covalent linkages in the side chain were synthesized by radical copolymerization of DMAEMA, **2-1**, and **2-2**, and subsequent protonation of dimethylaminoethyl groups. Cross-linking reactions of water-soluble polymers in aqueous media were achieved by heating the polymer at 100 °C in closed systems, and gel structures obviously depended on the amounts of cross-linkable alkoxyamine units in the polymer chains and concentrations of the polymer. De-cross-linking reaction was also accomplished in aqueous media by radical exchange reaction between the cross-linked polymers and the water-soluble alkoxyamine compound. Since radical reactions are tolerant of many functional groups and solvents, the present system can be applied to more complicated system such as organic/aqueous two-phase system in the future.

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Chapter 3

Radical Exchange Reactions of Polymers with Dynamic Covalent Linkages under Bulk Condition

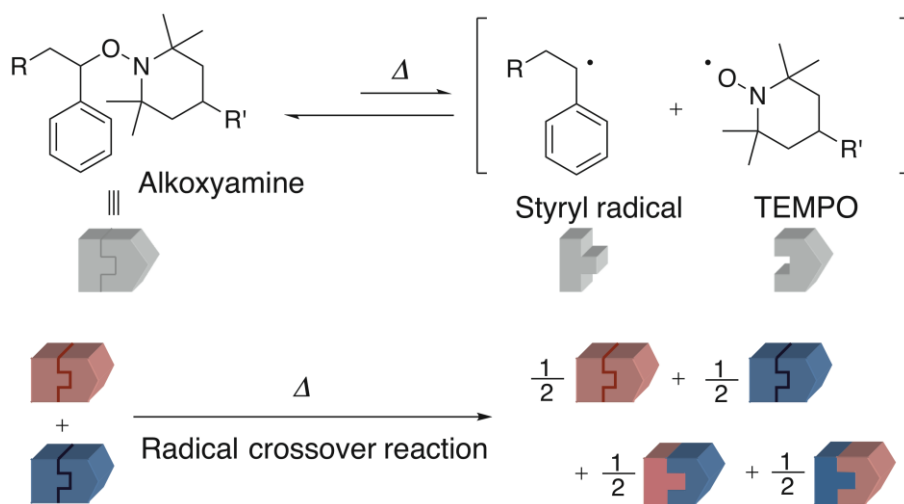
3.1. Introduction

Over the last few decades, polymers with reversible and dynamic covalent linkages have gained much attention in many fields of polymer science because they behave like supramolecular polymers in many respects, for example, in terms of reversibility and controllability.¹⁻⁵ Therefore, they have been widely used, e.g., in responsive assemblies,⁶ reactive polymers,⁷⁻¹⁰ and functional materials.^{11,12} In particular, cross-linked polymers with dynamic covalent linkages have been widely studied and have been used to prepare responsive polymers with particular abilities, including ability to realize network structure variations¹³⁻¹⁵ and sol–gel transitions,^{16,17} and self-healing properties.¹⁸⁻²⁶ Polymer reactions involving dynamic covalent linkages in bulk states, however, have been desired to produce functional materials: some works on reactions based on imine bonds,²⁷ Diels-Alder reactions,²⁸⁻³⁰ and disulphide bonds^{20,31} were reported because of the low reactivity of the robust reversible covalent bonds.

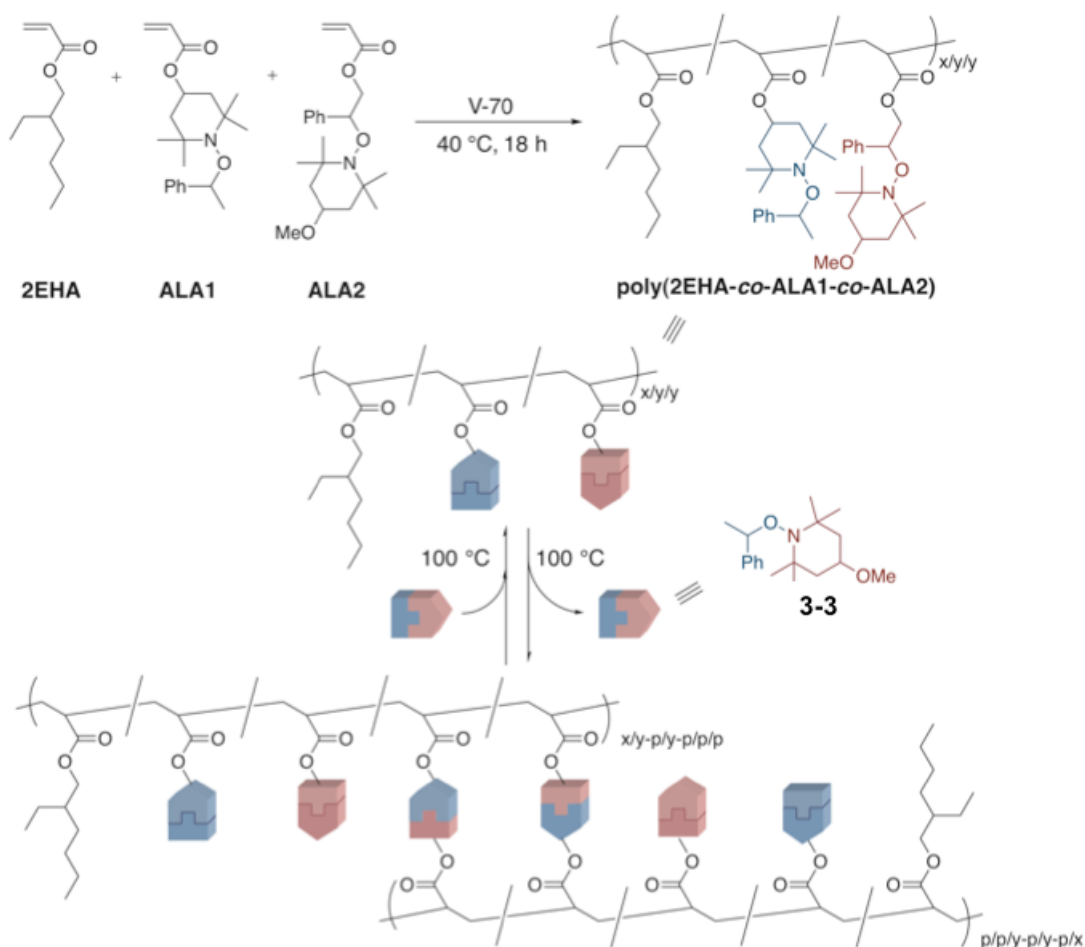
Recently, stiffness-controllable responsive polymers have attracted considerable attention. These polymers can be used to prepare smart materials, including solvent-free pressure-sensitive adhesives (PSA), actuators, and biomaterials for tissue engineering. Polymers can exist in several physical states, i.e., glassy, rubbery, and flowable states, and the mechanical properties of the polymers significantly depend on their state. Although transition between the flowable and rubber-like states can be controlled simply by cross-linking and de-cross-linking polymers with low glass transition temperatures (T_g), there are a few reports on the use of dynamic covalent linkages.

In previous works, reversible cross-linking and de-cross-linking reactions of polymers with alkoxyamine units in the side chains in organic solvents were demonstrated.¹⁶ In Chapter 2, radical exchange reactions of polymers with dynamic covalent linkages were demonstrated in an aqueous system.³² Because alkoxyamine compounds consisting of styryl radicals and nitroxide radicals undergo dissociation, radical exchange reactions can occur upon heating (**Scheme 3-1**). This leads to the formation of cross-linking points in the polymer chains. All reversible reactions of alkoxyamines, however, were achieved in a solvent system. On the other hand, bulk polymeric materials have higher mechanical properties and higher concentration of functional groups than polymer solutions and gels. Furthermore, non-solvent reversible cross-linking systems are environmentally benign. In the case of alkoxyamine cross-linking reversible system, parent polymers can be prepared by radical polymerization under mild conditions and their reversible cross-linking can be performed by radical reactions upon heating. Since radical exchange reactions are tolerant of many functional groups, radical exchange reaction between alkoxyamines occurs in the bulk state of polymers, thereby producing functional materials.

In this chapter, a novel reversible cross-linking system under bulk conditions using a low- T_g alkoxyamine-containing polymer subjected to radical exchange reactions is described. To carry out the reactions in the bulk system, cross-linkable alkoxyamine units were introduced into the side chains of polymers with low T_g , as represented in **Scheme 3-2**.



Scheme 3-1. Radical crossover reaction of TEMPO-based alkoxyamine derivatives.



Scheme 3-2. Cross-linking and de-cross-linking reactions of alkoxyamine-appended polymers with low glass transition temperature under bulk conditions.

3.2 Experimental

3.2.1 Materials

Alkoxyamines (**3-1** and **3-2**),³³ 4-methoxy-1-((1'-phenylethyl)oxy)-2,2,6,6-tetramethyl-piperidine,³⁴ (**3-3**) and 4-methoxy-2,2,6,6-tetrapethylpyperidine-1-oxy (4-methoxy-TEMPO)³⁵ were synthesised and purified as previously reported. Acryloyl chloride was purchased from Wako Pure Chemical Industries and used without further purification. Triethylamine (99%) and anisole (99%) were purchased from Wako Pure Chemical Industries and purified by distillation over calcium hydride. Tetrahydrofuran (THF, 99.5%) was purchased from Wako Pure Chemical Industries and purified through a Glass Contour solvent purification system. 2-Ethylhexyl acrylate (2EHA) was purchased from Tokyo Chemical Industry and purified by distillation under vacuum. 2,2-Azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70, 95%) was purchased from Wako Pure Chemical Industries and used without further purification.

3.2.2 Measurement

¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectroscopic measurements in chloroform-*d* (CDCl₃) were carried out at 25 °C on a Bruker spectrometer, using tetramethylsilane as an internal standard. The monomer conversion was determined by ¹H NMR spectroscopy of the crude reaction mixtures. IR spectra were obtained on a Perkin-Elmer Spectrum One infrared spectrometer using thin films on NaCl or neat samples. Number- and weight-average molecular weights (M_n and M_w , respectively) and polydispersities (M_w/M_n) were estimated by gel permeation chromatography (GPC) in THF at 40 °C on a polystyrene gel column [TOSOH TSKgel SuperH2500, TSKgel SuperH4000, and TSKgel SuperH6000 (6–150 mm), nominal

maximum molecular weight at which separation occurs: 40,000,000]. The column was connected to a TOSOH system equipped with a refractive index detector and the mobile phase was maintained at a flow rate of 0.6 mL min⁻¹. The column was calibrated against six standard polystyrene samples (M_n : 1060–3,690,000; M_w/M_n : 1.02–1.08). DSC measurement was performed on an EXSTAR6000 unit (SII Nanotechnology Inc.) at 153 to 323 K at a heating rate of 10 K min⁻¹. Dynamic viscoelastic measurements were carried out at 25 °C with a Physica MCR101 rheometer with a parallel circular plate (12 mm diameter). The storage shear modulus (G') and loss shear modulus (G'') were evaluated on the basis of the average values of numerous measurement results.

