

## FOCUS REVIEW

# Reorganization of polymer structures based on dynamic covalent chemistry: polymer reactions by dynamic covalent exchanges of alkoxyamine units

Hideyuki Otsuka<sup>1,2</sup>

The recent progress of research on polymer reactions utilizing dynamic covalent exchanges of alkoxyamine units—adducts of styryl and stable nitroxide radicals—is reviewed. The alkoxyamine derivatives derived from 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, a stable free radical) are frequently utilized as unimolecular initiators for the nitroxide-mediated radical polymerizations. In the absence of monomers, however, the alkoxyamine derivatives can undergo intermolecular crossover reactions via a radical process upon heating. The central C–ON bonds in the alkoxyamine derivatives reversibly cleave and reform upon heating, and a mixture of alkoxyamine derivatives is able to equilibrate thermally, meaning that the covalent bonds in the alkoxyamine derivatives are considered as ‘dynamic covalent bonds.’ Unlike conventional polymers, the structures and constitutions of polymers with dynamic covalent bonds, dynamic covalent polymers, can be reorganized under appropriate conditions even after polymerization. In the present review, various types of macromolecular design, polymer reactions based on dynamic covalent exchanges of alkoxyamine units and their related research are described. Various examples of polymer reactions of main-chain-type, side-chain-type, crosslinked and star-shaped poly(alkoxyamine)s are systematically shown. Furthermore, the progress of the polymer reactions can be confirmed by diverse characterization techniques, such as spectroscopic, chromatographic, microscopic and scattering methods.

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## INTRODUCTION

Reorganizable polymers have attracted considerable attention in recent decades because their primary structures and properties can be changed and manipulated even after polymerization. However, most conventional polymers are structurally unchangeable because their molecular structures are composed of strong and fixed covalent bonds. Therefore, reorganizable polymers should consist of monomer units reversibly connected by exchangeable covalent and/or non-covalent bonds, and they have the potential to be applied to the design of intelligent materials, chemical recycling systems, polymer hybridization and so on. ‘Supramolecular polymers’ are representative successful examples of reorganizable polymers, and are constructed by secondary non-covalent interactions such as hydrogen bonding. The pioneering example of a supramolecular polymer was first reported by Fréchet and Kato in 1989.<sup>1</sup> Lehn *et al.*<sup>2</sup> synthesized the first main-chain-type supramolecular polymer based on hydrogen bonding; since then, many examples of supramolecular polymers have been reported.<sup>3–6</sup> For instance, Meijer *et al.*<sup>7</sup> developed supramolecular main-chain polymers with very high molecular weights by using a

quadruple hydrogen-bonding system. Unlike conventional polymers, supramolecular polymers connected by hydrogen bonds are not very stable, but rather, are mutable, particularly in the solution state. Their superstructures and their molecular weights are strongly dependent on concentration and solvent quality. Therefore, it is relatively difficult to characterize their detailed structures further.

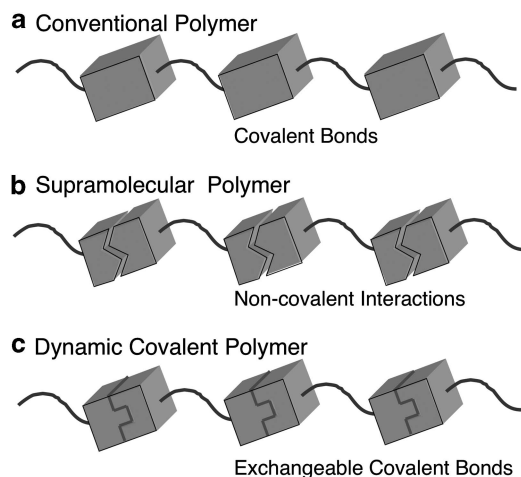
On the other hand, successful applications of reversible covalent chemistry have been seen in the development of dynamic combinatorial libraries,<sup>8–14</sup> interlocked molecules,<sup>15–21</sup> drug discovery<sup>22</sup> and controlled release of fragrances.<sup>23</sup> Rowan *et al.*<sup>24</sup> introduced the concept of dynamic covalent chemistry, which offered the possibility of ‘doing supramolecular chemistry’ at the level of covalent bonds. When the main chain of a polymer consists of reversible covalent bonds instead of non-covalent interactions, the polymer is expected to behave as a reorganizable polymer, similarly to supramolecular polymers (Figure 1).<sup>25,26</sup> In contrast to supramolecular polymers, one can manipulate the stability and reorganizability of ‘dynamic covalent polymers’<sup>27</sup> by selecting the proper reversible covalent bonds. If a thermally reversible covalent system is employed, the polymers are

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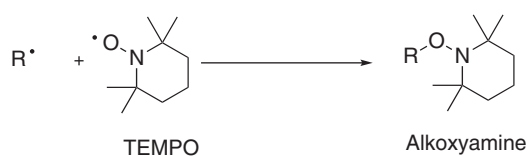
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**Figure 1** Schematic representation of (a) conventional polymers, (b) supramolecular polymers and (c) dynamic covalent polymers.



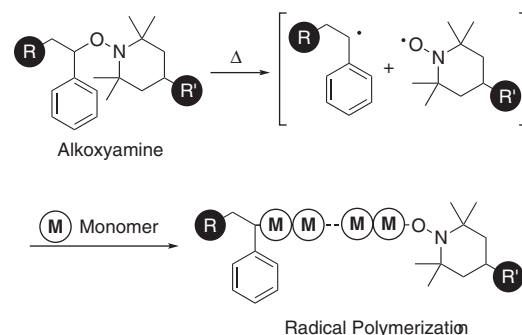
**Scheme 1** Formation of alkoxyamine from TEMPO.

stable under normal conditions and even at high dilution. Nevertheless, once they are exposed to an external stimulus (heating), they start to reorganize to reflect the chemical and physical environmental conditions.

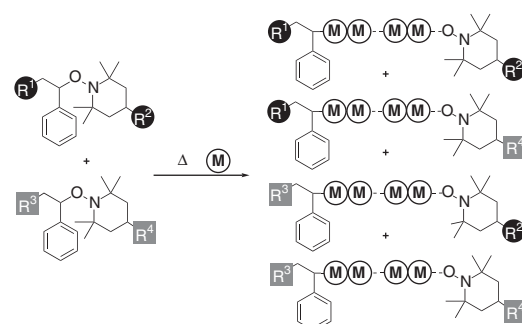
Although some reversible covalent bonds have been used for structural change in the field of polymer chemistry,<sup>28–45</sup> this review focuses on polymer reactions by dynamic covalent exchanges of alkoxyamine units derived from 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, a stable free radical) derivatives (Scheme 1). The fundamental radical exchange reaction of alkoxyamine derivatives is shown by a model reaction using low-molecular-weight alkoxyamine compounds. Then, various types of macromolecular design and polymer reactions based on dynamic covalent exchanges of alkoxyamine units and their related research are described. Main-chain-type, side-chain-type, crosslinked and star-shaped alkoxyamine-containing dynamic covalent polymers are systematically described by diverse characterization techniques, such as spectroscopic, chromatographic, microscopic and scattering methods.

