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Intelligent Build-Up of Complementarily Reactive Diblock Copolymers via Dynamic Covalent Exchange toward Symmetrical and Miktoarm Star-like Nanogels

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ABSTRACT: The formation of symmetrical and asymmetrical (miktoarm) star-like nanogels by the cross-linking reaction of complementarily reactive diblock copolymers via a radical crossover reaction of alkoxyamine units was successfully accomplished. Four types of diblock copolymers with alkoxyamine units connected at different positions and different chemical compositions were prepared by random copolymerization of methyl methacrylate and methacrylic esters with alkoxyamine from poly(methyl methacrylate) or polystyrene prepolymers using the atom transfer radical polymerization method. Star-like nanogels were formed by dynamic covalent exchange among alkoxyamine units when heating a mixture of two different types of diblock copolymers in anisole. It was revealed that one block of diblock copolymers complementarily reacted; the formation of star-like arms and nanogel parts was revealed by small-angle X-ray scattering (SAXS) measurements and scanning force microscopic (SFM) observations. Furthermore, miktoarm star-like nanogels with different molecular weights and chemically asymmetrical chains were also formed by using several types of diblock copolymers. At the same time, structural transformation from star-like nanogels to diblock copolymers was successfully accomplished by dynamic covalent exchange among alkoxyamine units in the star-like nanogels and excess added alkoxyamine compounds. The molecular weights and sizes of the diblock copolymers and star-like nanogels were evaluated by gel permeation chromatography−multiangle light scattering (GPC−MALS), quasi elastic light scattering (QELS), and SAXS measurements, and their molecular conformations were estimated from SAXS profiles and SFM images.

Introduction

Molecular assemblies have been extensively investigated and several functions that cannot be obtained from the individual constituent molecules have been realized.[1] In developing fields such as host−guest chemistry, DNA−RNA, and self-assembly, the constituent molecules or units play complementary roles, with the desired compound being formed after the several components are brought together, and the configurations of the desired molecules are controlled by cleverly designing the constituent molecules. Additionally, in macromolecular science, the formation of molecular assemblies has been achieved by controlling intermolecular attraction and hydrophobic interaction. It should be noted that the development of controlled polymerization[2] such as atom transfer radical polymerization (ATRP) makes it possible to synthesize well-defined polymers such as those with uniform molecular weights and designed chemical compositions, and to discuss the effect of polymer composition on macromolecular aggregation. For example, diblock copolymers with segments that respond to specific stimuli such as pH,[3] heat,[4] and ion strength[5] can form highly ordered structures such as micelles and core−shell particles. Interestingly, the size of the final product is intelligently determined according to the polymer design at the synthetic stage, and the interconversion between the constituent polymers and macromolecular aggregations is controlled by the environment.

On the other hand, covalent bonds with the ability to dissociate into their units in response to a specific external stimulus and then to reform bonds such as disulfide bonds,[6] ester bonds,[7] and carbon−carbon double bonds[8] have attracted much attention. Rowan et al. proposed the concept of dynamic covalent (bond) chemistry (DCC)[9] to purposely incorporate these bonds into compounds and control the structures of molecular assemblies based on covalent bond systems. Dynamic covalent chemistry enables the compounds not only to behave typical organic compounds but also to form their molecular architecture under thermodynamic control in response to specific stimuli, similarly to supramolecular systems.[9] These systems have been used for many molecular systems, such as dynamers,[10] dendrimers,[11] macrocycles,[12] graft polymers,[13] and cross-linking systems.[14]

The authors have applied dynamic covalent chemistry to polymer reactions,[15] especially using alkoxyamine units, which are adducts of styryl radicals and 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) radicals, and are well-known as initiators for living radical polymerization.[16] Although alkoxyamine units behave as typical covalent bonds under normal conditions, the central C−O bonds can radically and reversibly dissociate when heated to temperatures over 60 °C, and their units can be exchanged between alkoxyamine units. By incorporating alkoxyamine units into the main chains or side chains of polymers, several polymer architectures have been synthesized, such as

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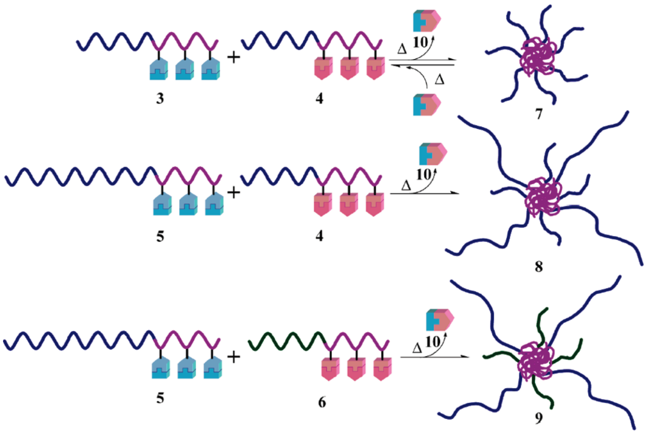


Figure 1. Schematic representation of symmetrical and miktoarm star-like nanogels formed via the dynamic covalent exchange reaction of several types of complementarily reactive diblock copolymers.