3.2.3 Synthesis of alkoxyamine-appended acrylate monomers (ALA1)

Acryloyl chloride (0.54 g, 6.0 mmol) was added to a solution of **3-1** (1.39 g, 5.0 mmol) and triethylamine (0.6 g, 6.0 mmol) in dry THF (20 mL) at 0 °C. The solution was stirred at room temperature under nitrogen for 16 h and then evaporated to dryness. To the residue, water and dichloromethane were added. Subsequently, the organic phase was washed with water and dried over anhydrous magnesium sulphate. The solution was evaporated to dryness and the crude product was purified by flash chromatography by eluting with ethyl acetate/hexane (1/1, v/v) to give the acrylic ester monomer (ALA1) as a colourless viscous liquid (1.23 g, 74% yield). ¹H NMR (400 MHz, CDCl₃), δ /ppm 0.67 (3 H, s, CH₃), 1.14 (3 H, s, CH₃), 1.28 (s, 3H, CH₃), 1.34 (3 H, s, CH₃), 1.48 (3 H, d, J = 6.7 Hz, CH₃), 1.55 (1 H, d, J = 7.4 Hz, CH₂), 1.63 (1 H, d, J = 12 Hz, CH₂), 1.78 (1 H, d, J = 12 Hz, CH₂), 1.90 (1 H, d, J = 12 Hz, CH₂), 4.77 (1 H, q, J = 6.7 Hz, CH), 5.05–5.11 (1 H, m, CH), 5.79 (1 H, d, J = 10 Hz, vinyl proton), 6.07 (1 H, dd, J =

10 and 17 Hz, vinyl proton), 6.36 (1 H, d, J = 17 Hz, vinyl proton), 7.21–7.31 (5 H, m, aromatic proton). ^{13}C NMR (100 MHz, CDCl_3), δ / ppm 21.12, 23.30, 34.07, 34.38, 44.59, 44.65, 59.98, 60.23, 67.00, 83.37, 126.66, 126.99, 128.07, 128.88, 130.37, 145.34, 165.78 (C=O). FT-IR (neat, cm^{-1}), 3105–2860, 1721 (C=O), 1636, 1328, 1184 (C–O), 770 (C–H), 702 (C–H).

3.2.4 Synthesis of alkoxyamine-appended acrylate monomers (ALA2)

Acryloyl chloride (0.54 g, 6.0 mmol) was added to a solution of **3-2** (1.54 g, 5.0 mmol) and triethylamine (0.6 g, 6.0 mmol) in dry THF (20 mL) at 0 °C. The solution was stirred at room temperature under nitrogen for 16 h and then evaporated to dryness. To the residue, water and dichloromethane were added. Subsequently, the organic phase was washed with water and dried over anhydrous magnesium sulphate. The solution was evaporated to dryness and the crude product was purified by flash chromatography by eluting with ethyl acetate/hexane (1/1, v/v), and dried *in vacuo* to give the acrylic ester monomer (ALA2) as a colourless viscous liquid (1.72 g, 95% yield). ^1H NMR (400 MHz, CDCl_3), δ / ppm 0.69 (3 H, s, CH_3), 1.08 (3 H, s, CH_3), 1.23 (3 H, s, CH_3), 1.37 (4 H, dd, J = 12 and 17 Hz, CH_2), 1.38 (3 H, s, CH_3), 3.29 (3 H, s, OCH_3), 3.39–3.44 (1 H, m, CH), 4.31–4.36 (1 H, m, CH_2), 4.65–4.69 (1 H, m, CH_2), 4.96 (1 H, t, J = 5.9 Hz, CH), 5.76 (1 H, d, J = 10 Hz, vinyl proton), 6.03 (1 H, q, J = 10 Hz, vinyl proton), 6.30 (1 H, d, J = 17 Hz, vinyl proton), 7.26–7.32 (5 H, m, aromatic proton). ^{13}C NMR (100 MHz, CDCl_3), δ / ppm 21.29, 34.11, 45.16, 45.31, 55.70, 60.23, 60.57, 66.22, 71.59, 84.03, 127.74, 127.81, 128.06, 128.33, 130.72, 140.23, 165.82 (C=O). FT-IR (NaCl, cm^{-1}), 3105–2817, 1728 (C=O), 1181 (C–O), 1098 (C–O), 763, 700.

3.2.5 Synthesis of poly(2EHA-*co*-ALA1-*co*-ALA2)

Under an argon atmosphere, 2EHA (1.66 g, 9 mmol), ALA1 (0.17 g, 0.5 mmol), ALA2 (0.18 g, 0.5 mmol), and toluene (2 mL) were added to a round-bottom flask containing a magnetic stirring bar. The initiator V-70 (0.15 g, 0.48 mmol) was added to the mixture. The copolymerisation was carried out at 40 °C for 18 h, and the product poly(2EHA-*co*-ALA1-*co*-ALA2) was washed with methanol (1.66 g, 83 % yield, $M_n = 22\,000$ and $M_w/M_n = 3.33$). ^1H NMR (400 MHz, CDCl_3), δ / ppm 0.66 (3 H, s, CH_3), 0.89 (3 H, s, CH_3), 0.91 (3 H, s, CH_3), 1.05–1.10 (3 H, m, CH_3), 1.29 (brs, R-CH_3), 1.47–1.48 (3 H, m, CH_3), 1.58 (brs, R-CH), 1.91 (brs, CH_2), 2.30 (1 H, brs, CH), 3.31 (s, OCH_3), 3.43 (1 H, m, CH), 3.90–3.96 (2 H, m, CH_2), 4.78 (brs, CH), 4.91 (brs, CH), 7.28 (s, aromatic proton), 7.31 (brs, aromatic proton). ^{13}C NMR (100 MHz, CDCl_3), δ / ppm 10.70, 10.75, 14.07, 21.08 (br), 23.47, 23.62, 28.88, 30.13, 34.17, 35.41, 36.45, 38.51, 38.54, 41.54, 44.44, 45.22, 55.65, 59.98, 60.04, 60.15, 60.49, 66.97, 71.61, 83.22, 126.63, 126.94, 128.03, 140.36, 145.36, 174.30 (C=O), 174.36 (C=O), 174.48 (C=O). FT-IR (NaCl, cm^{-1}), 3106–2860, 1733 (C=O), 1165 (C-O), 763 (C-H), 699 (C-H).

3.2.6 Cross-linking reaction of poly(2EHA-*co*-ALA1-*co*-ALA2)

Poly(2EHA-*co*-ALA1-*co*-ALA2) (0.10 g, $M_n = 22000$ and $M_w/M_n = 3.33$) was charged into a glass tube, degassed by freeze–pump–thaw cycles, sealed off under vacuum, and then heated at 100 °C for 24 h under bulk conditions.

3.2.7 De-cross-linking reaction of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2)

De-cross-linking reactions of the cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) were carried out by heating the cross-linked polymer with alkoxyamine compound **3-3** or 4-methoxy-TEMPO. Typically, cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) (0.1 g, 0.1 mmol) and alkoxyamine-containing compound **3-3** (0.58 g, 2 mmol) were charged into a glass tube. Afterwards, the glass tube was degassed by freeze–pump–thaw cycles and then heated at 100 °C for 48 h.

3.3 Results and Discussion

3.3.1 Design and synthesis of low- T_g polymer

To carry out radical exchange reactions under bulk conditions, cross-linkable alkoxyamine units were introduced into the side chains of the low- T_g polymers. In the present study, the author focused on poly(2-ethylhexyl acrylate) (P2EHA) with T_g of -70 °C. Acrylate monomer ALA1 with an alkoxyamine unit was synthesized from the corresponding alkoxyamine derivative **3-1**, which has a hydroxyl group and a polymerizable acryloyl group, in good yield. The acrylate monomer with alkoxyamine connected at the opposite position, ALA2, was also synthesized from **3-2** in 95% yield. Both the polymerizable acrylate moiety and the alkoxyamine moiety were clearly observed in ^1H NMR spectra of ALA1 and ALA2, as shown in **Figures 3-1** and **3-2**, respectively.

The alkoxyamine-appended polymer, poly(2EHA-*co*-ALA1-*co*-ALA2), was synthesised by radical copolymerisation of 2EHA and two kinds of alkoxyamine-containing acrylate monomers (ALA1 and ALA2) at a 2EHA/ALA1/ALA2 molar ratio of 18:1:1, as shown in **Scheme 3-2**. The polymerisation was carried out for 18 h in toluene in the presence of 2,2-azobis(4-methoxy-2,4-dimethylvaleronitrile) [V-70] as an initiator, at 40 °C to afford the corresponding copolymer (conversion of 2HEA was 93% and yield was 83%). The structure of the obtained polymer was characterised by ^1H NMR measurement, as shown in **Figure 3-3**. Since a low-temperature initiator, V-70, was used for the radical copolymerisation, no decomposition of alkoxyamine units was observed. The composition of 2EHA, ALA1, and ALA2 in the obtained polymer could be calculated from the peak area in the ^1H NMR spectra; there was a good agreement with the feed ratio of the monomers. These results indicate that the

radical copolymerisation of 2EHA and two kinds of alkoxyamine-containing acrylate monomers (ALA1 and ALA2) was successfully performed to afford poly(2EHA-*co*-ALA1-*co*-ALA2) with a 2EHA/ALA1/ALA2 molar ratio of 18:1:1.

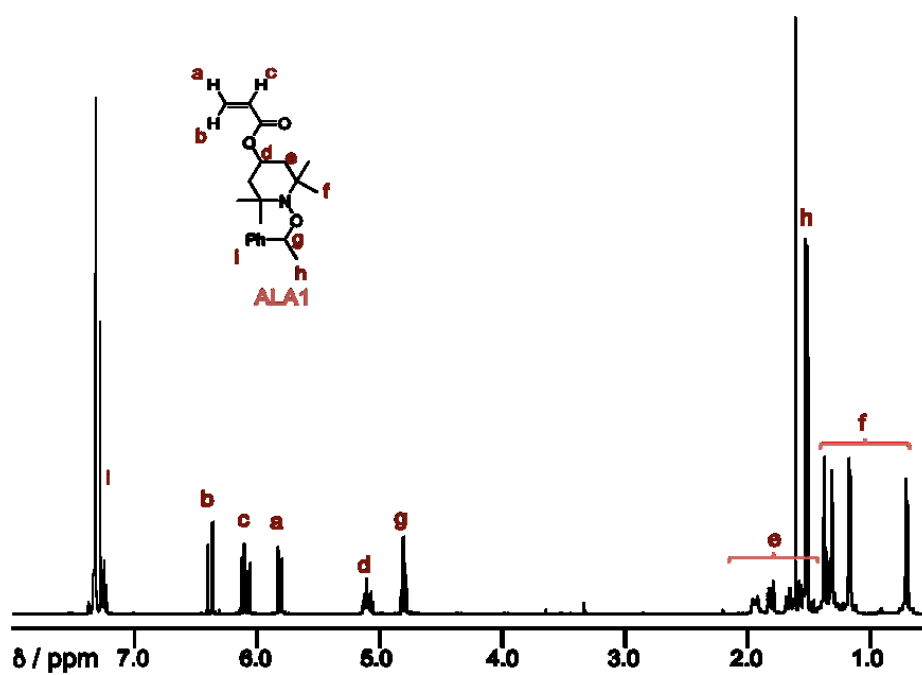


Figure 3-1. ^1H NMR spectrum of alkoxyamine-containing acrylate monomer ALA1 in CDCl_3 .