### ALKOXYAMINES AS DYNAMIC COVALENT EXCHANGE UNITS

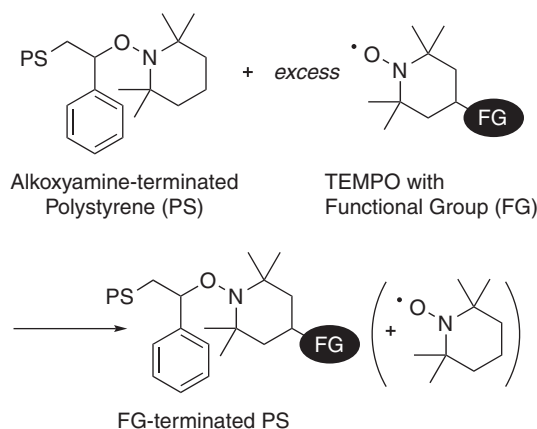
Since the discovery of nitroxide-mediated radical polymerization (NMP)<sup>46,47</sup> using TEMPO, alkoxyamines have been well known as structures of the propagating chain ends in NMP.<sup>48–54</sup> The key step in NMP is the reversible capping of the polymer chain end by a stable nitroxide free radical species.<sup>55</sup> Another significant advance with NMP was the recognition of an alkoxyamine as a unimolecular initiating agent, providing both the reactive initiating radical and the stable mediating nitroxide radical.<sup>56</sup> By using the NMP method, monomers such as styrene and acrylate derivatives can be polymerized from alkoxyamine initiators (Scheme 2).<sup>57</sup> In the case of the radical polymerization of styrene with two different unimolecular alkoxyamine initiators, Hawker *et al.*<sup>58</sup> reported that the radical crossover of the mediating nitroxide moieties occurred at



**Scheme 2** Nitroxide-mediated radical polymerization (NMP) from alkoxyamine.



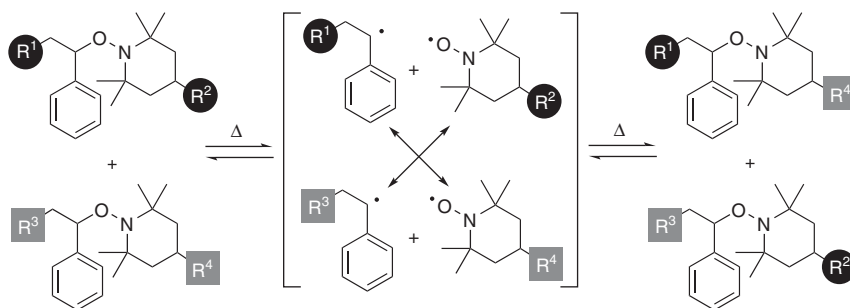
**Scheme 3** Radical crossover of the mediating nitroxide moieties occurred at the termini of the growing polymer chains during NMP.



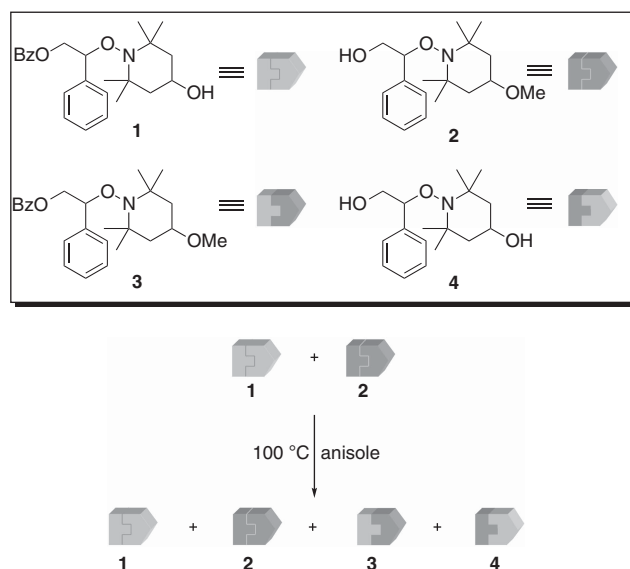
**Scheme 4** Exchange reaction with an excess amount of other nitroxide derivatives at the terminal group of the polystyrene prepared by NMP.

the termini of the growing polymer chains during polymerization, as shown in Scheme 3. Furthermore, an exchange reaction with an excess amount of other nitroxide derivatives at the terminal group of the polystyrene prepared by NMP was also reported by Turro *et al.*<sup>59</sup> (Scheme 4). 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 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 was reported to be  $\sim 30 \text{ kcal mol}^{-1}$ .

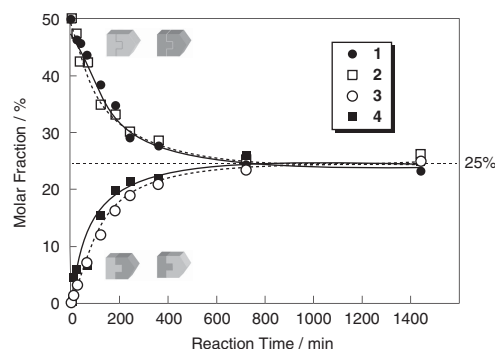
To evaluate the exchangeability of alkoxyamine units, model exchange reactions using low-molecular-weight alkoxyamines were



**Scheme 5** Radical crossover of alkoxyamine derivatives in the absence of monomers.



**Scheme 6** Model reaction of radical crossover using alkoxyamine derivatives 1–4 in anisole at 100 °C.



**Figure 2** Molar fractions of alkoxyamine derivatives 1–4 after heating a mixture of 1 and 2 in anisole at 100 °C.

amount of the carbon–carbon coupling product is still small compared with that of alkoxyamines, the total crossover reactions seem to be highly specific.

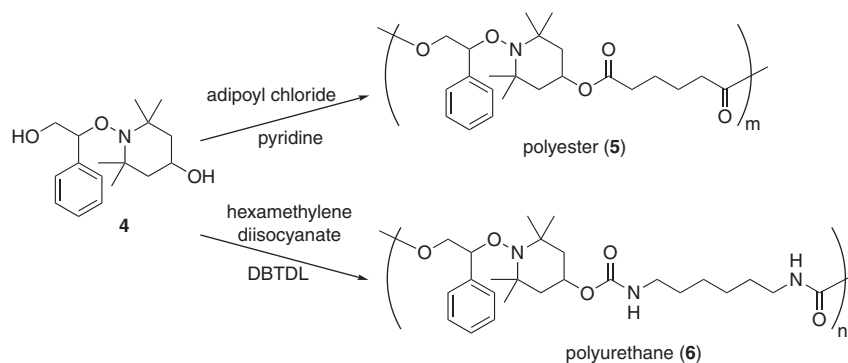
The ratio of compounds 1–4 was estimated from the normalized peak areas in the high performance liquid chromatography analysis. As shown in Figure 2, the molar fractions of alkoxyamines 1–4 attained equilibrium after 12 h at 100 °C. In this equilibrium state, the molar fractions were nearly identical, 25%, for the four different alkoxyamine derivatives. Furthermore, the reaction rate strongly depended on the reaction temperature. The results revealed that the crossover reaction only occurred above 60 °C and the molar fractions attained equilibrium earlier at higher reaction temperatures.

From these model experiments, it was inferred that alkoxyamines, via the exchange reaction, were promising candidates as the fundamental units in dynamic covalent polymers.