hybrid polymers,[17] graft copolymers,[18] block copolymers,[19] and cyclic polymers.[20] Additionally, in a mixture of two types of linear polymers with alkoxyamine units connected at different points in their side chains, it was found that macroscopic gels were formed as a result of the dynamic covalent exchange reaction of the alkoxyamine units, and linear polymers were reversibly regenerated.[21] Furthermore, we previously reported the reversible formation of star-like nanogels,[22] which are defined as internally cross-linked single macromolecules with dimensions similar to the parent, linear polymer chains,[23] by designing diblock copolymers with alkoxyamine units in their side chains. In the case of two types of complementarily reactive diblock copolymers, the molecular weight of the star-like nanogels depended on the mixing ratio and concentrations of the diblock copolymers.[24,25]

This paper discusses the formation of symmetrical and asymmetrical (miktoarm) star-like nanogels using complementarily reactive diblock copolymers, as shown in Figure 1. The effects of the primary structures of the diblock copolymers on the molecular architectures of the formed star-like nanogels were systematically investigated. Furthermore, the structural transformation from star-like nanogels to diblock copolymers was also accomplished, because the cross-linking points consist of alkoxyamine units, which can behave as dynamic covalent bond units.

Experimental Section

Materials. 4-(2′-Methacryloyloxyethylcarbamyl)-1-((1′-phenylethyl)oxy)-2,2,6,6-tetramethylpiperidine (**1**),[22] 4-Methoxy-1-((2′-(2″-Methacryloyloxyethylcarbamyl)-1′-phenylethyl)oxy)-2,2,6,6-tetramethylpiperidine (**2**),[22] and 4-methoxy-1-((1′-phenylethyl)oxy)-2,2,6,6-tetramethylpiperidine (**10**)[18] were prepared and purified as previously reported. (−)-Sparteine (Sp, 99%) was purchased from Nacalai tesque and used without further purification. Ethyl 2-bromoisobuthylate (2-(EiB)Br, 98%) was purchased from Tokyo Chemical Industry Co. and used without further purification. Methyl methacrylate (MMA, 98%), styrene (98%), and anisole (99+%) were purchased from Wako Pure Chemical Industries and purified by distillation under reduced pressure over calcium hydride. Cu(I)Br (99+%) was purchased from Wako Pure Chemical Industries and purified by stirring in acetic acid (Wako Pure Chemical Industries, 99+%), washing with ethanol (Wako Pure Chemical Industries, 99+%), and then drying in vacuo. All of the other reagents were purchased from commercial sources and used as received.

Measurements. ^{1}H (300 MHz) NMR spectroscopic measurements were carried out at 25 °C with a JEOL JNM-AL300 spectrometer using tetramethylsilane (TMS) as an internal standard in chloroform-*d* ($CDCl_3$).

The relative number-average molecular weights (M_n) and molecular weight distributions (M_w/M_n) of the linear polymers were estimated by gel permeation chromatographic (GPC) analysis. GPC measurements were carried out at 40 °C on a TOSOH HLC-8220 GPC system equipped with a guard column (TOSOH TSK guard column Super H-L), three columns (TOSOH TSK gel SuperH 6000, 4000, and 2500), and a UV−vis detector. Tetrahydrofuran (THF) was used as the eluent at a flow rate of 0.6 mL min^{-1}. Polystyrene (PSt) standards (M_n = 1060−1 090 000; M_w/M_n = 1.02−1.08) were used to calibrate the GPC system.

The absolute weight-average molecular weight ($M_{w,\ MALS}$) and radius of gyration ($R_{g,\ MALS}$) of each polymers were evaluated by gel permeation chromatography−multiangle light scattering (GPC−MALS) in THF at 40 °C on a Dawn EOS instrument (Wyatt Technology; Ga−As laser; λ = 690 nm). The specific refractive index increment ($\partial n/\partial c$), which is necessary for the analysis of GPC−MALS, was measured with an Otsuka Electric DRM-3000 at 40 °C. The wavelength of the irradiation light λ was 633 nm. The measured $\partial n/\partial c$ of the star-like nanogels in THF was 0.0895 cm^3 g^{-1} and 0.0876 cm^3 g^{-1}, corresponding to **7** and **9**, respectively.

The hydrodynamic radius (R_h) of each star-like nanogel was evaluated by quasi elastic light scattering (QELS) measurements using a Wyatt QELS. The four concentrations of polymer solutions in acetone were measured, and the diffusion coefficients were determined by zero extrapolation in concentration to obtain R_h values by the Stokes−Einstein formula.

Small-angle X-ray scattering (SAXS) was carried out at the BL40B2 beamline of SPring-8 using an incident X-ray with a wavelength λ = 0.150 nm. Scattered X-rays were detected using a 300 mm ×300 mm imaging plate with a resolution of 0.1 mm/pixel and a 2162 mm sample-to-detector distance calibrated by the average of 11 peaks of collagen. The measured samples were four concentrations of star-like nanogels in acetone contained in 2 mm diameter glass capillaries. The scattering vector (q) was defined as $4\pi(\sin\theta)/\lambda$. The scattering intensities of polymers ($\Delta I(q)$) were calculated by subtracting the scattering intensities of solvent from that of solution adjusted through transmittance, and extrapolating in zero concentration of four samples. The radius of gyration (R_g) values of the polymers were evaluated by the initial slopes and intercepts of Berry plots ($(c/\Delta I(q))^{1/2}$ vs q^2).