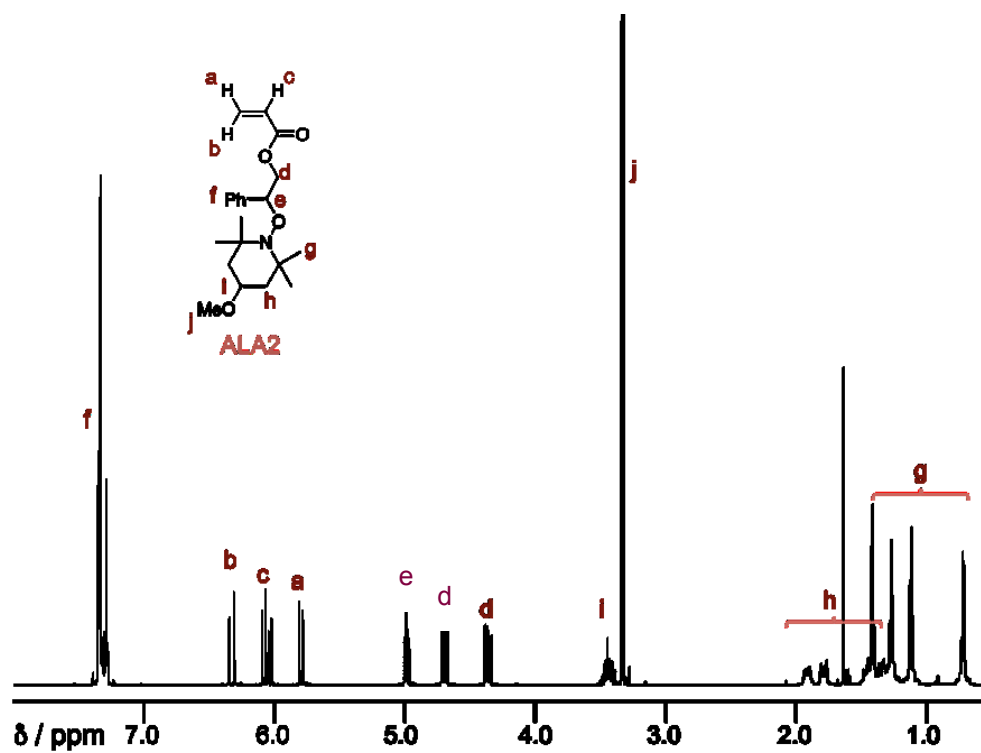


Figure 3-2. ^1H NMR spectrum of alkoxyamine-containing acrylate monomer ALA2 in CDCl_3 .

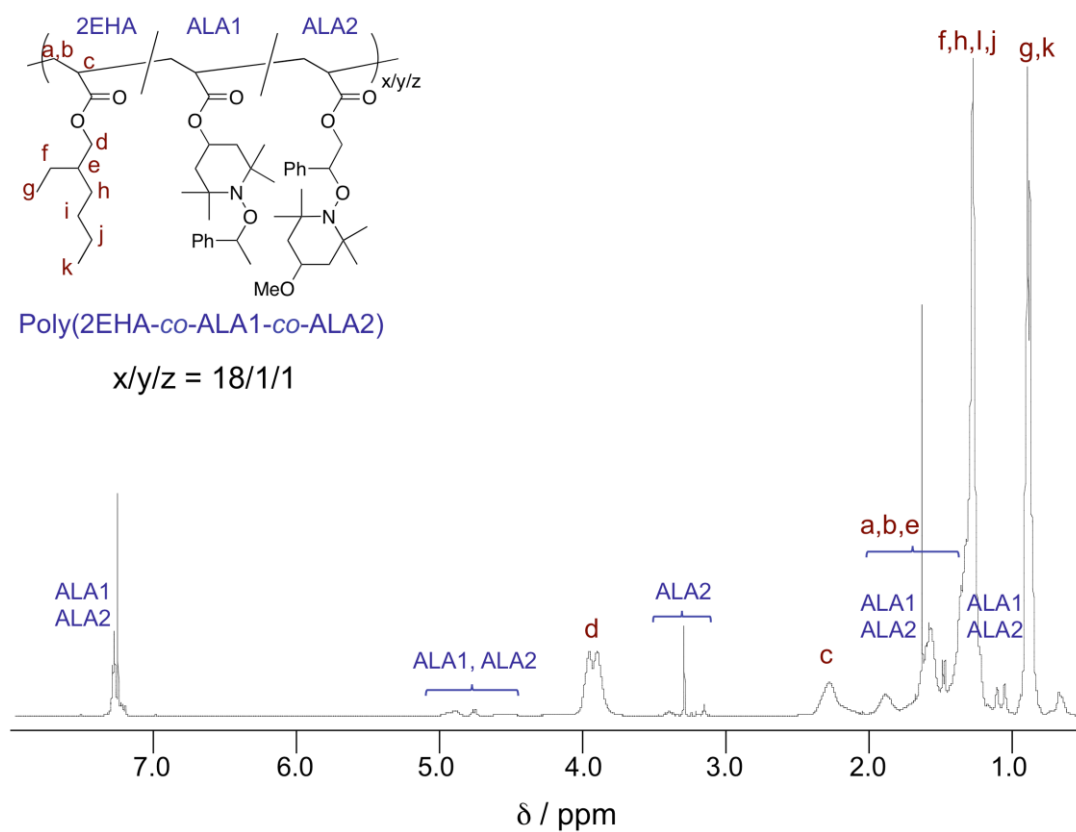


Figure 3-3. ^1H NMR spectrum of poly(2EHA-*co*-ALA1-*co*-ALA2) in CDCl_3 .

GPC measurement of poly(2EHA-*co*-ALA1-*co*-ALA2) revealed that the estimated values of M_n and M_w/M_n were 22,000 and 3.33, respectively. A single peak with no shoulder was present in the corresponding chromatogram, indicating that no detectable cross-linking reaction occurred. From the result of the DSC measurement, T_g of poly(2EHA-*co*-ALA1-*co*-ALA2) was estimated to be $-48\text{ }^{\circ}\text{C}$. This value is much higher than that for P2EHA ($-70\text{ }^{\circ}\text{C}$) because of the incorporation of ALA1 and ALA2 components. However, poly(2EHA-*co*-ALA1-*co*-ALA2) is still a low- T_g polymer. This result suggests that poly(2EHA-*co*-ALA1-*co*-ALA2) has flowability and adhesiveness at room temperature.

3.3.2 Cross-linking reaction of poly(2EHA-*co*-ALA1-*co*-ALA2)

The cross-linking reaction of poly(2EHA-*co*-ALA1-*co*-ALA2) was carried out at $100\text{ }^{\circ}\text{C}$ for 24 h under bulk conditions. Before heating, the polymer bulk sample was highly viscous liquid at room temperature, as shown in **Figure 3-4a**. In contrast, the product did not flow at all after heating (**Figure 3-4b**). The progress of the cross-linking reaction was further confirmed by the results of a swelling experiment. Although poly(2EHA-*co*-ALA1-*co*-ALA2) could be completely dissolved in chloroform and anisole before heating, the polymer product after heating could only be swollen in chloroform and anisole to form gels. The swelling ratios of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) were 313% for CHCl_3 and 278% for anisole (**Figure 3-5**). These results clearly revealed that the cross-linking reaction of poly(2EHA-*co*-ALA1-*co*-ALA2) occurred upon heating under bulk conditions.

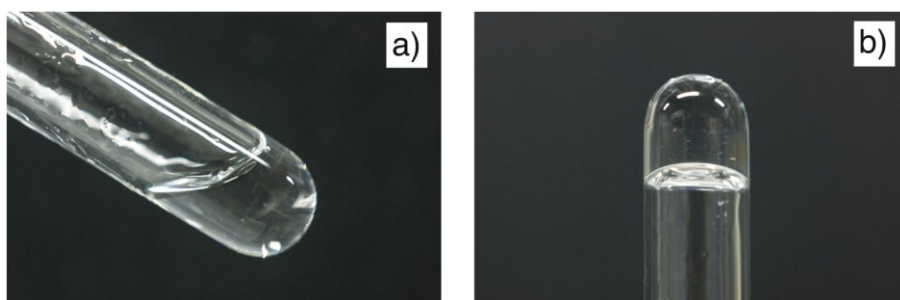


Figure 3-4. Photographs of poly(2EHA-*co*-ALA1-*co*-ALA2) (a) before and (b) after heating at 100 °C for 24 h.

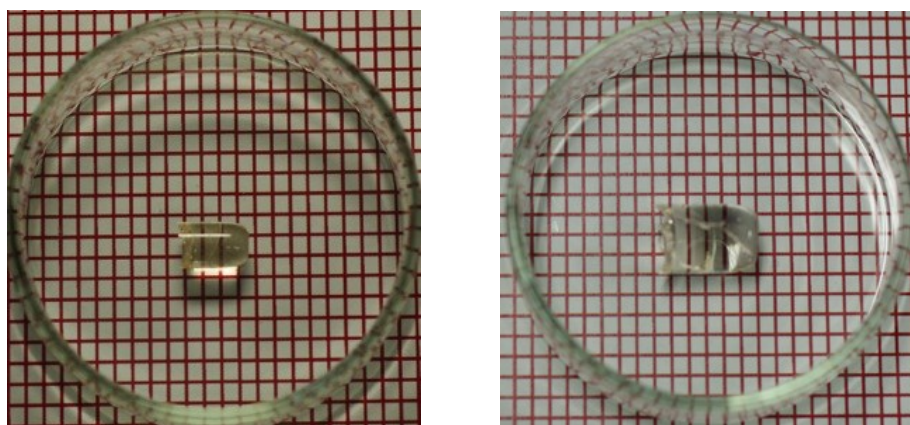


Figure 3-5. Photographs of poly(2EHA-*co*-ALA1-*co*-ALA2) (left) before and (right) after swelling with anisole.

Styryl and nitroxide radicals are formed at 100 °C from the side-chain alkoxyamine units, and these radical species undergo exchange to form cross-linking points (**Scheme 3-1**). If side reactions such as styryl–styryl coupling take place, then the concentration of residual nitroxide radical increases and the colour of the reaction mixture gradually changes to orange. However, the obtained cross-linked polymer was colourless and transparent. Therefore, the author can conclude that such carbon–carbon coupling scarcely occurred in the present system, which can be explained by the persistent radical effect (PRE)³⁶. PRE is a general principle that explains the highly specific formation of the cross-coupling product R^1-R^2 between R^1 and R^2 when one species is persistent (R^1) and the other is transient. PRE is observed when the persistent radical exists in excess over the transient radical. In the case of the crossover reaction between alkoxyamine derivatives, at the initial stage, a trace amount of coupling reaction inevitably occurs between the transient carbon radical species generated from the C–ON bond, and then generates a small amount of TEMPO radical, which serves as the persistent radical. Since the amount of the carbon–carbon coupling product is still small compared with that of alkoxyamines, the total crossover reactions seem to be highly specific.