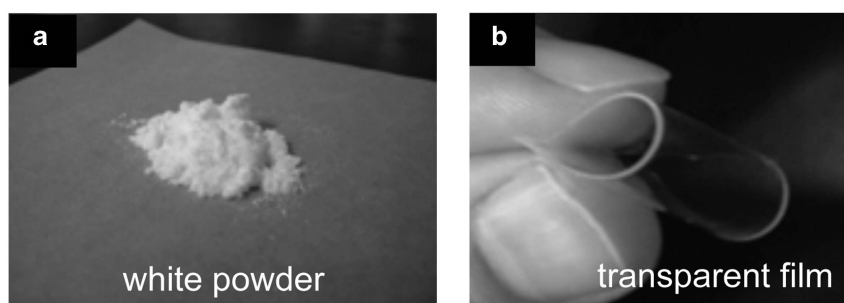
## REACTIONS OF MAIN-CHAIN-TYPE POLY(ALKOXYAMINE)S

Main-chain-type alkoxyamine-containing dynamic covalent polymers were synthesized by step-growth polymerization (Scheme 7). Alkoxyamine-containing polyester (5) was prepared by polycondensation of diol 4 and adipoyl chloride in dichloromethane in the presence of pyridine at room temperature.<sup>60,65</sup> Polyurethane 6, containing alkoxyamine units in the main chain, was prepared by the polyaddition of diol 4 with hexamethylene diisocyanate in the presence of dibutyltin dilaurate as a catalyst.<sup>66</sup> The chemical structures of the obtained main-chain-type alkoxyamine-containing dynamic covalent polymers were fully characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR and IR measurements. As alkoxyamine moieties are stable at room temperature, measurement of the polymer by gel permeation chromatography (GPC) successfully yielded the number-average molecular weight ( $M_n$ ) and weight-average molecular weight ( $M_w$ ).

performed.<sup>60</sup> 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 6. For example, equimolar amounts of 1 and 2 were mixed together in anisole as a 0.18 mol l<sup>−1</sup> solution, and then heated at 100 °C. The reaction was followed by high performance liquid chromatography. From the results of these measurements, two additional peaks, assignable to 3 and 4, appeared soon after heating. Thin layer chromatographic analysis also supported the high performance liquid chromatography results. Significantly, the radical crossover reaction proceeded without any detectable side reaction such as carbon–carbon coupling under these conditions. This observation is clearly explained by the persistent radical effect.<sup>47,61–64</sup> Persistent radical effect is a general principle that explains the highly specific formation of the crosscoupling product R<sup>1</sup>–R<sup>2</sup> between R<sup>1</sup> and R<sup>2</sup> when one species is persistent (R<sup>1</sup>) and the other is transient. Persistent radical effect is observed when the persistent radical exists in excess over the transient radical. In the case of the crossover reaction of 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 slight amount of TEMPO radical, which serves as the persistent radical. As the



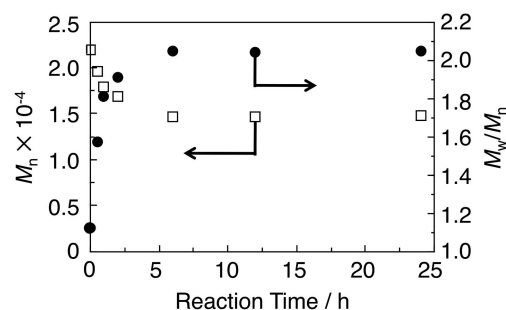
**Scheme 7** Preparation of main-chain-type alkoxyamine-containing dynamic covalent polymers, polyester **5** and polyurethane **6**, by step-growth polymerization.



**Figure 3** Photographs of alkoxyamine-containing polyurethane (**6**); (a) white powder obtained after reprecipitation and (b) transparent film prepared from a chloroform solution.

Under the experimental GPC conditions of 40 °C, no peak tailing and no drastic change of peak shape upon concentration change of the sample solutions were observed that would otherwise imply decomposition or reorganization of the polymer chains. Actually, the polymer was obtained as a white powder, and a transparent film could be prepared by slow evaporation of a chloroform solution, as shown in Figure 3. These results indicated that one can treat the alkoxyamine-containing dynamic covalent polymers at ambient temperature like conventional polymers due to their stability below 60 °C.

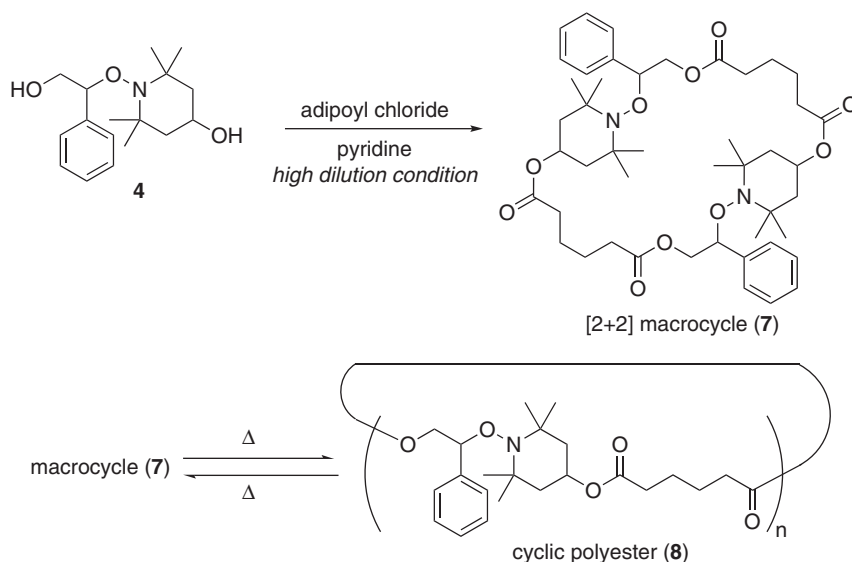
The thermal reaction behavior of the alkoxyamine-containing dynamic covalent polymers was completely different from conventional polymers. To investigate the thermal reactivity of the alkoxyamine-containing dynamic covalent polymers, polyester **5** was fractionated by preparative high performance liquid chromatography. The fractionated polyester **5a** ( $M_n = 12\,000$ ,  $M_w/M_n = 1.21$ ) was heated in anisole at 100 °C after degassing, and GPC and  $^1\text{H}$  NMR measurements of the reacted polymers were carried out. Although the NMR spectrum did not change after heating for 24 h, the GPC profiles drastically changed upon heating. The molecular weight distribution broadened with no significant change in the peak tops as the reaction proceeded. The phenomenon was undoubtedly attributed to the radical crossover reaction of the alkoxyamine units between the main chains. Figure 4 shows the  $M_n$  vs reaction time and the  $M_w/M_n$  vs time plots for the thermal reaction behavior of polyester **5a** in anisole at 100 °C. Although a slight change was observed for  $M_n$ ,  $M_w/M_n$  drastically increased to  $\sim 2.0$ , which is the theoretical value for step-growth polymerization. No further changes in  $M_n$  and  $M_w/M_n$  were observed after 6–12 h, indicating attainment of an equilibrium state.<sup>65</sup> Furthermore, heating a mixture of a high-