The morphologies of the star-like nanogels on mica were observed in air at room temperature by a SFM (SII Nanotechnology Inc., SPA 400) in a dynamic force microscopic (DFM) mode. A 20 μm × 20 μm scanner and a diamondlike carbon (DLC) tip on a cantilever (resonance frequency ≈150 kHz, spring constant 2.5−10 N m^{-1}) were used with an amplitude set point of ca. 0.8. The samples for the SFM observations were prepared by spin-casting (2000 rpm, 20 s) of 1 × 10^{-4} wt % chloroform solutions of the star-like nanogels onto freshly cleaved mica.

Poly(methyl methacrylate) (PMMA) and Polystyrene (PSt) Prepolymers. PMMA and PSt prepolymers with bromine atoms at the end were synthesized by reference to the ATRP methods.[2]

PMMA-*b*-poly(MMA-*co*-1) (3). In a typical run, Cu(I)Br (3.2 mg, 0.022 mmol) was charged into a test tube containing a magnetic stirring bar. The air was then removed by evacuation and it was backfilled with argon three times. Then, MMA (0.428 mL, 4.00 mmol), methacrylic ester with alkoxyamine moiety **1** (0.173 g, 0.400 mmol), anisole (0.63 mL), and Sp (10.3 mg, 0.0440 mmol) were added. The mixture was degassed by five freeze−pump−thaw cycles, the test tube was immersed in an oil bath at 50 °C under argon, and the PMMA prepolymer (0.245 g, M_n = 22 300, M_w/M_n = 1.13) dissolved in degassed anisole (0.95 mL) was added. After 3.5 h, the reaction mixture was quenched rapidly to 0 °C and diluted with acetone, and the solution was filtered through an Al_2O_3 column. The filtrate was concentrated and poured into excess methanol. The precipitation was then collected and dried in vacuo to give the purified polymer (242.1 mg) as a white powder (M_n = 33 500, M_w/M_n = 1.07).

PMMA-*b*-poly(MMA-*co*-2) (4). Diblock copolymer **4** was synthesized by the same procedure as **3** by using alkoxyamine monomer **2**. After precipitation, purified polymer (246.9 mg) was obtained as a white powder (M_n = 34 500, M_w/M_n = 1.08).

PSt-*b*-poly(MMA-*co*-1) (6). Diblock copolymer **6** was prepared by the same procedure as **3** by using PSt prepolymer (M_n = 18 800, M_w/M_n = 1.18). After passing through an Al_2O_3 column, the polymer solution was purified by reprecipitation into hexane/cyclohexane (= 1/4, v/v) five times to remove any unreacted PSt prepolymer, to give a white powder (M_n = 31 600, M_w/M_n = 1.28).

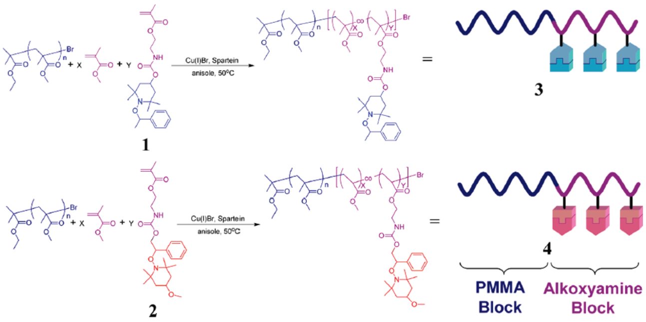
Cross-Linking Reaction. In a typical run, a 10 wt % anisole solution of diblock copolymers **3** and **4** was charged into a glass tube, degassed by seven freeze−pump−thaw cycles, and sealed off under vacuum. The solution was heated at 100 °C for 24 h. No macroscopic gelation was observed, and the reaction mixture was precipitated from hexane to afford core cross-linked polymer (star-like nanogel) **7** in a 95% yield.

De-Cross-Linking Reaction. In a typical run, star-like nanogel **7** (9 mg) was dissolved in anisole solution (10 wt %) with an excess of alkoxyamine (16.2 mg, 0.0556 mmol, 40 equiv/alkoxyamine units in star-like nanogel) and charged into a glass tube. The solution was degassed by seven freeze−pump−thaw cycles, sealed off under vacuum, and heated at 100 °C for 48 h.

Results and Discussion

Design and Synthesis of Complementarily Reactive Random and Diblock Copolymers with Alkoxyamine. Four types of complementarily reactive diblock copolymers (**3**−**6**) with alkoxyamine units in their side chains were designed and synthesized as initial polymers. Two types of methacrylic esters with alkoxyamine moieties connected at different positions by polar urethane groups (**1** and **2**), which were expected to aggregate in cross-linking reaction, were separately polymerized with MMA from PMMA or PSt prepolymers with bromine atoms in their chain ends using ATRP techniques. The polymerizations were performed under 50 °C conditions, because the central C−O bonds in the alkoxyamine units are thermally exchangeable above 60 °C.

Scheme 1. Preparation of Diblock Copolymers 3 and 4 by Random Copolymerization of MMA and 1 or 2 from PMMA Prepolymer with a Bromine Atom at the Chain End Using ATRP Methods



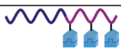
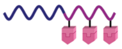
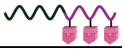
In a model polymerization, the random copolymerization of MMA and **1** was performed using the ATRP technique. The ATRP of a 10/1 mixture of MMA/**1** was carried out in anisole at 50 °C using 2-(EiB)Br as an initiator and Cu(I)Br/Sp as the catalyst complex. The polymerization was well controlled, and a copolymer with a relatively low molecular weight distribution (M_w/M_n < 1.2) was obtained. Using the ^{1}H NMR spectrum, the copolymerization ratio of the polymer was calculated as [MMA]/[**1**] = 10.2/1, indicating that the copolymerization proceeded according to the prepared monomer ratio and the designed polymer structure was obtained. In a complementarily reactive system, it is very important that the prepared monomer ratio of $[\mathrm{MMA}]_0/[\mathbf{1}]_0$ is equal to the copolymerization ratio of the random copolymer, because the structure of the copolymer, as well as the number of alkoxyamines in the polymer, should be specified.