To obtain further insight into the cross-linking reaction, the chloroform-soluble part of the heated poly(2EHA-*co*-ALA1-*co*-ALA2) was analysed. In the ¹H NMR spectrum of the chloroform-soluble products (**Figure 3-6**), peaks for alkoxyamine by-product **3-3** derived from ALA1 and ALA2 units were clearly observed, in addition to the peaks for insufficiently cross-linked soluble polymers. These features clearly indicate that cross-linking reaction occurred as a result of radical exchange reactions between ALA1 and ALA2 units. The degree of cross-linking in poly(2EHA-*co*-ALA1-*co*-ALA2) can be estimated by the generation of

by-product **3**, although it is impossible to distinguish between intermolecular and intramolecular cross-linking reactions. The estimated degree of cross-linking was 12% after heating poly(2EHA-*co*-ALA1-*co*-ALA2) at 100 °C for 24 h.

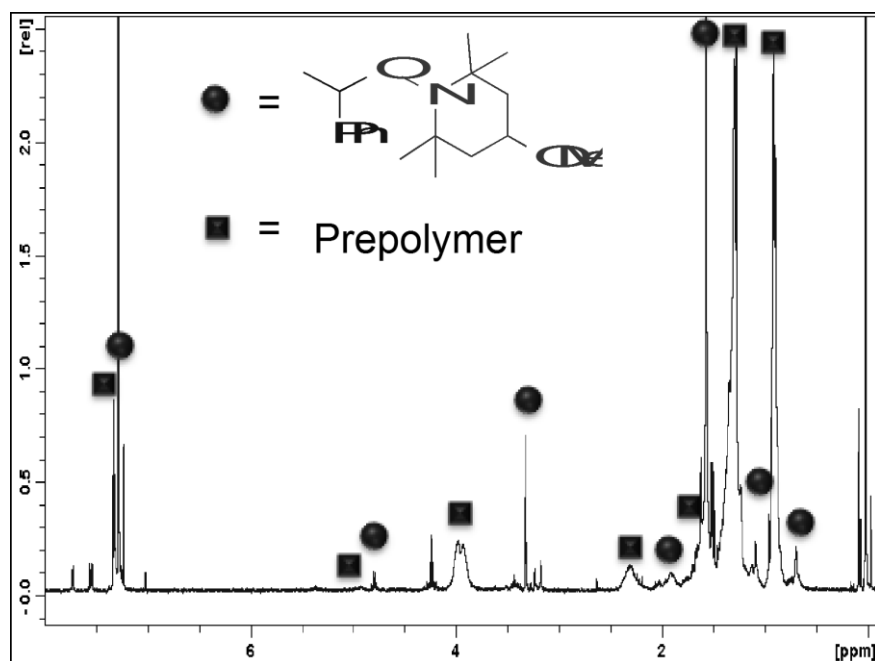


Figure 3-6. ^1H NMR spectrum of chloroform-soluble part of heated poly(2EHA-*co*-ALA1-*co*-ALA2) in CDCl_3 .

3.3.3 Rheological studies of cross-linking reactions of poly(2EHA-co-ALA1-co-ALA2)

The progress of the cross-linking reaction was also followed by dynamic viscoelastic measurement. The storage shear modulus (G') and loss shear modulus (G'') were evaluated on the basis of the results of frequency sweep experiments at constant environmental temperature.

Figure 3-3a shows the relationships between G' and angular frequency (ω) of the polymer heated for different reaction times at 100 °C. In the case of the polymer before heating (0 h), the values of G' increased with ω , and a relationship of $G' \propto \omega^2$ at low angular frequency became apparent. This is typical behaviour of linear polymers in a flowable liquid state. With increasing reaction time, G' of the cross-linked polymer increased. After 24 h, G' did not change significantly as a function of angular frequency, and the estimated average value of the G' was 1.18×10^5 Pa. This property is characteristic of cross-linked networks in rubber-like state, indicating that the product does not flow. Plots of G' and G'' at 1 Hz against reaction time are shown in **Figure 3-7b**. The value of G' was less than G'' before reaction (0 h), and increased with reaction time. After 4 h, G' became higher than G'' due to the gelation,³⁷ indicating that an efficient network formed after 4 h *via* radical exchange reactions. Interestingly, G' after 24 h heating was over 100 times higher than that of the initial polymer, suggesting sufficient changes in stiffness. These viscoelastic properties suggest that the polymer was successfully converted from a flowable liquid state to a rubber-like state *via* radical exchange reactions of alkoxyamine units.

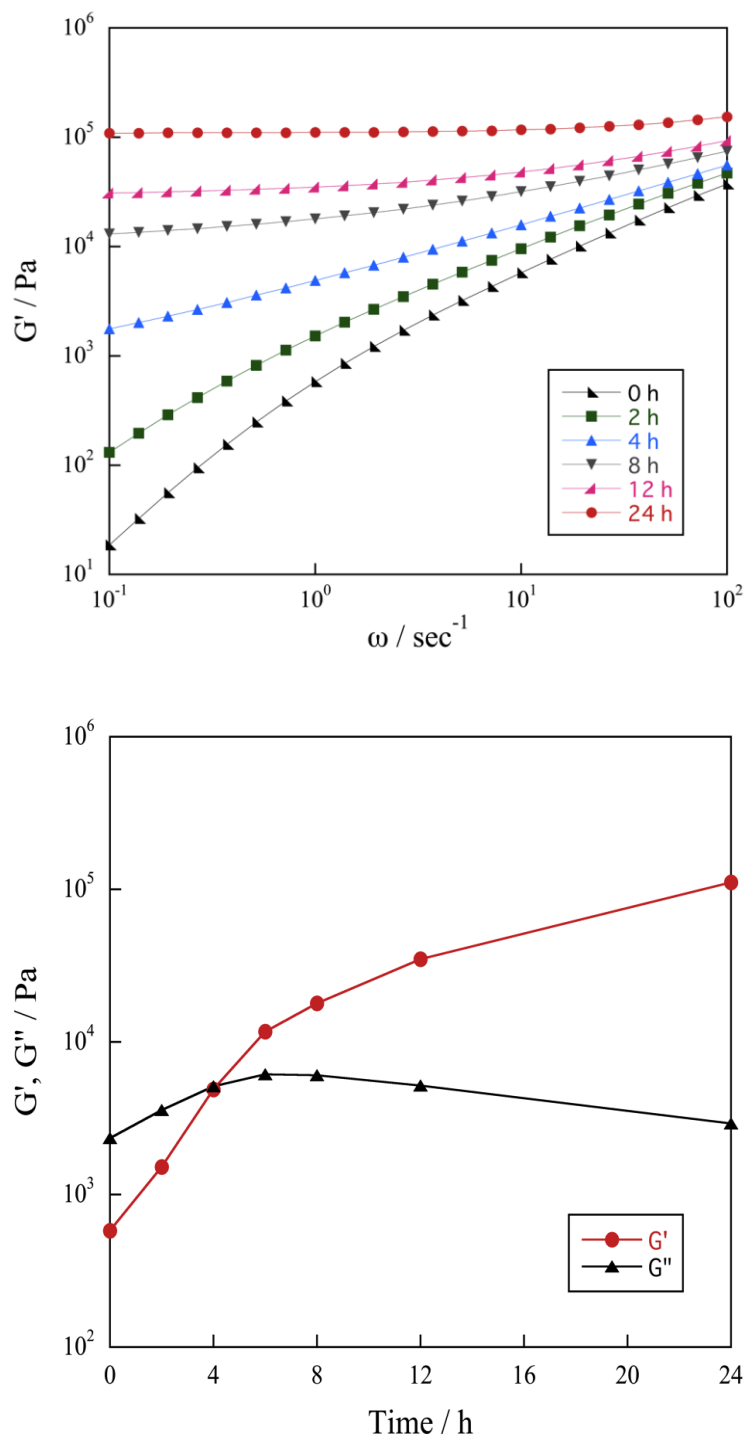
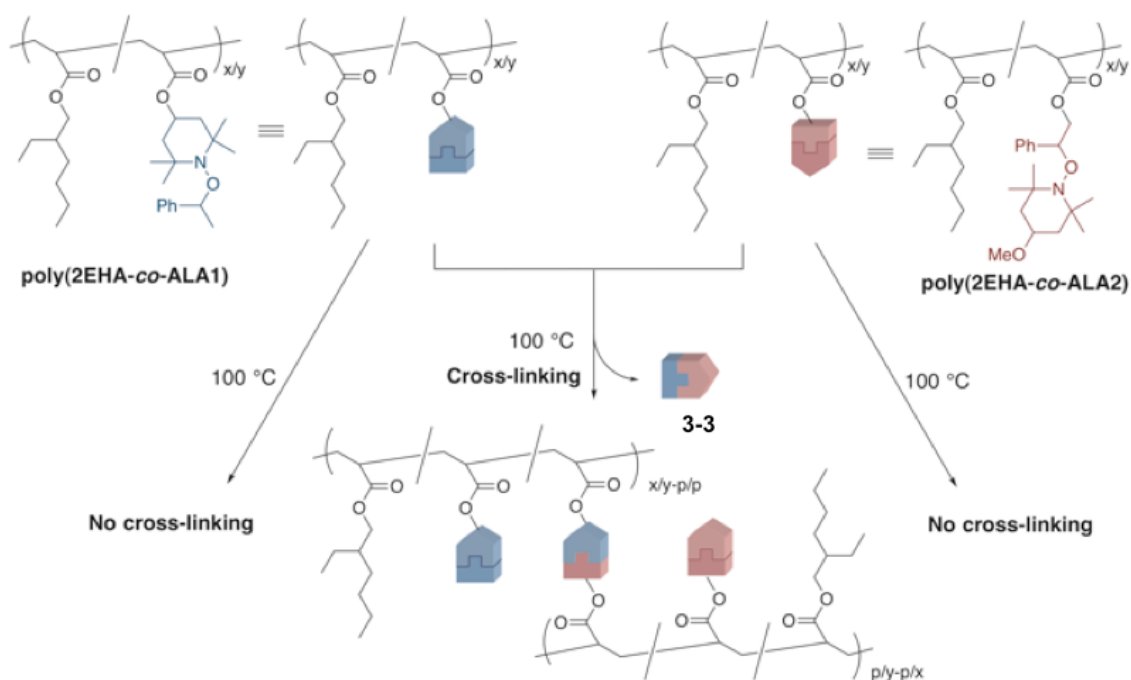


Figure 3-7. (a) Storage shear modulus (G') vs. angular frequency (ω) of the low- T_g polymer heated for 0, 2, 4, 8, 12, and 24 h measured at 25 °C. (b) G' and loss shear modulus (G'') of the low- T_g polymer heated for 0, 2, 4, 8, 12, and 24 h were at 1 Hz at 25 °C.