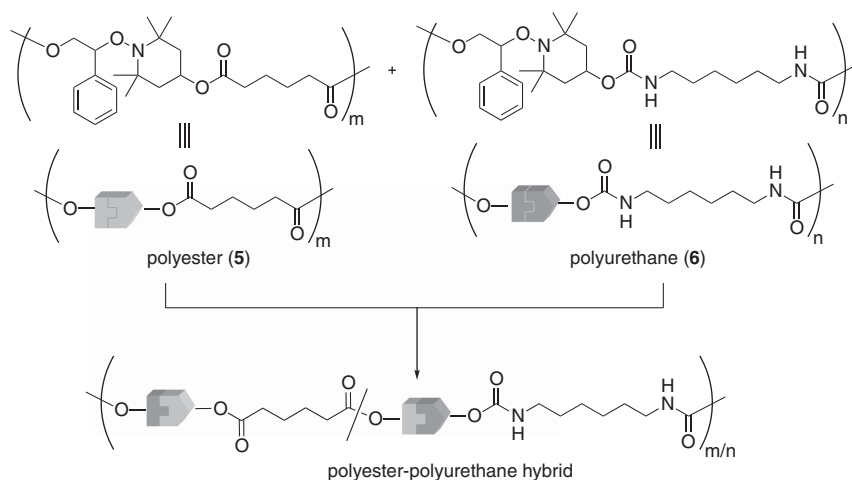
**Figure 4** Changes in  $M_n$  and  $M_w/M_n$  of alkoxyamine-containing polyester (**5a**), ( $M_n = 12\,000$ ,  $M_w/M_n = 1.21$ ) heated in anisole at 100 °C.

molecular-weight polymer and a low-molecular-weight polymer in anisole at 100 °C for 24 h successfully resulted in the formation of the middle- molecular-weight polymer.

The concentration effect on the reorganization behavior of alkoxyamine-containing dynamic covalent polymers was investigated by using macrocyclic alkoxyamines. A macrocycle with alkoxyamine units was synthesized and its dynamic polymerization behavior was evaluated.<sup>67,68</sup> For example, a macrocyclic alkoxyamine, the [2 + 2] adduct (**7**), was synthesized by condensation of an alkoxyamine-based diol (**4**) with adipoyl chloride under high-dilution conditions. Macrocycle **7** acted as a monomer for ‘ring-crossover’ polymerization to afford the corresponding cyclic oligomer or polymer (**8**) with  $M_n = 2000$ –18 000 due to the intermolecular radical crossover reaction. The structure of polymer **8** was identical to that of polymer **5** except that it was linear rather than cyclic.



**Scheme 8** Preparation and ring-crossover polymerization of macrocyclic alkoxyamine **7**.



**Scheme 9** Hybridization of polyester **5** and polyurethane **6** by polymer scrambling.

The polymerization behavior strongly depended on concentration. Furthermore, under high-dilution conditions, polymer **7** depolymerized to the monomer or oligomers mainly by the intramolecular radical exchange process (Scheme 8).

The above-mentioned exchange process is applicable to polymers with many functional groups because of the high tolerance of radical reactions for varying functionality. If the two different dynamic covalent polymers are mixed and the system is thermally reorganized, it can be expected that they will afford one hybridized polymer. These reorganizable polymers can facilitate a new polymer synthetic method—in particular, a method that is effective for the preparation of polymeric hybrid materials at the nanometer level. An innovative method for the hybridization of different dynamic covalent polymers by ‘polymer scrambling’ at the main-chain level was demonstrated by an alkoxyamine-containing dynamic covalent polyester and polyurethane (Scheme 9).<sup>69</sup> By this method, the composition and blockiness of the polymers could be controlled, allowing the preparation of novel polymer nanohybrids by a combinatorial approach.

These findings strongly suggest that the main-chain-type alkoxyamine-containing dynamic covalent polymers are thermally reorganizable polymers. They can dissociate and associate reversibly in the

main chain similarly to supramolecular polymers when triggered by external stimuli (in the present system, upon heating). This concept was further applied to other dynamic covalent chemistries, such as acylhydrazone exchange by acid treatment or heating,<sup>25,70–78</sup> carbene dimerization by heating,<sup>79–81</sup> olefin metathesis by metal catalyst,<sup>82</sup> disulfide exchange by photoirradiation<sup>83</sup> and so on.<sup>84</sup>

## REACTIONS OF SIDE-CHAIN-TYPE POLYMERS WITH ALKOXYAMINES

The exchange reaction between polymer chains with alkoxyamine units is considered as a novel reversible polymer reaction system when it is applied to side-chain reactions. The composition of product polymers can be expected to depend on equilibrium control. This adaptability potentially offers the development of ‘smart’ materials that can respond to external stimuli through the use of reversible covalent bonds.<sup>85</sup> To demonstrate the reorganization, side-chain-type alkoxyamine-containing polymers were synthesized and their reversible reactions were investigated.

Alkoxyamine-containing methacrylic ester (**9**) was prepared by the condensation reaction of alkoxyamine alcohol derivative **10** and methacryloyl chloride. To control the molecular weight via a facile

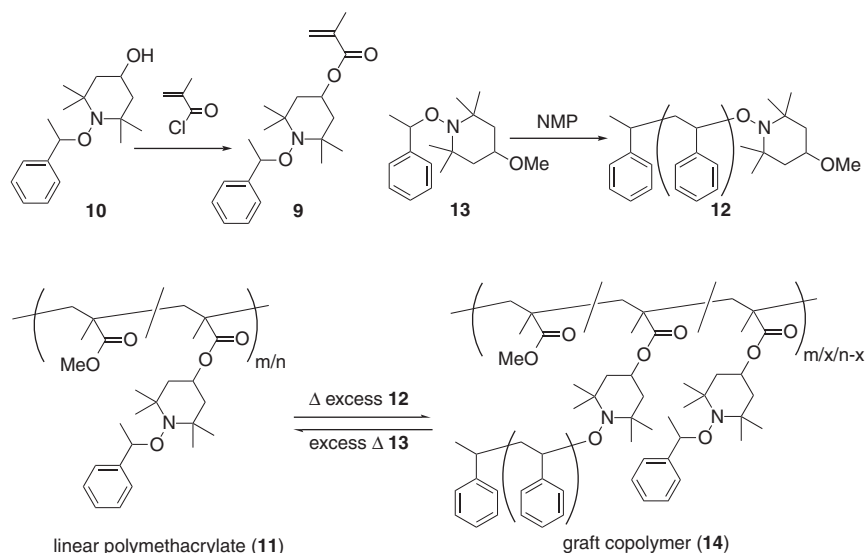
procedure, metal-catalyzed living radical polymerization has been used.<sup>86</sup> For the preparation of well-defined polymers with alkoxyamine units in the side chain, atom-transfer radical polymerization (ATRP)<sup>87–90</sup> was employed. As mentioned above, the TEMPO-based alkoxyamine units do not dissociate below 60 °C. Therefore, the ATRP of methyl methacrylate (MMA) and methacrylic ester **9** was presumed to proceed without dissociation of the alkoxyamine units by conducting the polymerization below 60 °C, affording linear polymers (**11**) incorporating alkoxyamine units in the side chains with a high degree of molecular weight control.<sup>91</sup> Accordingly, the ATRP of a 5:1 mixture of MMA and **9** was conducted in anisole at 50 °C using ethyl 2-bromoisobutyrate as the initiator and Cu(I)Br/sparteine as the catalyst complex. The observed  $M_n$ s increased linearly with conversion and were in good agreement with those calculated, while polydispersities were relatively low ( $M_w/M_n < 1.23$ ). The <sup>1</sup>H NMR spectrum of the resulting polymer revealed that the copolymer composition approximately corresponded to the feed ratio of the monomers (copolymer composition: MMA/**9** = 4.6/1).