Diblock copolymers consisting of PMMA or PSt blocks and alkoxyamine blocks were synthesized by the random copolymerization of MMA and methacrylic ester with alkoxyamine moieties from PMMA or PSt prepolymers using the ATRP methods, as shown in Scheme 1. PMMA and PSt prepolymers with bromine atoms at their ends were prepared by ATRP using alkyl bromide and the Cu(I)Br/Sp system. The random copolymerization of MMA and **1** or **2** to prepare block copolymers was carried out in anisole at 50 °C using PMMA or PSt prepolymer and the Cu(I)Br/Sp system, and diblock copolymers with relatively low polydispersities (M_w/M_n < 1.3) were obtained.

Table 1 summarizes the M_n and M_w/M_n values of four kinds of diblock copolymers. Diblock copolymers **3** and **4** have almost identical degrees of polymerization, with the only difference being the direction of the alkoxyamine units. In addition, compared with diblock copolymer **3**, diblock copolymer **5** was designed and synthesized to have a higher molecular weight PMMA block and the same alkoxyamine block. Diblock copolymer **6** has a polystyrene block instead of a PMMA block, although its other structures are almost the same as diblock copolymer **4**.

Cross-Linking Reaction of 3 and 4. As we have previously reported,[21,22,24,25] cross-linking reactions via the dynamic covalent exchange reaction of alkoxyamine units were carried out by heating the polymers with alkoxyamine units in their side chains. First, as a fundamental reaction system, a reaction was attempted between two types of diblock copolymers, **3** and **4**, which have almost the same degree of polymerization but with the opposite directions for their alkoxyamine units. The dynamic covalent exchange reaction was carried out by heating an anisole solution with a mixture of **3** and **4** at 100 °C. After heating, no gelation of the system was observed, even at high concentrations such as 15 wt %. Due to the existence of the PMMA block, excess gelation was

Table 1. M_n and M_w/M_n of Complementarily Reactive Diblock Copolymers 3−6 Prepared by ATRP Methods with Different Alkoxyamine Unit Directions, Molecular Weights, and Chemical Compositions

	PMMA prepolymer		PSt prepolymer		Diblock Copolymer				
	M_n	M_w/M_n	M_n	M_w/M_n	M_n	M_w/M_n	$[\mathrm{MMA}]_0/[\mathbf{1}]_0$	$[\mathrm{MMA}]_0/[\mathbf{2}]_0$	Structure Model
3	22 300	1.11	-		33 500	1.08	10/1	-	
4	22 300	1.11	-		34 500	1.07	-	10/1	
5	54 800	1.15	-		66 900	1.13	10/1	-	
6	-		18 800	1.18	31 600	1.28	-	10/1	

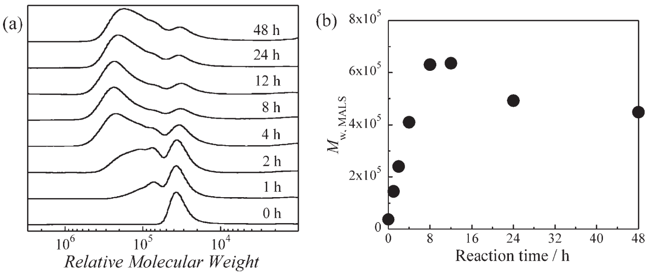


Figure 2. Reaction time dependence of (a) GPC curves, and (b) $M_{\mathrm{w,\,MALS}}$ of the cross-linking products (**7**) after heating the mixture of **3** and **4** ([**3**]/[**4**] = 5/5 (w/w)) in anisole (10 wt %) at 100 °C.

depressed and the cross-linking reaction occurred, not on a macroscale, but on a nanoscale. Indeed, no detectable red coloration, corresponding to the generation of TEMPO derivatives by a carbon–carbon coupling reaction of the styryl radical, was observed. These results indicated that the dynamic covalent exchange reaction proceeded with few detectable side reactions in the present system and this observation can be explained by the persistent radical effect (PRE).[26] 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. In the case of the crossover reaction of alkoxyamine derivatives, nitroxide radical is persistent and styryl radical is transient.

Figure 2a shows the time variation of the GPC curves of the polymers after heating a mixture of **3** and **4** ([**3**]/[**4**] = 5/5 (w/w)) in anisole (10 wt %) at 100 °C. As the reaction time passed, the molecular weight increased, with a maximum at 8 h, and the peaks for the diblock copolymer gradually decreased. After that, the peaks gradually broadened and became practically constant at 24 h. From the GPC curves, conversion = 79% was estimated. The absolute molecular weight (M_w) was determined by GPC-MALS measurements, because the retention time of GPC is affected, not only by the molecular weight but also by the cross-linked and/or branched structure, and a calibration curve for linear polymers will not give the real molecular weight for cross-linked polymers. Figure 2b shows the reaction time dependence of M_w for polymers prepared under the same conditions as above with the diblock copolymer components removed by fractionation using a preparative HPLC system with GPC columns. Similarly to the GPC measurement results, M_w increased until 12 h, and then decreased gradually. Indeed, the M_w of MALS was much larger than that of GPC (for examples, after 24 h, $M_{\mathrm{w,\,MALS}} = 493\,000$ and $M_{\mathrm{w,\,GPC}} = 96\,200$), indicating the formation of highly branched and/or cross-linked polymers corresponding to star polymers and nanogels.