3.3.4 Cross-linking reaction of poly(2EHA-co-ALA1) and poly(2EHA-co-ALA2)

To show the complementary reactivity of ALA1 and ALA2 groups in the cross-linking reaction of poly(2EHA-co-ALA1-co-ALA2), two types of random copolymers were also prepared. When poly(2EHA-co-ALA1) and poly(2EHA-co-ALA2) were separately heated at 100 °C for 24 h under bulk conditions, no cross-linking reaction was confirmed. Furthermore, rheological measurement (measured at 25 °C) gave G' and G'' vs. ω plots of poly(2EHA-co-ALA1) that did not change before and after heating. In contrast, the 1:1 mixture of poly(2EHA-co-ALA1) and poly(2EHA-co-ALA2) successfully afforded the corresponding cross-linked polymer (**Scheme 3-3**). This finding indicates that both of ALA1 and ALA2 units are indispensable for the cross-linking reaction.



Scheme 3-3. Cross-linking reactions using poly(2EHA-co-ALA1) and poly(2EHA-co-ALA2).

3.3.5 De-cross-linking reaction of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2)

The de-cross-linking reaction of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) was carried out by heating the sample with **3-3** (20 equiv. to alkoxyamine in polymer) at 100 °C. After 48 h, the flowable state was recovered and a product soluble in organic solvents was obtained. The polymer product was evaluated by ¹H NMR measurements. Similar NMR spectra of poly(2EHA-*co*-ALA1-*co*-ALA2) and of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) after the de-cross-linking reaction were observed, as shown in **Figure 3-8**. The efficiency of the de-cross-linking reaction was further evaluated by GPC measurement. **Figure 3-9** shows the GPC curves of the polymers before cross-linking and after de-cross-linking reactions. The peak of the polymer after de-cross-linking had almost the same retention time as that of the polymer before cross-linking, and a peak over exclusion limit was not seen. M_n values before cross-linking and after de-cross-linking reaction were estimated to be 22,000 and 34,000, respectively. These results suggest that de-cross-linking reaction successfully occurred through radical crossover reaction between alkoxyamines, and a change from the rubber-like state to the flowable state was accomplished.

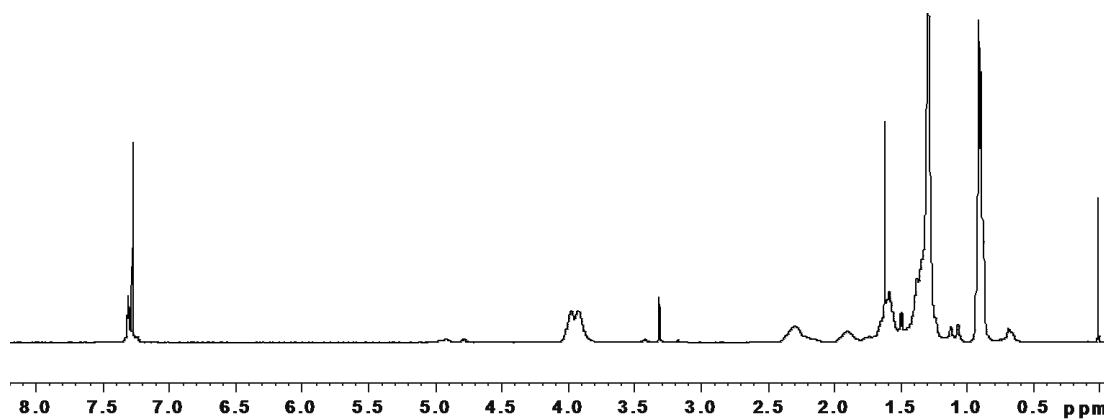


Figure 3-8. ^1H NMR spectrum of the polymer product after de-cross-linking reaction of cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2).

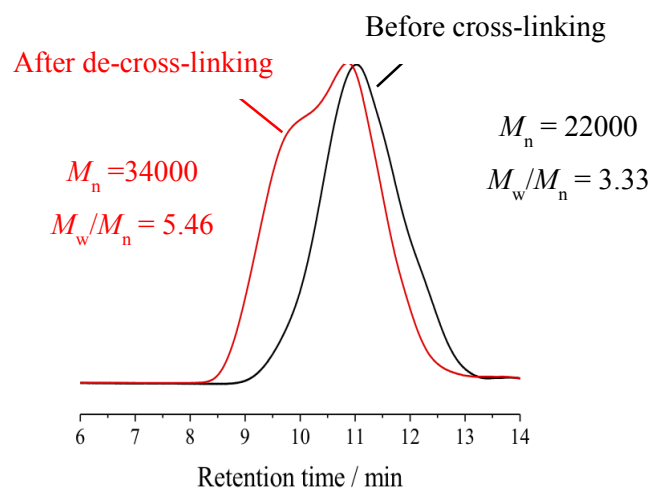


Figure 3-9. GPC curves of poly(2EHA-*co*-ALA1-*co*-ALA2) and the polymer product after de-cross-linking reaction of cross-linked polymer(2EHA-*co*-ALA1-*co*-ALA2) with **3-3**.

To achieve more effective de-cross-linking, nitroxide radical was directly reacted with the cross-linked polymer. The cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) was heated in the presence of 4-methoxy-TEMPO (20 equiv. to alkoxyamine in polymer) at 100 °C. After 48 h, the sample was transformed from the viscoelastic solid state to a flowable liquid state, as shown in **Figure 3-10**. The M_n after the de-cross-linking reaction ($M_n = 23000$, $M_w/M_n = 5.18$) almost corresponded to that of the starting polymers ($M_n = 22000$, $M_w/M_n = 3.33$), as shown in **Figure 3-5**. Although the M_n after the de-cross-linking reaction ($M_n = 23000$, $M_w/M_n = 5.18$) was slightly higher than that of the starting polymers ($M_n = 22000$, $M_w/M_n = 3.33$) as shown in **Figure 3-5**, the efficiency of the de-cross-linking reaction using 4-methoxy-TEMPO was higher than the case using compound **3-3**. These results prove that the cross-linked points are thermally dissociable and that the reaction system is almost reversible under stoichiometric control.

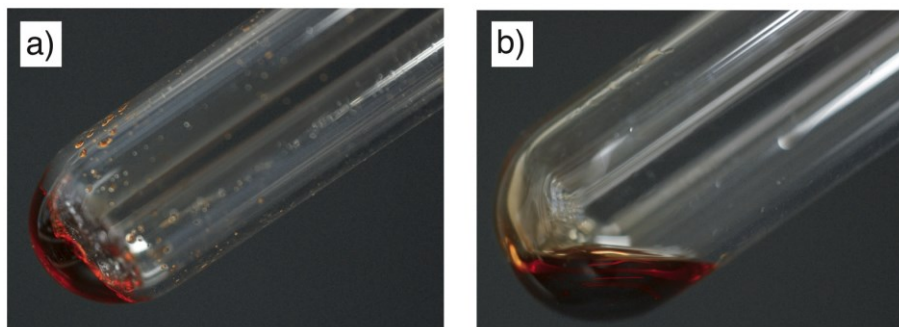


Figure 3-10. Photographs of the cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) swollen with an excess amount of 4-methoxy-TEMPO (20 equiv./alkoxyamine units) (a) before and (b) after heating at 100 °C for 48 h.

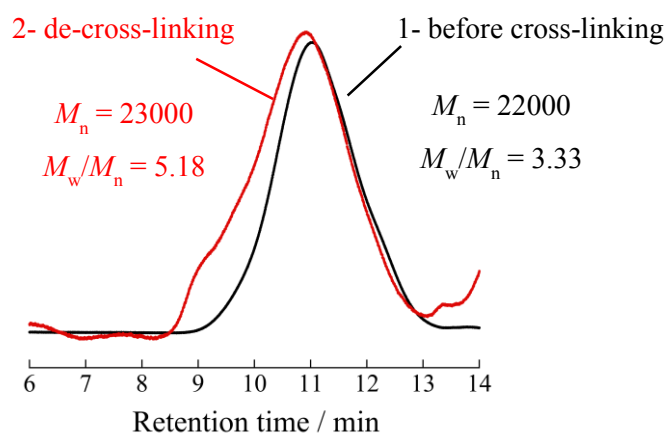


Figure 3-11. GPC curves of poly(2EHA-*co*-ALA1-*co*-ALA2) and de-cross-linked polymer by treatment with the network polymer prepared from poly(2EHA-*co*-ALA1-*co*-ALA2) with 4-methoxy TEMPO.

3.4 Conclusion

Since polymers with reversible and dynamic covalent linkages have gained much attention in many fields of science because of their supramolecular polymer-like behaviour, polymer reactions with dynamic covalent linkages in bulk states have been desired to produce novel functional materials. Further, although transition between the flowable and rubber-like polymers states can be controlled simply by cross-linking and de-cross-linking polymers with low glass transition temperatures (T_g), there are a few reports on the use of dynamic covalent linkages. Reversible cross-linking reactions of polymers with alkoxyamines under bulk conditions have been demonstrated. Cross-linking reactions of the polymers under bulk conditions proceeded by heating the polymer at 100 °C, *via* radical crossover reaction between alkoxyamines. The reactions caused rheological tuning, and the viscoelastic property changed with an accompanying change in the polymer state from flowable to rubber-like. De-cross-linking reaction was achieved by radical exchange reaction between the cross-linked poly(2EHA-*co*-ALA1-*co*-ALA2) and alkoxyamine compound or 4-methoxy-TEMPO. Because radical reactions are tolerant of many functional groups, this reaction may be employed to produce other stimuli-responsive smart materials, including solvent-free PSAs and thermoplastic cross-linked polymers.

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Chapter 4

Radical Exchange Reactions of Polymers with Dynamic Covalent Linkages in the Presence of Plasticizers

4.1 Introduction

Reorganizable polymers have attracted considerable attention in a few decades because their structures and properties can be altered and tuned up even after polymerization.¹⁻⁵ They have the potential to be applied to the design of intelligent materials such as stimuli-responsive systems,^{6,7} chemical recycling systems,^{8,9} polymer hybridization,¹⁰⁻¹² and mendable systems.¹³⁻¹⁷ However, most of conventional polymers are structurally unchangeable due to their strong and fixed covalent bonds. Therefore, reorganizable polymers should contain exchangeable covalent^{3,18,19} and/or non-covalent bonds in their main chains, side chains, cross-linking points, or other positions.

In particular, polymeric materials cross-linked by stimuli-responsive reversible covalent bonds can be expected to possess the similar stability to static materials under normal conditions due to covalent connections as well as the reorganizability as with dynamic materials under the external stimulation. Dynamic covalent polymers that structure is stable under normal conditions, and is changeable by the crossover reaction of covalent bonds upon heating have been developed.¹⁹ In the course of these studies on dynamic covalent polymers, 2,2,6,6-tetramethylpiperidiny-1-oxyl (TEMPO)-based alkoxyamine unit has been employed as fundamental exchangeable unit. Although the alkoxyamine unit behaves as a typical covalent bond at room temperature, it homolytically cleaves and reaches an equilibrium state between dissociation/association upon heating. According to the model reaction results, radicals generated by the alkoxyamine dissociation can exchange, leading to an equilibrium state without side reactions and/or deactivation.

In previous works, reversible cross-linking and de-cross-linking reactions of polymers with alkoxyamine units in the side chains in organic solvents were reported.¹⁹ In Chapter 2, the reversible cross-linking and de-cross-linking reactions of alkoxyamine-appended polymers were demonstrated in an aqueous system.²⁰ In Chapter 3, the radical exchange reactions of alkoxyamine-appended dynamic covalent polymers in the bulk state by careful macromolecular design have been achieved.²¹ However, such polymer design is very limited, therefore, more general material design is required.