On the other hand, the alkoxyamine-terminated polystyrene (**12**) was prepared through the conventional NMP procedure.<sup>56</sup> Polymerization of styrene was conducted in bulk with the unimolecular initiator **13** at 125 °C under argon to give a polystyrene with predictable molecular weight and low polydispersity. The <sup>1</sup>H NMR spectrum of **12a** ( $M_n = 1700$ ,  $M_w/M_n = 1.15$ ) showed that the alkoxyamine units were attached to the chain end of **12a**. A mixture of **11a** ( $M_n = 11\,800$ ,  $M_w/M_n = 1.18$ , MMA/**9** = 4.6/1) and **12a** (5.0 equiv. per alkoxyamine units) was dissolved in anisole and heated at 100 °C under argon (Scheme 10). GPC measurement indicated an increase in the molecular weight of **11a** caused by grafting via the radical crossover reaction of the alkoxyamine units. Confirmation of structure of the separated polymer **14a** ( $M_n = 24\,000$ ,  $M_w/M_n = 1.16$ ) was accomplished by <sup>1</sup>H NMR and IR measurements. By comparing the integral ratio of the signal for the unreacted alkoxyamine units and that for the methyl ester, the degree of grafting was estimated to be 58%. The molecular weight calculated from the <sup>1</sup>H NMR spectrum was found to be 28 200. On the other hand, the  $M_n$  estimated by GPC measurement

was 24 000, which was smaller than that estimated by <sup>1</sup>H NMR. This discrepancy in molecular weights is, however, fully consistent with the proposed structure, as the hydrodynamic volume of a graft polymer is less than that of a comparable linear polymer.<sup>92,93</sup>

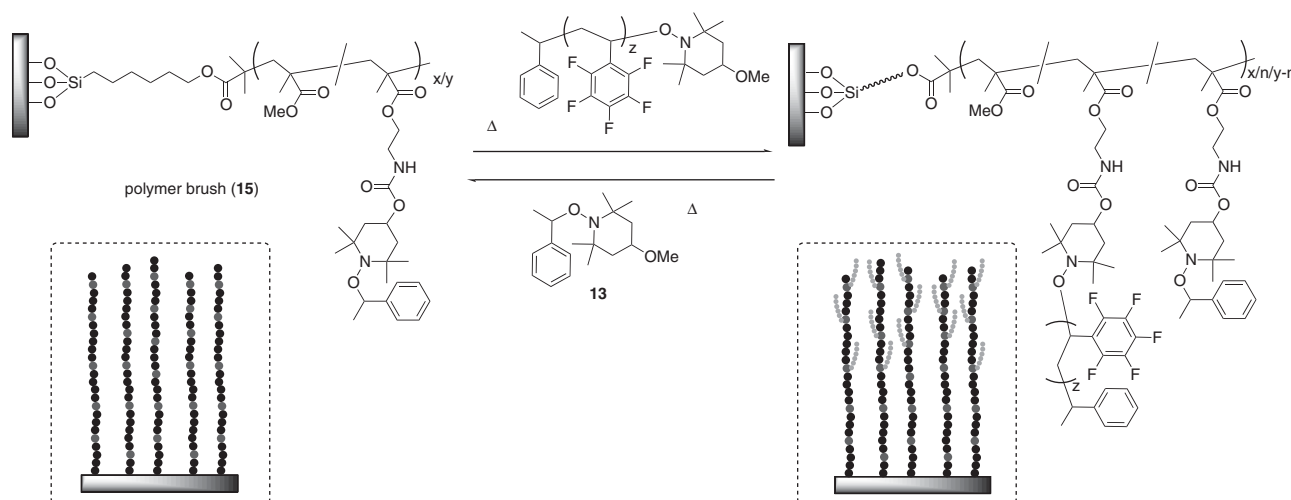
To investigate the reversibility of the reaction system, a mixture of graft copolymer **14** and an excess amount (8.3 equiv. per alkoxyamine unit) of alkoxyamine derivative **13** was dissolved in anisole and heated at 100 °C under argon. As the reaction proceeded, the peak derived from **14** in the GPC profile shifted to the lower molecular weight region. Significantly, the GPC profile corresponding to the eliminated polystyrene ( $M_n = 1700$ ,  $M_w/M_n = 1.15$ ) appeared, and the integral ratio of the profile to the graft polymer increased with increasing reaction time. The de-grafting system reached equilibrium after 30 h. Interestingly, the equilibrium  $M_n$  nearly corresponded to the initial  $M_n$  of **11a**. These results indicated that the grafting system was produced by the exchange reaction of alkoxyamine groups and that the reaction was apparently reversible and under equilibrium control.

Side-chain-type reactions were further applied in a polymer brush to reversibly alternate its surface properties.<sup>94,95</sup> Reactive poly(methacrylate)-based polymer brushes (**15**) with radically exchangeable alkoxyamine units in the side chains were prepared on flat silicon substrates, and their reactivities and surface properties were investigated (Scheme 11). The reactive polymer brushes (**15**) were prepared by surface-initiated ATRP, and the graft density of the brushes was estimated to be  $\sim 0.36$  chains  $\text{nm}^{-2}$ . Radical crossover reactions between the alkoxyamine units in the side chains of the polymer brushes and at the ends of the fluorinated polymer chains were carried out to afford polymer brushes with low surface free energies. In addition, de-grafting of the fluorinated polymer chains was also performed to confirm the reversibility of the radical crossover reactions. The surface properties of the polymer brushes after the grafting and de-grafting processes were characterized by X-ray photoelectron spectroscopy (XPS) and contact angle measurements. The composition calculated from XPS indicated that the reversible grafting of the fluorinated polymer chains had proceeded successfully. The surface wettability of the polymer brushes also changed after the grafting of the fluorinated polymers. Furthermore, after the de-grafting of the fluorinated polymer chains, the peaks

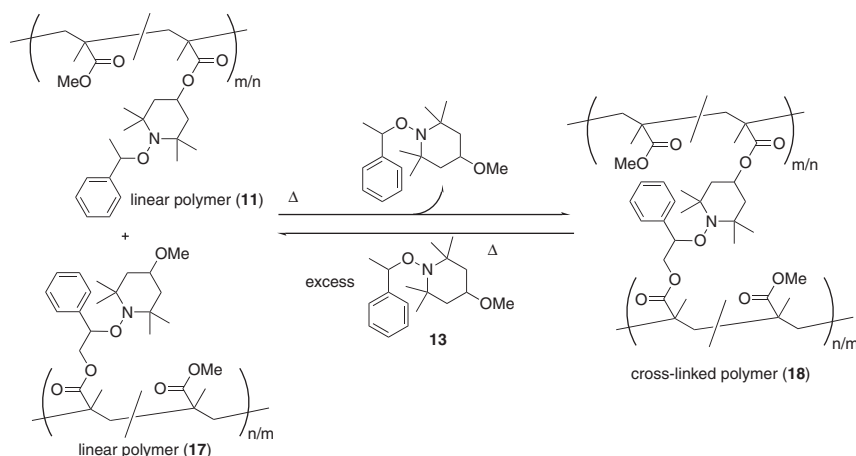


**Scheme 10** Preparation and dynamic grafting reaction of linear polymethacrylate with alkoxyamine units in the side chains and alkoxyamine-terminated polystyrene.