In order to obtain further information about the star-like nanogels, the sizes (R_g and R_h) in acetone solutions were evaluated by SAXS and QELS measurements, respectively. Figure 3 summarizes the R_g and R_h values of the star-like nanogels for several reaction times. As with the M_w results, R_g and R_h increased until 8 h, and then gradually decreased. Indeed, the ρ ($=R_g/R_h$) parameter, which represents the structure of the polymers and decreases by branching, of the star-like nanogels could be obtained so as to discuss their structures. In the case of a mixture of diblock copolymers **3** and **4**, $\rho = 1.55$ was estimated, which was well related to the Gaussian chain model. In contrast, in the case of the star-like nanogels, ρ gradually decreased with reaction time, and approached 0.94 at 24 h, supporting the assumption that star-like nanogels formed higher branched structures with reaction time.

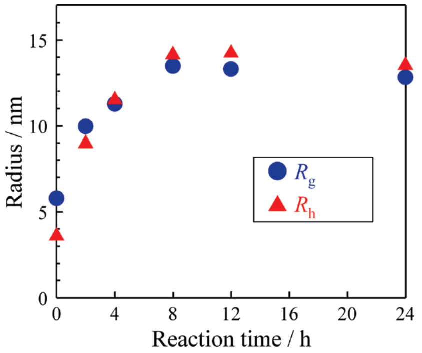


Figure 3. Time dependence of R_g and R_h in acetone of the cross-linking product (**7**) prepared by heating a mixture of **3** and **4** ([**3**]/[**4**] = 5/5 (w/w)) in anisole (10 wt %) at 100 °C.

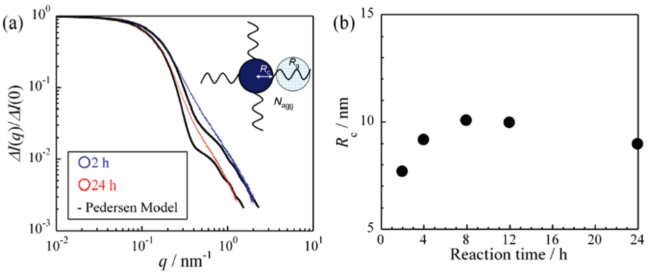


Figure 4. (a) Scattering profiles of star-like nanogel **7** and their fitting curves described by eq 1 and (b) radius of rigid sphere (core) for several reaction times.

In the SAXS measurements, a larger range of q values makes clear the smaller structure of molecules or structure of polymers in solution, which can provide important information about macromolecular architectures. Figure 4a shows the SAXS profiles of star-like nanogels for several reaction times, along with their fitting curves by the scattering function of the Pedersen model,[27] which describes a rigid sphere (core) and several connecting Gaussian chains without interchain interaction, as follows.

$$\begin{aligned} F_{Pedersen}(q) &= N_{agg}{}^2 \rho_{core}{}^2 F_{core}(q, R_c) \\ &+ N_{agg} \rho_{chain}{}^2 F_{chain}(q, R_{g,\,chain}) \\ &+ 2N_{agg}{}^2 \rho_{core} \rho_{chain} S_{core-chain}(q, R_c, R_{g,\,chain}) \\ &+ N_{agg}(N_{agg}-1) \rho_{chain}{}^2 S_{chain-chain}(q, R_c, R_{g,\,chain}) \qquad (1) \end{aligned}$$

where N_{agg} is the chain aggregation number, ρ is the electron density, R_c is the radius of the rigid sphere (core), and $R_{g,\mathrm{chain}}$ is the radius of gyration of the Gaussian chain. Furthermore, F_{core} and F_{chain} are form factors of the core and chain, and $S_{\mathrm{core-chain}}$ and $S_{\mathrm{chain-chain}}$ are structure factors between the core and chain, and chain and chain, respectively (refer to details of equations in original papers[27]). Because N_{agg} ($=M_{\mathrm{w,\ star\text{-}like\ nanogel}}/M_{\mathrm{w,\ diblock\ copolymer}}$), ρ, and $R_{g,\mathrm{chain}}$ (radius of gyration of PMMA) could be estimated by the theoretical and observed data, only R_c was treated as a fitting parameter. The disagreement of fitting curves in the range of $q = 0.3-0.8\ \mathrm{nm}^{-1}$ was derived from their polydispersity. Figure 4b represents the time variation of the R_c of **7**. Along with the M_w and size values, the trend that R_c increased until 8 h and then decreased gradually could be confirmed. In the case of the 24 h, the R_c corresponding to the sizes of the gel parts was estimated to be about 9 nm.