To overcome this problem, the mobility of polymer chains was focused on. When the low glass transition temperature (T_g) polymers were employed as a main skeleton of the thermally cross-linkable dynamic covalent polymer, the cross-linking reaction successfully proceeded under bulk conditions.⁴ Since the exchange reaction between the appended alkoxyamine units of the polymers is based on the intermolecular process, the reaction seems to require high mobility of the polymer chains to react one another. If one can increase the mobility of the polymer chains by the additive, the cross-linking ability can be expected to be controlled. In this chapter, the plasticizer-promoted cross-linking of a dynamic covalent polymer with complementarily reactive alkoxyamine units in the side chain under bulk conditions is described.

2. Experimental

4.2.1 Materials

Alkoxyamine-containing methacrylate monomers, ALMA1 and ALMA2, were synthesised and purified as previously reported. Triethylamine (99%) were purchased from Wako Pure Chemical Industries and purified by distillation over calcium hydride. Tetrahydrofuran (THF, 99.5%) was purchased from Wako Pure Chemical Industries and purified through a Glass Contour solvent purification system. Toluene was purchased from Wako Pure Chemical Industries and purified through a Glass Contour solvent purification system. Methyl methacrylate (MMA) was purchased from Tokyo Chemical Industry and purified by distillation under vacuum. 2,2-Azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70, 95%) was purchased from Wako Pure Chemical Industries and used without further purification.

4.2.2 Measurement

^1H NMR (400 MHz) spectroscopic measurement in chloroform-*d* (CDCl_3) were carried out at 25 °C on a Bruker spectrometer, using tetramethylsilane as an internal standard. The monomer conversion was determined by ^1H NMR spectroscopy of the crude reaction mixtures. Number- and weight-average molecular weights (M_n and M_w , respectively) and polydispersities (M_w/M_n) were estimated by gel permeation chromatography (GPC) in THF at 40 °C on a polystyrene gel column [TOSOH TSKgel SuperH2500, TSKgel SuperH4000, and TSKgel SuperH6000 (6–150 mm), nominal maximum molecular weight at which separation occurs: 40,000,000]. The

column was connected to a TOSOH system equipped with a refractive index detector and the mobile phase was maintained at a flow rate of 0.6 mL min^{-1} . The column was calibrated against six standard polystyrene samples (M_n : 1060–3,690,000; M_w/M_n : 1.02–1.08). DSC measurement was performed on an EXSTAR6000 unit (SII Nanotechnology Inc.) at 153 to 323 K at a heating rate of 10 K min^{-1} .

4.2.3 Synthesis of alkoxyamine-containing methacrylate monomers ALMA1.

Methacryloyl chloride (0.44 mL, 4.5 mmol) was added to a solution of alkoxyamine alcohol **4-1** (0.83 g, 3.0 mmol) and triethylamine (0.63 mL, 4.5 mmol) in anhydrous tetrahydrofuran (10 mL), and then the solution was stirred at room temperature under nitrogen for 16 h and then evaporated to dryness. The residue was partitioned between water and dichloromethane. Then the aqueous layer was washed with dichloromethane, and the combined organic layers were dried with magnesium sulfate and evaporated to dryness. The crude product was purified by a flash chromatography eluting with ethyl acetate/hexane (1/20, v/v) and dried in vacuo to give the acrylic ester (ALMA1) as a colorless viscous oil (0.623 g, 60% yield). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm 0.67 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.49 (d, 3H, CH_3), 1.40–2.00(m, 4H, CH_2), 1.85 (d, 1H, CH_3), 4.77 (q, 1H, CH), 5.08 (m, 1H, CH), 5.52 (s, 1H, vinyl proton), 6.08 (d, 1H, vinyl proton), 7.10–7.39 (m, 5H, aromatic proton).

4.2.4 Synthesis of alkoxyamine-containing methacrylate monomers ALMA2.

Methacryloyl chloride (0.44 mL, 4.5 mmol) was added to a solution of alkoxyamine alcohol **4-2** (0.79 g, 3.0 mmol) and triethylamine (0.63 mL, 4.5 mmol) in anhydrous tetrahydrofuran (10

mL), and then the solution was stirred at room temperature under nitrogen for 16 h and then evaporated to dryness. The residue was partitioned between water and dichloromethane. Then the aqueous layer was washed with dichloromethane, and the combined organic layers were dried with magnesium sulfate and evaporated to dryness. The crude product was purified by a flash chromatography eluting with ethyl acetate/hexane (1/10, v/v) and dried in vacuo to give the acrylic ester (ALMA2) as a colorless viscous oil (0.31 g, 31% yield). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm 0.71 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 3.33(s, 1H, CH), 3.45(m, 2H, CH_2), 4.35 (d, 1H, CH_3), 4.67 (q, 1H, CH), 5.05 (m, 1H, CH), 5.52 (s, 1H, vinyl proton), 6.05 (s, 1H, vinyl proton), 7.10-7.39 (m, 5H, aromatic proton).

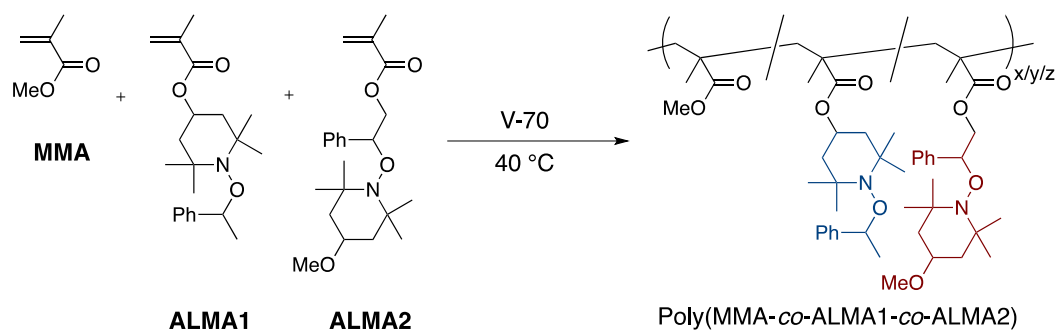
4.2.5 Synthesis of poly(MMA-*co*-ALMA1-*co*-ALMA2).

Under argon condition, MMA (4.8 mL, 4.512 g, 45 mmol), ALAM1 (0.85 g, 2.5 mmol), ALAM2 (0.90 g, 2.5 mmol), and toluene (20 mL) were added into a round-bottom flask containing a magnetic stirring bar and V-70 (0.0675 g, 0.22 mmol) as an initiator was added into the mixture (**Scheme 4-1**). The copolymerization was carried out at 40 °C for 16 h, and the product was precipitated with methanol to afford poly(MMA-*co*-ALMA1-*co*-ALMA2). Then, the white fiber-like poly(MMA-*co*-ALMA1-*co*-ALMA2) was obtained (4.58g, yield : 73 %, $M_n = 21000$ and $M_w/M_n = 1.88$). The structure was confirmed by $^1\text{H-NMR}$. Number-average molecular weight (M_n) as well as polydispersity index (M_w/M_n) were estimated by size exclusion chromatography (SEC) in THF at 40 °C. $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm (3 H, s, CH_3), 0.84 (3 H, s, CH_3), 1.03 (3 H, s, CH_3), 1.08–1.16 (3 H, m, CH_3), 1.25 (brs, R- CH_3), 1.47–1.51 (3 H, m, CH_3), 1.56 (brs, R-CH), 1.81 (brs, CH_2), 3.31 (s, OCH_3), 3.42 (1 H, m, CH), 4.77 (brs,

CH), 4.87 (brs, CH), 7.26 (s, aromatic proton), 7.31 (brs, aromatic proton).

4.2.6 Cross-linking of poly(MMA-*co*-ALMA1-*co*-ALMA2)

Poly(MMA-*co*-ALMA1-*co*-ALMA2) [$M_n = 21,000$, $M_w/M_n = 1.88$] and an additive were mixed together and the mixtures were heated at 100 °C for 24 h under nitrogen atmosphere.



Scheme 4-1. Preparation of poly(MMA-*co*-ALMA1-*co*-ALMA2) by radical copolymerization of MMA, ALMA1, and ALMA2 (18/1/1) by azo-type initiator V-70 at 40 °C.

4.3 Results and Discussion

4.3.1 Design and synthesis of poly(MMA-*co*-ALMA1-*co*-ALMA2)

In this chapter, an alkoxyamine-appended polymer with higher T_g than the reaction temperature (100 °C) was designed to investigate the influence of additives. An alkoxyamine-appended polymer was synthesized at 40 °C by radical copolymerization from methyl methacrylate (MMA) and alkoxyamine-containing methacrylate monomers (ALMA1 and ALM2) [MMA/ALMA1/ALMA2 = 18/1/1] (**Scheme 4-1**). Low-temperature azo-type initiator, 2,2'-azobis(4-methoxy-2,4-dimethyl valeronitrile (V-70), was employed and the corresponding copolymer, poly(MMA-*co*-ALMA1-*co*-ALMA2), was successfully isolated (yield 73%) from the reaction mixture after 16 h at 40 °C by reprecipitation from methanol. Alkoxyamine-containing methacrylate monomers, ALMA1 and ALMA2, were synthesised and purified as previously reported.²

The structure of poly(MMA-*co*-ALMA1-*co*-ALMA2) was confirmed by ¹H-NMR measurement, as shown in **Figure 4-1** and its composition was in agreement with the feed ratio (MMA/ALMA1/ALMA2 = 18/1/1). Gel permeation chromatographic (GPC) measurement revealed that the number average molecular weight (M_n), weight average molecular weight (M_w), and polydispersity (M_w/M_n) were 21000, 39500, and 1.88, respectively. By differential scanning calorimetric (DSC) analysis, the T_g of poly(MMA-*co*-ALMA1-*co*-ALMA2) was estimated to be 125 °C, which is higher than poly(methyl methacrylate) (PMMA) due to the introduction of rigid alkoxyamine moieties.