**Scheme 11** Radical crossover reactions between alkoxyamine-containing polymer brushes and alkoxyamine-terminated fluorinated polymer. A full color version of this scheme is available at *Polymer Journal* online.



**Scheme 12** Reversible crosslinking reactions between linear polymethacrylate with complementarily reactive alkoxyamine units in their side chains.

attributed to fluorine atoms completely disappeared from the XPS spectrum and the wettability of the surface returned to that observed before grafting.

## REACTIONS OF POLYMERS CROSSLINKED BY ALKOXYAMINE UNITS

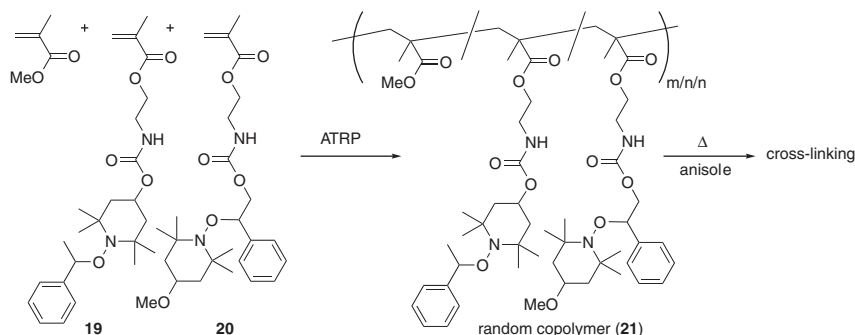
Crosslinked polymers have been widely applied in various fields due to their attractive properties, such as adsorption of solvents<sup>96</sup> and/or other substances,<sup>97</sup> and their useful functionalities.<sup>98–101</sup> Because the crosslinking points of typical crosslinked polymers such as poly(styrene-*co*-divinylbenzene)<sup>102</sup> 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 crosslinked polymers. For example, a thermodynamic covalent crosslinking system based on the radical exchange reaction of alkoxyamine units was constructed, as represented in Scheme 12.<sup>103</sup>

The ATRP of MMA and methacrylic ester **9** or other methacrylic ester **16**, which has been prepared by condensation of alkoxyamine alcohol derivative **2** and methacryloyl chloride, with the alkoxyamine moiety connected at different positions was performed with a

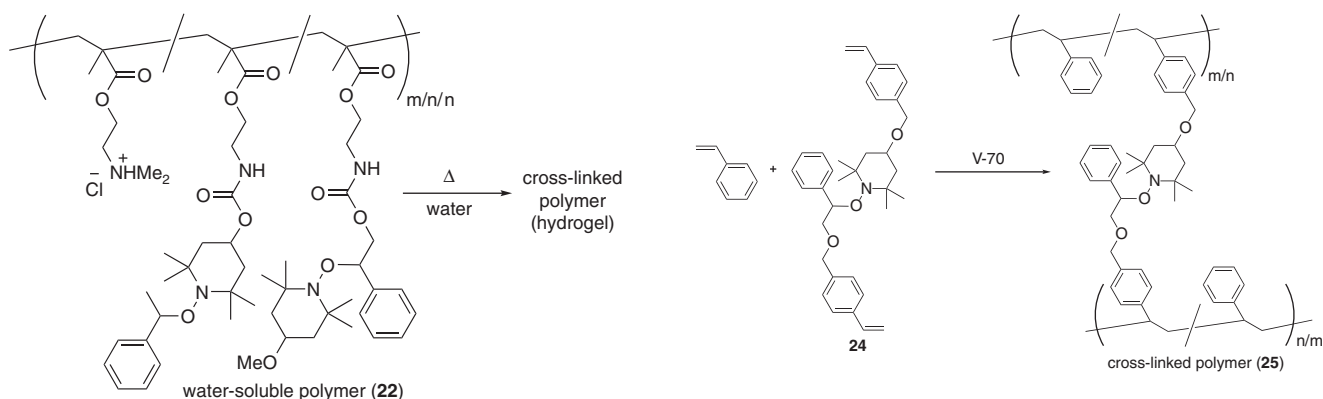
20/1 mixture of MMA and **9** or **16** in anisole at 50 °C, using ethyl 2-bromoisobutyrate as the initiator and Cu(I)Br/sparteine as the catalyst complex. <sup>1</sup>H NMR measurement revealed that the composition of the resulting copolymers **11** and **17** approximately corresponded to the feed ratio of the monomers (copolymer composition: MMA/alkoxyamine-containing monomer = 19/1).

Before the polymer reaction between **11b** ( $M_n = 16\,200$ ,  $M_w/M_n = 1.19$ , MMA/**9** = 19/1) and **17a** ( $M_n = 15\,500$ ,  $M_w/M_n = 1.12$ , MMA/**16** = 19/1), 10 wt% anisole solutions of each polymer were heated independently at 100 °C. In these cases, there was no change in the molecular weight or the molecular weight distribution. Crosslinking reactions were carried out by heating an anisole solution of the mixture of **11b** and **17a** at 100 °C (Scheme 12). After heating, the solution was transformed into a gel at high concentrations. The crosslinking behavior remarkably depended upon the concentration.<sup>103</sup>

The reverse reaction, transformation from gel to solution, was examined through stoichiometric control. The crosslinked polymer **18** was swollen with anisole solution containing an excess amount of alkoxyamine **13** (20 equiv. per alkoxyamine unit) and heated at 100 °C for 48 h. After heating, the sample was transformed from a gel state to a colorless solution. The molecular weight after the



**Scheme 13** Crosslinking reaction of linear polymethacrylate with complementarily reactive alkoxyamine units in the side chains.

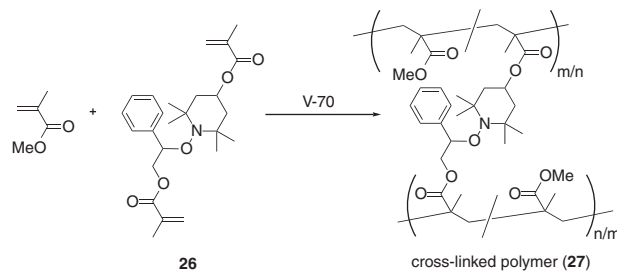


**Scheme 14** Crosslinking reaction of water-soluble linear polymers with complementarily reactive alkoxyamine units in the side chains.

de-crosslinking reaction ( $M_n = 17\,200$ ,  $M_w/M_n = 1.24$ ) almost corresponded to that of a mixture of the starting polymers ( $M_n = 15\,800$ ,  $M_w/M_n = 1.17$ ).

A smarter system was constructed by using random copolymers of methacrylic esters containing complementarily reactive alkoxyamine units (Scheme 13).<sup>104</sup> The random copolymers of MMA and two types of methacrylic esters (19 and 20) with alkoxyamines at different positions were synthesized by the ATRP method. A radical crossover reaction of random copolymer 21 was carried out by heating a degassed anisole solution of 21 at 100 °C at various concentrations. At high concentrations (above 5 wt%), 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, even after 24 h. At 0.5 wt% concentration, the relative molecular weight did not increase, but rather decreased and peak broadening was observed. 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.