This molecular weight and size information for time variations makes clear the formation process of star-like

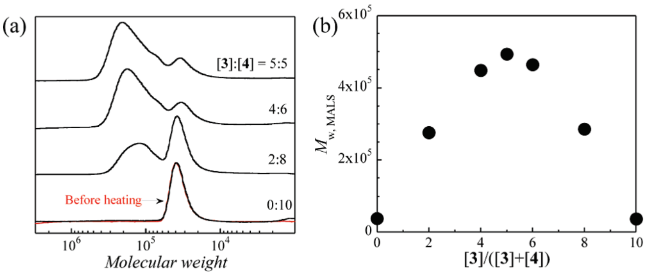


Figure 5. Mixing ratio dependence of (a) GPC curves before (red line) and after heating (black lines) and (b) M_w of star-like nanogel **7** prepared by heating several mixing ratios of the diblock copolymers **3** and **4** in anisole (10 wt %) for 24 h at 100 °C.

nanogels as three stages. In the first stage, the dynamic covalent exchange reaction of the alkoxyamine units between the diblock copolymers makes the linear polymer form micellelike assembled polymers. Next, excess cross-linking reaction and the formation of larger assembled polymer were depressed by the effect of the PMMA blocks, and an intramolecular cross-linking reaction in the assembled polymer proceeded preferentially to form the nanosized cross-linking structures. Finally, due to the decrease in the size and increase in the steric repulsion of the PMMA block, some diblock copolymers were eliminated. From the viewpoint of above process, it was obvious that star-like nanogels were formed under thermodynamic control, because the cross-linking points of the star-like nanogels consisted of alkoxyamine units as dynamic covalent units.

In the present complementarily reactive system, the objective substance was obtained only when two components existed together. To investigate the complementarity of two types of diblock copolymers, model reactions under several mixing ratio conditions were carried out. Figure 5a shows the GPC curves of reaction products after heating mixtures of diblock copolymers **3** and **4** at different mixing ratios in anisole (10 wt %) for 24 h. In the case of heating only diblock copolymer **4** ([**3**]/[**4**] = 0/10), it was hard to observe any change in the GPC curve, indicating that the cross-linking reaction did not occur. However, increases in the molecular weight and decreases in the diblock copolymer peaks were observed in the other mixing conditions. Additionally, the mixing ratio dependence of the molecular weight ($M_{w,\ MALS}$) was estimated, showing symmetric bell-shaped plots, as seen in Figure 5b. Under an equal mixing ratio condition ([**3**]/[**4**] = 5/5, w/w), M_w showed a maximum value, which means larger star-like nanogels were formed. This is because there was almost same number of alkoxyamine units in the two types of diblock copolymers. In other words, the cross-linking reaction was the result of the dynamic covalent exchange reaction of alkoxyamine units in diblock copolymers, and it proceeded as a complementarily reactive system.

In order to investigate the effect of mixing ratio of the diblock copolymers on the size of star-like nanogels, the sizes of the star-like nanogels were estimated by SAXS and QELS measurements. Figure 6 summarizes the R_g, R_h, and R_c values of star-like nanogel **7** for several mixing ratios of diblock copolymers **3** and **4**. As with the molecular weight results, the plots of R_g and R_h show bell-shapes, supporting the complementarily reactive system of diblock copolymers **3** and **4**. Interestingly, the core sizes (R_c) also indicated symmetric plots. It is proposed that the size of a star-like nanogel can be controlled by its mixing ratio.

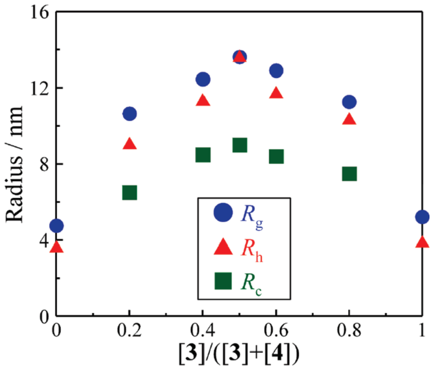


Figure 6. Mixing ratio dependence of R_g, R_h, and R_c of star-like nanogel **7** prepared by heating several mixing ratios of diblock copolymers **3** and **4** in anisole (10 wt %) for 24 h at 100 °C.

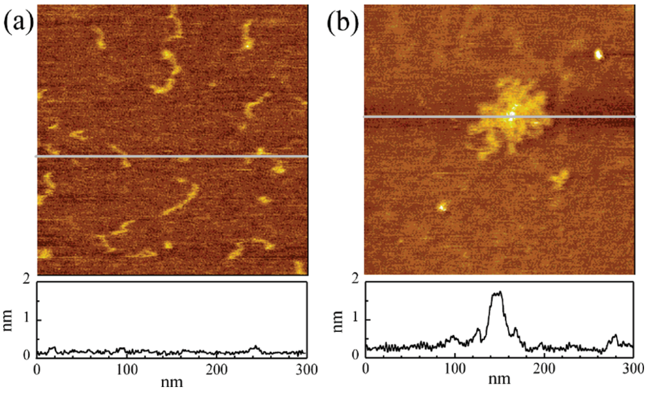


Figure 7. SFM images of post polymers after heating (a) only diblock copolymer **4** ([**3**]:[**4**] = 0:10), and (b) a mixture of diblock copolymers **3** and **4** ([**3**]:[**4**] = 5:5) in anisole (10 wt %) at 100 °C for 24 h.