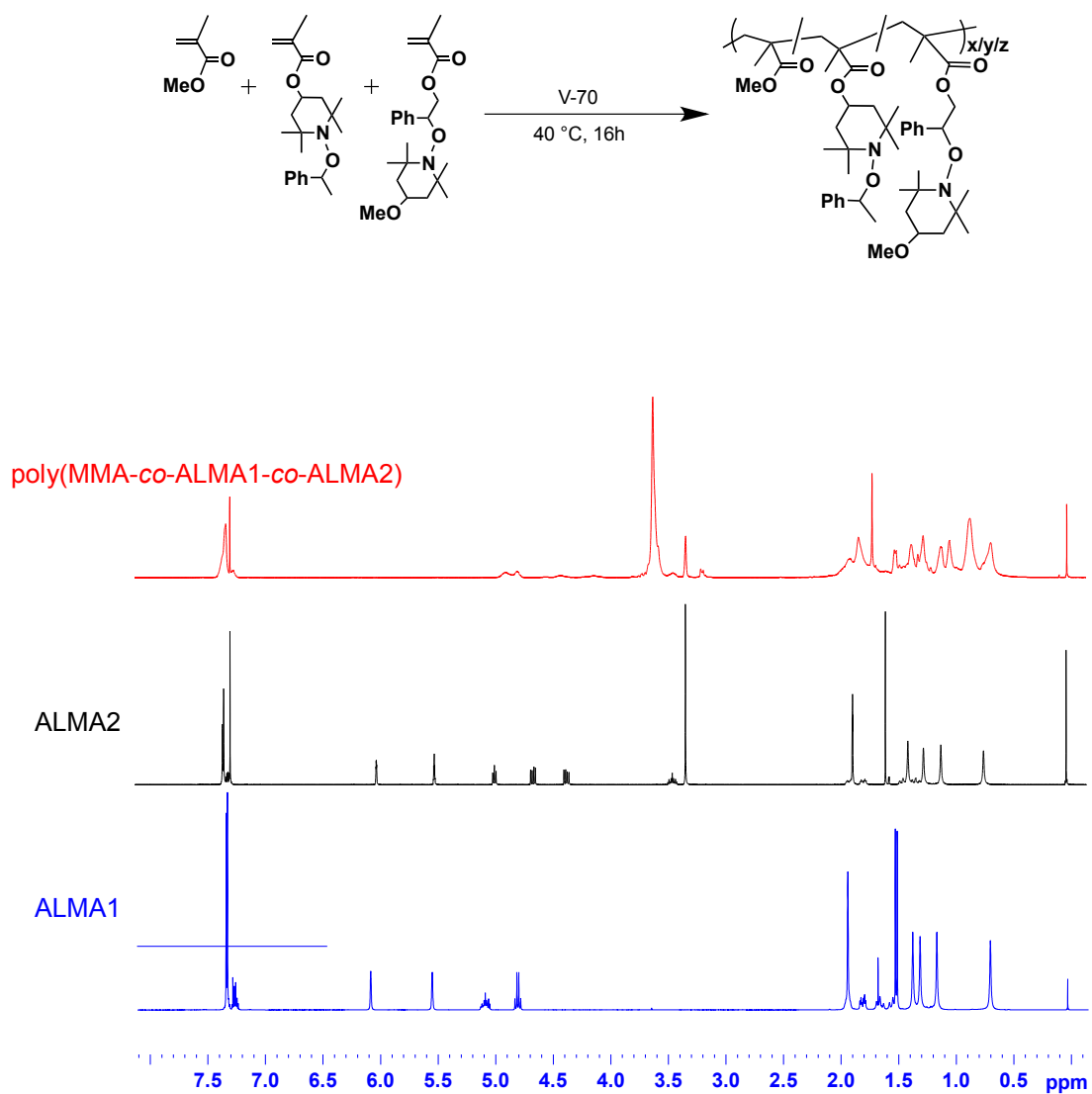


Figure 4-1. ^1H -NMR spectrum of ALMA1, ALMA2, and poly(MMA-co-ALMA1-co-ALMA2) in CDCl_3 .

As a plasticizer, dibutyl phthalate (DBP) was employed, because DBP shows good miscibility with PMMA. Thin film was prepared from a chloroform solution of the mixture of poly(MMA-*co*-ALMA1-*co*-ALMA2) and DBP (2/1, 1.26 g/0.63 g.). As shown in **Figure 4-2 (a)**, homogeneous, transparent, and colorless film was obtained after evaporation of the solvent. The T_g of the polymer film was 52 °C due to the addition of DBP. As a control sample, poly(MMA-*co*-ALMA1-*co*-ALMA2) bulk film without any additive was also prepared.

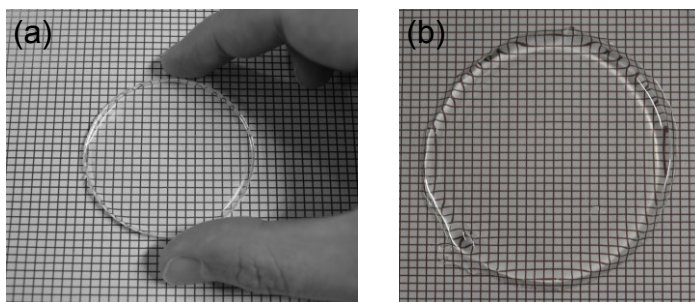
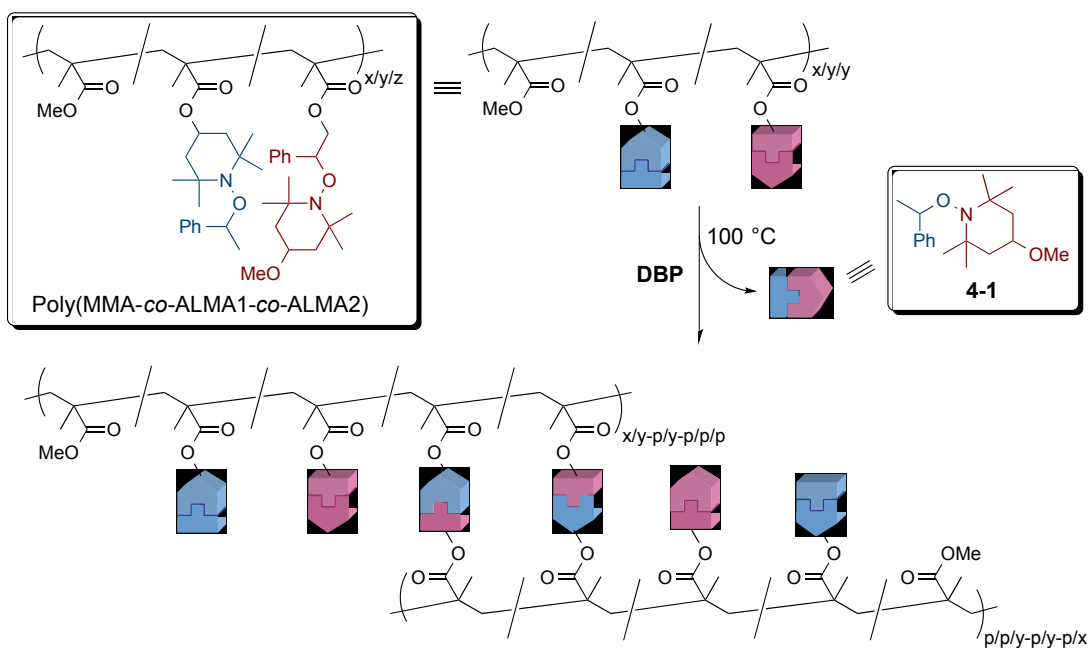


Figure 4-2. Photograph of polymer film prepared from a chloroform solution of the mixture of poly(MMA-*co*-ALMA1-*co*-ALMA2) and DBP (2/1, 1.26 g/0.63 g), before heating (a) and after swelling (b).

The polymer film was heated under nitrogen atmosphere at 100 °C for 24 h. In the case of poly(MMA-*co*-ALMA1-*co*-ALMA2) bulk film without plasticizer, the heated film was completely dissolved into chloroform. From the GPC and NMR measurements, no progress of the cross-linking reaction was observed. In contrast, the polymer film with DBP did not dissolve into chloroform but it was swollen with chloroform to afford a gel, as shown in **Figure 4-2 (b)**. The swelling ratio was 479%, when the solvent was chloroform. This is clearly due to the progress of the cross-linking reaction of polymer chains, promoted by the addition of the plasticizer. NMR measurement of the chloroform-soluble part of the heated film revealed that the presence of alkoxyamine (**4-1**) (**Figure 4-3**), which can be generated by the exchange reaction between the alkoxyamine moieties derived from ALMA1 and ALMA2 as shown in **Scheme 4-2**.



Scheme 4-2. Cross-linking reaction of poly(MMA-co-ALMA1-co-ALMA2) in the presence of DBP as a plasticizer at 100 °C.

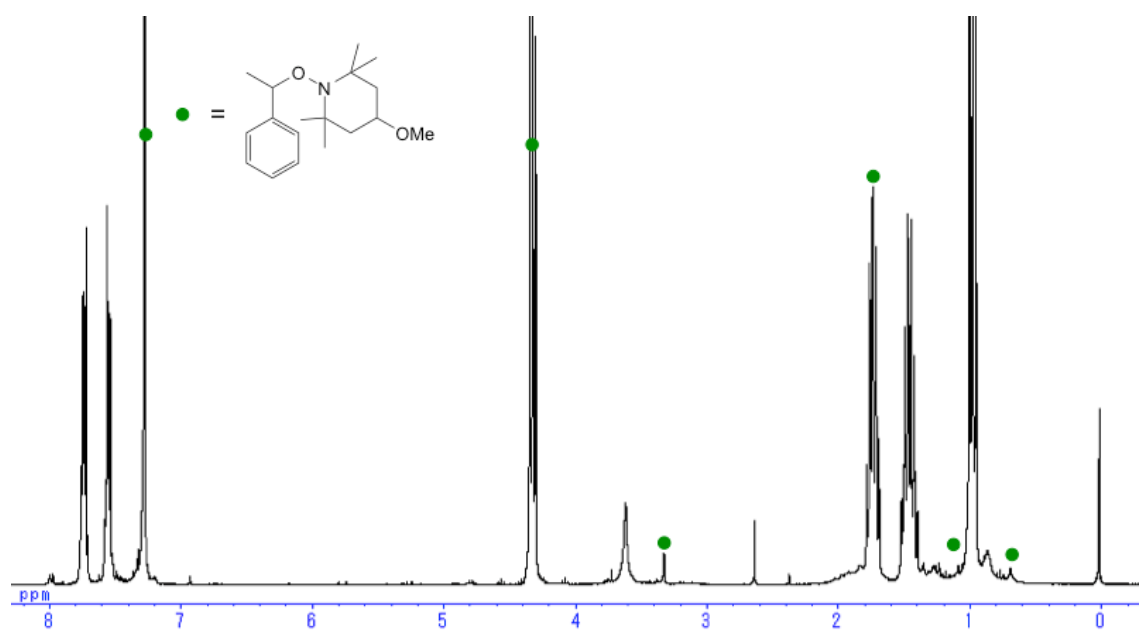


Figure 4-3. ^1H -NMR spectrum of chloroform-soluble part of heated poly(MMA-*co*-ALMA1-*co*-ALMA2) in CDCl_3 .

To obtain further insight into the cross-linking reaction, other additives were used. **Table 4-1** summarizes the results of the cross-linking reactions of poly(MMA-*co*-ALMA1-*co*-ALMA2) in the presence of various additives. Poly(butyl acrylate) (PBA, $M_n = 13400$) and poly(2-ethylhexyl acrylate) (P2EHA, $M_n = 10800$) were added into poly(MMA-*co*-ALMA1-*co*-ALMA2). Although PBA and P2EHA are low T_g polymers, the miscibility with poly(MMA-*co*-ALMA1-*co*-ALMA2) are poor. The mixture was heterogeneous in both poly(MMA-*co*-ALMA1-*co*-ALMA2)/PBA and poly(MMA-*co*-ALMA1-*co*-ALMA2)/P2EHA systems. Even after heating the mixtures, the system was heterogeneous and no progress of the cross-linking reactions was observed in both cases. These results indicate that the mobility of the polymer chains of poly(MMA-*co*-ALMA1-*co*-ALMA2) was not enough due to the phase separation with PBA or P2EHA.