The reversible crosslinking of alkoxyamine-containing polymers in aqueous media was also accomplished (Scheme 14).<sup>105</sup> Water-soluble polymers (22) with alkoxyamine units in the side chains were synthesized by the radical copolymerization of 2-(dimethylamino)ethyl methacrylate and methacrylic esters with alkoxyamine units, and the subsequent protonation of the (dimethylamino)ethyl groups by hydrochloric acid. By heating the polymers in water at 100 °C in a closed system, hydrogels were formed by radical exchange reactions. Because radical reactions are tolerant of water, the exchange reactions of the alkoxyamine units in the side

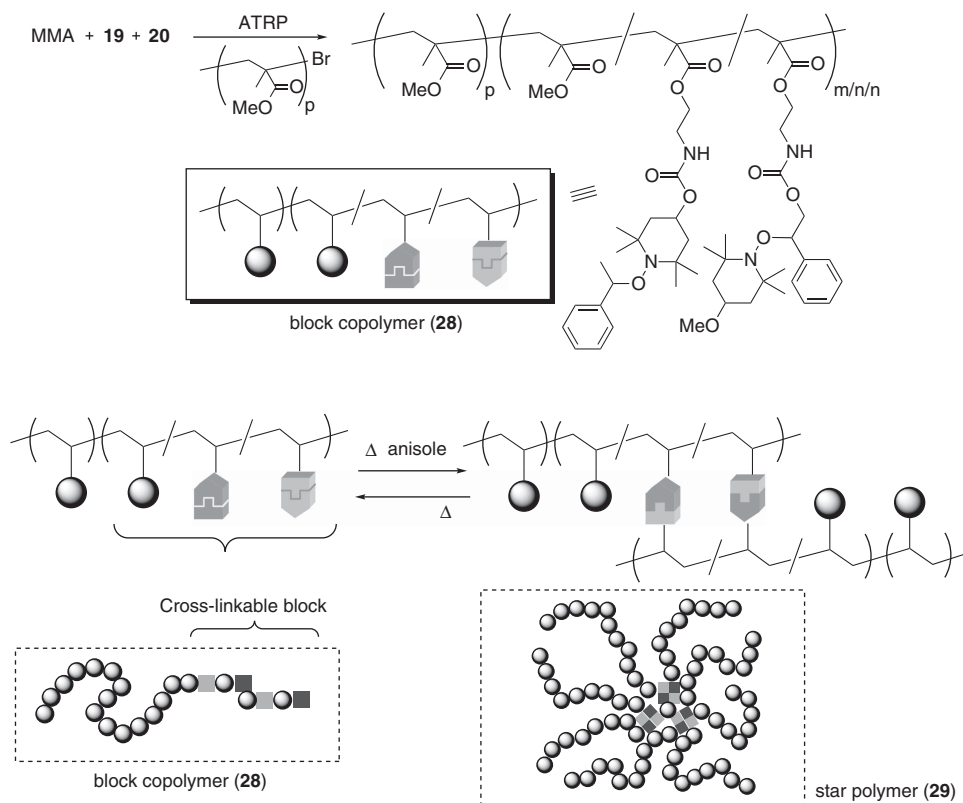


**Scheme 15** Preparation of crosslinked polymers by radical copolymerization of vinyl monomers and bifunctional monomers with an alkoxyamine spacer.

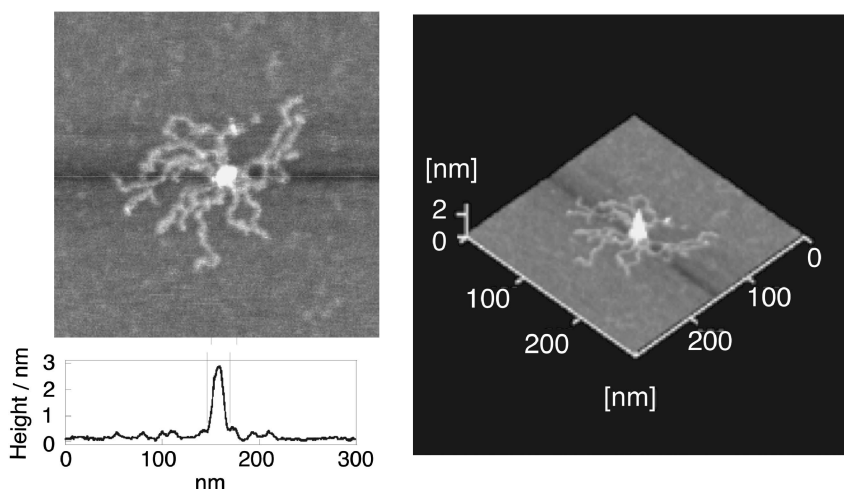
chains caused the crosslinking reaction even in aqueous media. A de-crosslinking reaction was also accomplished by a radical exchange reaction between the crosslinked polymer and an added hydrophilic alkoxyamine compound.

Crosslinked polymers can be synthesized not only by polymer reactions, but also by polymerization using bifunctional monomers as crosslinkers. Crosslinked polymers with alkoxyamine units at the crosslinking points were prepared by radical copolymerization of styrene and alkoxyamine-containing bifunctional monomer (24) (Scheme 15).<sup>106</sup> The copolymerization was carried out in anisole at 40 °C with V-70 as an initiator, which can generate radicals at relatively low temperature, to afford the corresponding polystyrene-type crosslinked polymers (25). Poly(methyl methacrylate) (PMMA)-type crosslinked polymers (27) were also synthesized by radical copolymerization of MMA and alkoxyamine-containing bifunctional monomer (26) (Scheme 15).<sup>107</sup> In both cases, de-crosslinking reactions and monomer insertion reactions were performed. The progress of the reactions was successfully characterized by dynamic viscoelasticity and small angle X-ray scattering measurements to show the reorganizability of the alkoxyamine-containing crosslinked polymers.





**Scheme 16** Reversible formation of star polymers with crosslinked alkoxyamine core.

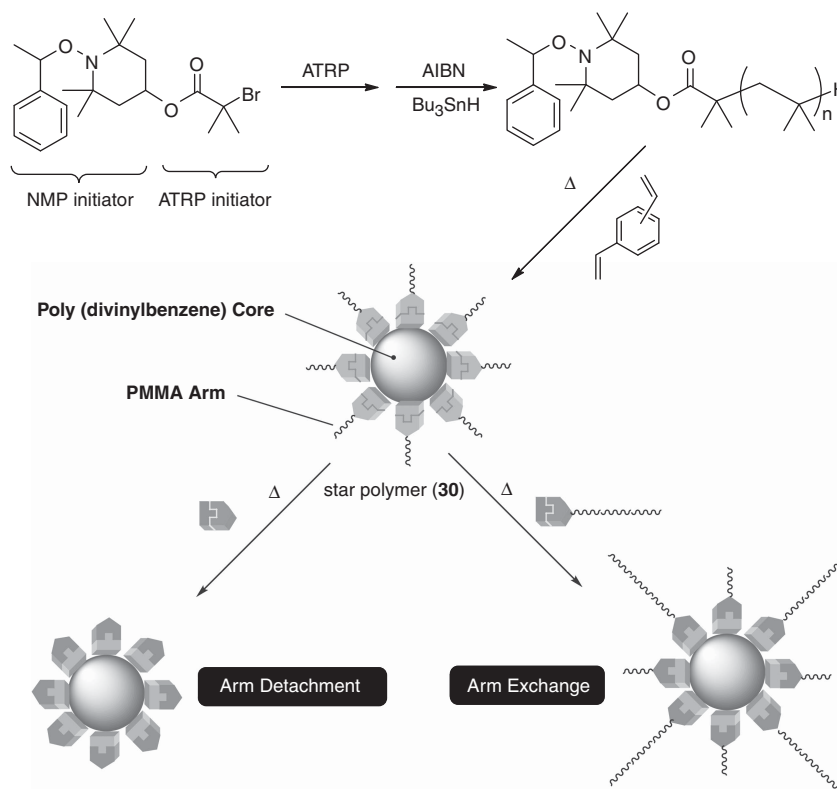


**Figure 5** Scanning force microscopic image of a star polymer molecule on a mica substrate deposited from a solution of **29**.