Recently, SFM observation has become one of the most powerful tools for revealing the structures of molecular assemblies and/or macromolecular architectures.[28] Figure 7 shows SFM images of polymers on mica, using sharp cantilevers, after heating different mixing ratios of the diblock copolymers ([**3**]:[**4**] = (a) 0:10, (b) 5:5). In the case of heating one type of diblock copolymer, simply several molecular chains corresponding to the diblock copolymer were observed. Under a mixing condition, however, macromolecular assemblies consisting of a core and several polymer chains could be confirmed. The core part was estimated to be about 1.5 nm in height and about 25 nm in diameter, and it must have corresponded to a nanogel part. In the SAXS measurement in acetone solution, it was estimated that R_c = 9.0 nm, corresponding to a diameter of 18 nm, and the core shape on mica was more flattened. Furthermore, several polymer chains connected to a core were clearly observed and their lengths were almost the same. These data strongly supported the expectation that star-like nanogels were formed in the present complementary system.

Cross-Linking Reaction of 5 and 4. In the present complimentarily reactive system, it was expected that various types of assemblies could be built up, with different structures and/or functionalities. In star polymer chemistry, asymmetrical (miktoarm) star polymers, which have different kinds of arms (molecular weights and/or chemical asymmetrical chains) in one star polymer, have been synthesized.[29] Therefore, the formation of an asymmetrical (miktoarm) star-like nanogel **8** with different molecular weight arms was attempted via the dynamic covalent exchange reaction of diblock copolymers **5** and **4** with different molecular weights of PMMA blocks. Figure 8a shows the GPC profiles of the polymers after heating the mixture of diblock copolymers **5**

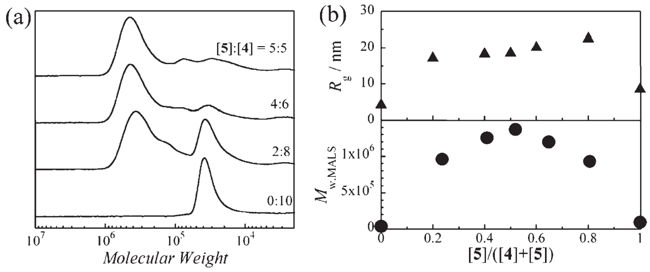


Figure 8. (a) GPC curves, and (b) $M_{w,\ MALS}$ and R_g of post polymers after heating mixtures of diblock copolymers **5** and **4** in anisole (10 wt %) at 100 °C for 24 h in several mixing ratios.

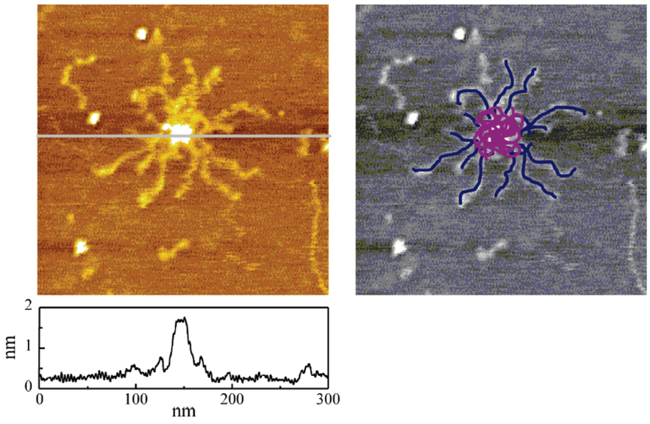


Figure 9. SFM image of star-like nanogel **8** prepared by heating an equal mixing ratio of diblock copolymers ([**5**]:[**4**] = 5:5), and their polymer chain image.

and **4**. When the ratio of **5** to **4** was increased, the top peaks increased toward higher molecular weights, and the diblock copolymer peaks decreased. Moreover, the molecular weights ($M_{w,\ MALS}$) showed bell-shaped plots, as seen in Figure 8b. These data show that the two types of diblock copolymers, **5** and **4**, reacted in a complementary system.[25] However, the sizes of the star-like nanogels (R_g) indicated no symmetrical plots. This is because the radius of gyration of the star-like nanogels increased with the ratio of diblock copolymer **5** to **4**, with higher molecular weight as well as a larger radius of gyration of the PMMA block.

Figure 9 shows an SFM image of star-like nanogel **8** prepared under an equal mixing ratio condition ([**5**]:[**4**] = 5:5). It was clearly observed that star-like nanogel **8** possessed two different lengths of polymer chains (long chains and short chains). The long chains and short chains must be derived from PMMA blocks of **5** and **4**, respectively. In the SFM images, the ratio of long chain increased with increasing the mixing ratio of **5**, and the structure of miktoarm star-like nanogels could be controlled by their mixing ratio of diblock copolymers. Interestingly, all of the star-like nanogels necessarily had two different types of molecular chains in the present system. The details about the polymer chain ratio of long chains and short chains were discussed in our previous report.[25]

Cross-Linking Reaction of 5 and 6. Herein, the preparation of another type of asymmetrical (miktoarm) star-like nanogel **9** with arms having different chemical compositions (PMMA and PSt) is reported. The reaction was performed by heating a mixture of diblock copolymers **5** and **6** in anisole at 100 °C for 24 h in several mixing ratios. As with star-like nanogels **7** and **8**, the GPC curves transformed toward higher molecular weights with an increase in the ratio of diblock copolymer **5**, as shown in Figure 10a. Indeed, the continuous variation of R_g and M_w with the mixing ratio, as seen in Figure 10b, indicated that the diblock copolymer reacted in the complementarily reactive system. The molecular weight ($M_{w,\ MALS}$) and size ($R_{g,\ MALS}$) peaks seemed to occur for a [**5**]:[**6**] = 4:6 condition. This is because the molecular weight of the alkoxyamine block was slightly different, as shown in Table 1, and the opposite directions of the alkoxyamine moieties were almost the same in this mixing condition. On the basis of the above knowledge, the preparation of star-like nanogels with asymmetrical chains (PMMA and PSt) was successfully accomplished. The expanded PMMA chains from gel parts could be confirmed in the AFM images, as well as in Figures 7 and 9. The conformation of the expanded PSt block, however, could not be observed, because of the difference of affinity toward mica substrates.