Also, poly(propylene glycol) (PPG-300, M_n is approximately 300) was also added into poly(MMA-*co*-ALMA1-*co*-ALMA2) and similar heating experiment was carried out. Although the heterogeneous mixture was obtained even after heating, the generation of trace amount of cross-linked product was observed. This is because the miscibility of PPG-300 and poly(MMA-*co*-ALMA1-*co*-ALMA2) is slightly better than the cases of PBA or P2EHA.

Table 4-1. Results of the cross-linking reactions of poly(MMA-*co*-ALMA1-*co*-ALMA2) in the presence of various additives at 100 °C for 24 h

Run	Additive ^a	poly(MMA- <i>co</i> -ALMA1- <i>co</i> -ALMA2) / Additive (w/w)	Appearance		Cross-linking ^b
			Before heating	After heating	
1	PBA	1 / 5	Heterogeneous	Heterogeneous	No
2	PBA	1 / 10	Heterogeneous	Heterogeneous	No
3	P2EHA	1 / 5	Heterogeneous	Heterogeneous	No
4	P2EHA	1 / 10	Heterogeneous	Heterogeneous	No
5	PPG300	1 / 5	Heterogeneous	Heterogeneous	Trace
6	PPG300	1 / 10	Heterogeneous	Heterogeneous	Trace
7	DBP	5 / 1	Heterogeneous	Heterogeneous	No
8	DBP	2 / 1	Heterogeneous	Homogeneous	Yes
9	DBP	1 / 1	Heterogeneous	Homogeneous	Yes
10	DBP	1 / 2	Homogeneous	Homogeneous	Yes
11	DBP	1 / 5	Homogeneous	Homogeneous	Yes
12	DBP	1 / 10	Homogeneous	Homogeneous	Yes

a. PBA: poly(butyl acrylate) [$M_n = 13400$], P2EHA: poly(2-ethylhexyl acrylate) [$M_n = 10800$], PPG300: poly(propylene glycol) [M_n is approximately 300], DBP: dibutyl phthalate. b. Heated samples were added into chloroform: “Yes” denotes the generation of gel, and “No” denotes the sample was completely dissolved. “Trace” denotes trace amount of chloroform-insoluble part was obtained.

4.4 Conclusion

In summary, “plasticizer-promoted” cross-linking reactions of an alkoxyamine-appended poly(methyl methacrylate) (PMMA)-based dynamic covalent polymer were demonstrated under bulk conditions. The homogeneous and transparent polymer films of poly(MMA-*co*-ALMA1-*co*-ALMA2) and DBP as a plasticizer were prepared and their cross-linking was confirmed upon heating at 100 °C under bulk conditions. The plasticizer approach is quite simple but the results are completely different from the case with no plasticizer. By the addition of the plasticizer, the mobility of polymer chains was improved. As a result, cross-linking reaction proceeded. The mobility of the polymer chains are undoubtedly important during the cross-linking reactions of poly(MMA-*co*-ALMA1-*co*-ALMA2) and this approach can be useful for the various polymer reactions systems.

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Chapter 5

Conclusion

5. Conclusion

Dynamic covalent bonds are powerful tool for the synthesis of impressively complex structures under thermodynamic controls and alkoxyamine as a dynamic covalent bond have been studied in various conditions such as organic system at high temperature. In this thesis, reversible cross-linking of alkoxyamine-containing dynamic covalent polymers in aqueous system and bulk system were demonstrated.

In chapter 2, the radical exchange reactions of polymers with alkoxyamine units in the side chain were successfully demonstrated in an aqueous media, because the radical reactions are tolerant of water. The cross-linking behavior depended on the amounts of alkoxyamine units in the polymers and the reaction concentrations. A de-cross-linking reaction was also accomplished by radical exchange reaction between the cross-linked polymer and added hydrophilic alkoxyamine compound (**Figure 5-1**).

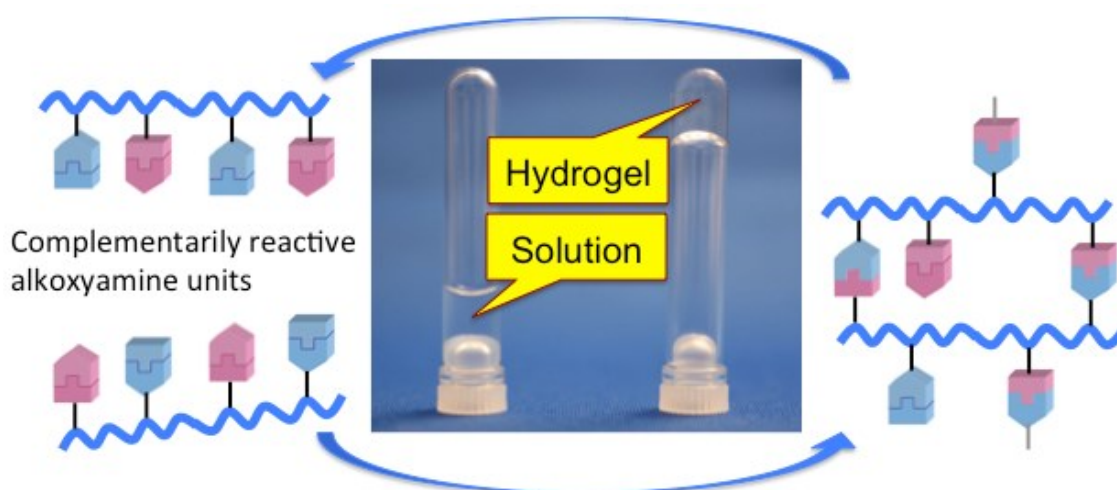


Figure 5-1. Graphical abstract of chapter 2.

In chapter 3, reversible cross-linking reactions of alkoxyamine-appended polymers with low glass transition temperature were successfully carried out under bulk conditions. Cross-linking reactions of the polymers under bulk conditions proceeded by heating the polymer at 100 °C, *via* radical crossover reaction between alkoxyamines. The reactions caused rheological tuning, and the viscoelastic property changed with an accompanying change in the polymer state from flowable to rubber-like. De-cross-linking reaction was achieved by radical exchange reaction between the cross-linked polymer and alkoxyamine compound or 4-methoxy-TEMPO (**Figure 5-2**).

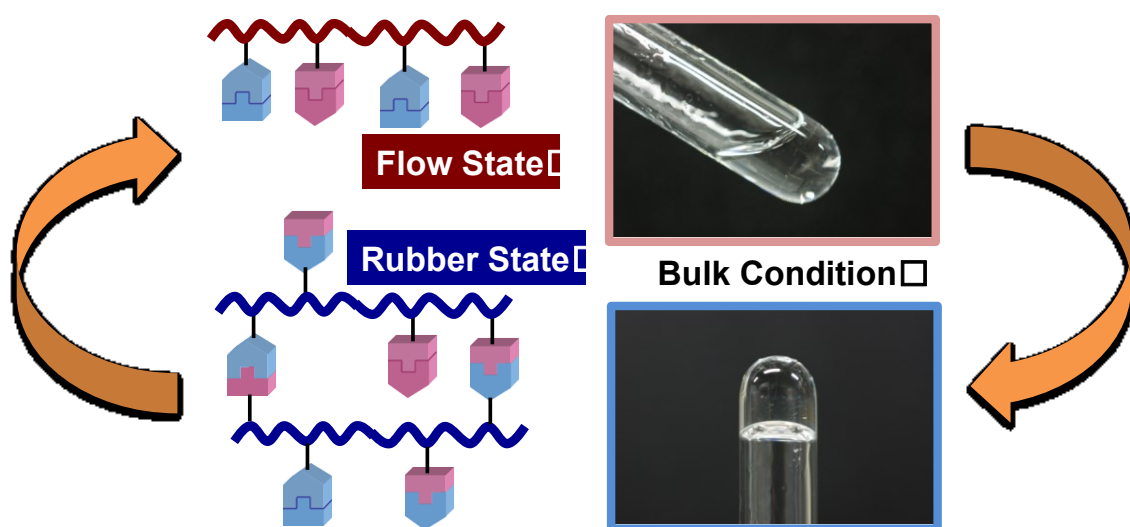


Figure 5-2. Graphical abstract of chapter 3.

In chapter 4, “plasticizer-promoted” cross-linking reactions of an alkoxyamine-appended poly(methyl methacrylate)-based dynamic covalent polymer were demonstrated under bulk conditions. The homogeneous and transparent polymer films of the polymer and dibutyl phthalate as a plasticizer were prepared and their cross-linking was confirmed upon heating at 100 °C under bulk conditions (**Figure 5-3**).

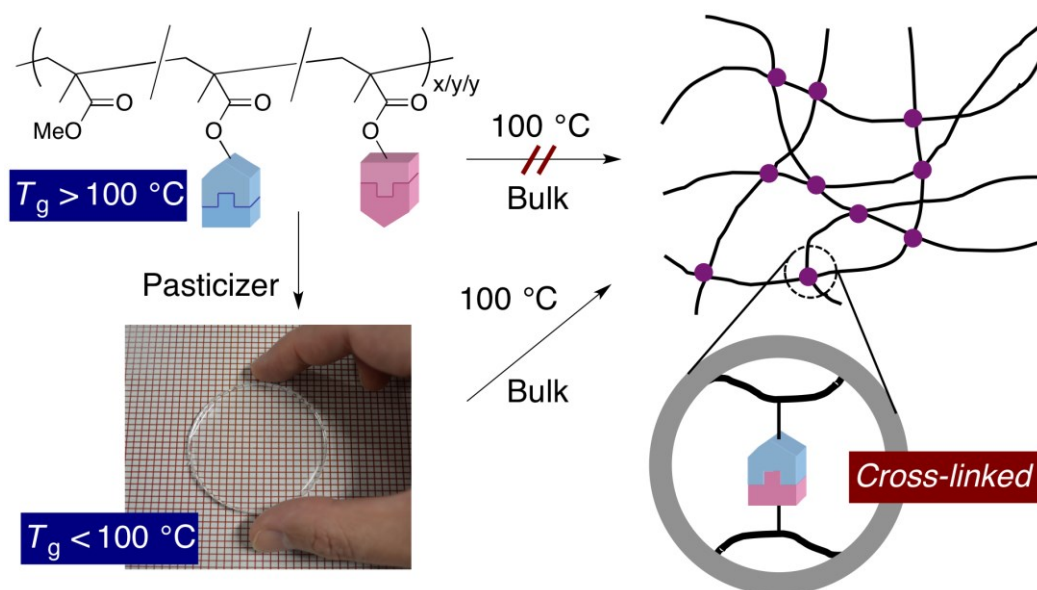


Figure 5-3. Graphical abstract of chapter 4.

These results are foundation of reversible cross-linking and de-cross-linking reactions based on dynamic covalent bonds. Since the radical reactions are tolerant of many conditions, alkoxyamine units in the side chain caused the reversible reactions under various conditions.

In the future, more complicated system such as organic/aqueous two-phase system can be applied under aqueous condition and other stimuli-responsive smart materials, including solvent-free PSAs and thermoplastic cross-linked polymers may be employed to produce by the bulk condition reaction.

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