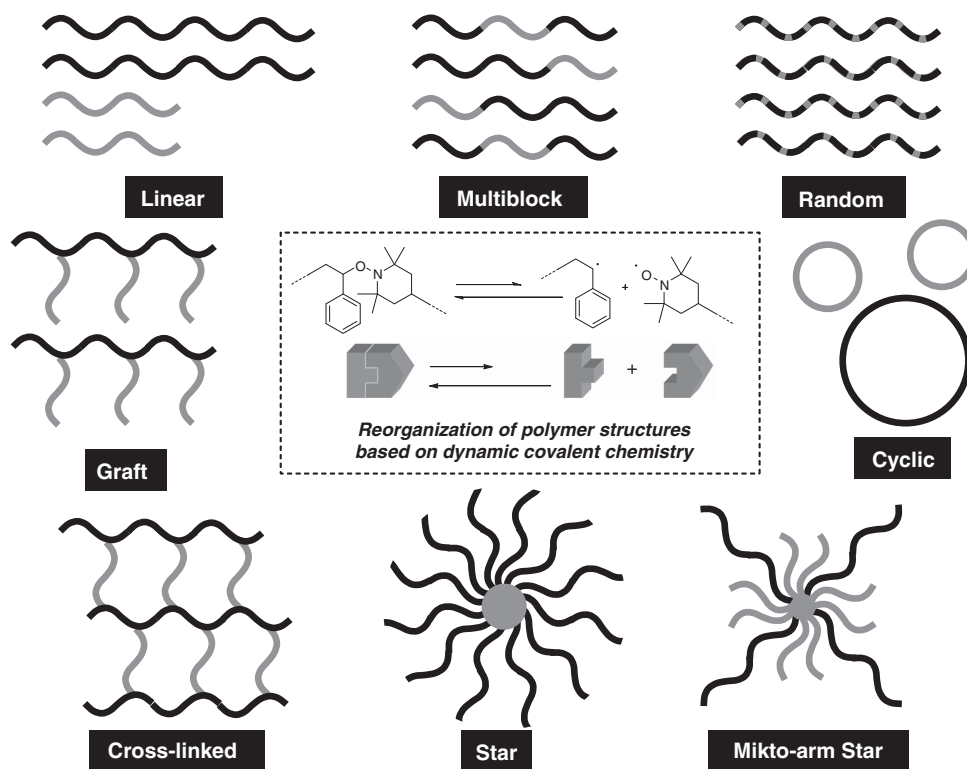
#### SYNTHESIS AND REACTIONS OF STAR POLYMERS WITH CORES CROSSLINKED BY ALKOXYAMINE UNITS

Star polymers were synthesized by radical crossover reactions of diblock copolymers with non-crosslinkable blocks and crosslinkable blocks.<sup>104,108–111</sup> For example, linear diblock copolymers that consisted of PMMA blocks and random copolymer blocks of MMA and methacrylic esters (**19** and **20**) with an alkoxyamine moiety were prepared by ATRP (Scheme 16).<sup>104</sup> By heating the diblock copolymers (**28**) in anisole, a crosslinking reaction occurred as a result of the radical crossover reaction of the alkoxyamine moieties to afford star polymers (**29**). The equilibrium structures of the star polymers were

controlled by the initial concentrations of the diblock copolymers and their compositions and molecular weights. Additionally, by heating the star polymers with excess alkoxyamine, linear polymers were successfully regenerated. The molecular weights and sizes of the star polymers were evaluated by GPC-multiangle laser light scattering and small angle X-ray scattering measurements, respectively. The morphologies of the star polymers were directly observed by scanning force microscopy, which revealed that the star polymers consisted of both a core part and branching molecular chains (Figure 5). By controlling the stoichiometric ratio of the alkoxyamine, the structural conversion of the star polymers to diblock copolymers



**Scheme 17** Arm detachment and arm exchange of alkoxyamine-containing star polymers with a poly(divinylbenzene) core by radical crossover reactions.



**Figure 6** Conceptual representation for reorganization of polymer structures by dynamic covalent exchanges of alkoxyamine units.

also proceeded, as the structures of the compound depend on the equilibrium state. Other dynamic covalent chemistries can also offer reversible transformations between diblock copolymers and star polymers.<sup>112–115</sup>

The formation of asymmetrical (miktoarm) star polymers by the crosslinking reaction of complementarily reactive diblock copolymers was also accomplished.<sup>109,110</sup> Furthermore, the solvent-controlled formation of star polymers via a dynamic covalent exchange reaction of PSt-*b*-PMMA diblock copolymers with alkoxyamine units in the PMMA block was demonstrated. The reaction was carried out in decalin (a good solvent for PSt and a poor solvent for PMMA) and in anisole (a good solvent for both PSt and PMMA).<sup>111</sup>

The reorganization of star polymers, such as arm detachment or arm exchange reactions, was successfully demonstrated.<sup>116</sup> Star polymers were designed and synthesized, and consisted of PMMA arms prepared by ATRP, and cores of poly(divinylbenzene) with alkoxyamine units at their branching points, prepared by NMP using functionalized PMMA as a macroinitiator (Scheme 17). Arm detachment reactions were carried out through radical crossover reactions by heating the star polymers (**30**) with excesses of small-molecule alkoxyamines, whereas arm exchange reactions were performed by heating the star polymers with higher molecular weight alkoxyamine-terminated PMMA.

## SUMMARY

In this review, various types of macromolecular designs and polymer reactions based on dynamic covalent exchanges of alkoxyamine units were described (Figure 6). The structures and constitutions of dynamic covalent polymers were reorganized under appropriate conditions even after polymerization. Main-chain-type, side-chain-type, crosslinked and star-shape alkoxyamine-containing dynamic covalent polymers were systematically introduced. The reorganization was confirmed by spectroscopic, chromatographic, microscopic and scattering methods. Furthermore, polymer reactions by dynamic covalent exchanges of alkoxyamine units were applied in an aqueous system. The dynamic crosslinking nature in aqueous media provides a foundation for a wide range of polymer reactions, and the process can be applied to environmentally benign dynamic materials. Polymer reactions by dynamic covalent exchange are being extended to other dynamic covalent chemistries. The research in this field is expected to expand and open the way to novel dynamic soft materials, such as self-healing polymers and mechano-responsive polymers.

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