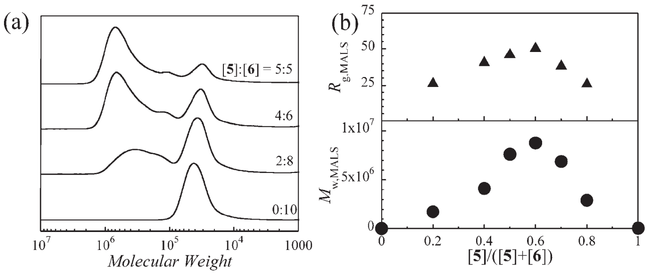


Figure 10. (a) GPC curves, and (b) $M_{w,\ MALS}$ and R_g of post polymers after heating mixtures of diblock copolymers **5** and **6** in anisole (10 wt %) at 100 °C for 24 h in several mixing ratios.

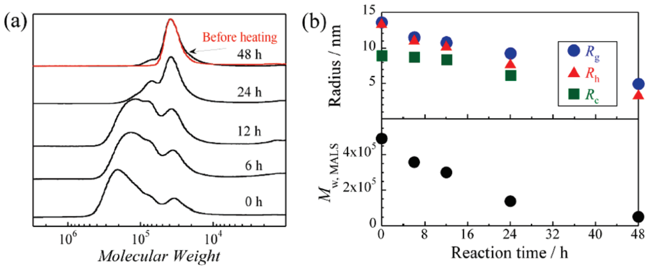


Figure 11. (a) GPC curves and (b) $M_{w,\ MALS}$, R_g, R_h, and R_c of polymers in the case of structural transformation from star-like nanogels to diblock copolymers by heating star-like nanogel **7** with excess alkoxyamine (40 equiv/alkoxyamine units in star-like nanogel) in anisole (10 wt %) for several reaction times at 100 °C.

Structure Transformation from Star-like Nanogels to Diblock Copolymers. The structures of compounds with dynamic covalent systems can be changed by a specific stimulus and external environment. In a previous report,[22] we demonstrated a transformation from star-like nanogels to diblock copolymers in a self-built-up system by a stoichiometric stimulus or the addition of excess alkoxyamine units. The transformation from star-like nanogel to diblock copolymer was attempted in a complementary system, as well as the self-built-up system. The decross-linking reaction was carried out by heating star-like nanogel **7**, which was prepared by heating an equal mixing ratio of diblock copolymers **3** and **4** in anisole (10 wt %) for 24 h at 100 °C, with excess alkoxyamine **10** (40 equiv/alkoxyamine units in star-like nanogels) in anisole (10 wt %) at 100 °C.

Figure 11a shows GPC curves of the reaction products for the above conditions. As the reaction proceeded, the peaks of the star-like nanogels decreased and those of the diblock copolymers increased gradually, and almost the same peak as diblock copolymers **3** and **4** before heating was obtained after 48 h. In addition, the $M_{w,\ MALS}$ and sizes (R_g, R_h, and

R_c) decreased with reaction time and indicated almost the same values as the diblock copolymers after 48 h (for example, after 48 h condition: $M_w = 52\ 260$: before heating: $M_w = 37\ 300$), as shown in Figure 11b. These results indicated that the diblock copolymers were obviously regenerated after 48 h via a dynamic covalent exchange reaction between the star-like nanogels and alkoxyamine **10**. From the above results, the transformation from star-like nanogels to diblock copolymers was accomplished in the present complementarily reactive system.

Conclusion

The authors demonstrated the systematic formation of symmetrical and asymmetrical (miktoarm) star-like nanogels via dynamic covalent exchange reaction among diblock copolymers with alkoxyamine units in their side chains. First, two types of diblock copolymers with the almost same degrees of polymerization but with opposite directions for their alkoxyamine units were reacted complementarily, and locally cross-linking polymers were formed with the thermodynamically stable structure in their systems. The chain conformation of these cross-linking polymers was revealed by SAXS measurements and SFM observations. In both the solution and bulk states, it was made clear that their structures consisted of a nanogel core part and radially extended PMMA chains from the core, corresponding to symmetrical star-like nanogels. Furthermore, by using different types of diblock copolymers with different molecular weights and/or chemical compositions, asymmetrical star-like nanogels were successfully formed. Moreover, in these systems, two types of diblock copolymers reacted complementarily. Furthermore, transformations from star-like nanogels to diblock copolymers were successfully accomplished by heating star-like nanogels with excess alkoxyamine moieties as a result of a dynamic covalent exchange reaction between added alkoxyamine units and the alkoxyamine of the core parts of the star-nanogels. Such intelligent reactive polymers show the potential to construct various shapes of molecular assemblies and/or macromolecular aggregates.

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