Synthesis and Self-Association of Stimuli-Responsive Diblock Copolymers by Living Cationic Polymerization

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Summary: The living cationic polymerization of several functional monomers in the presence of an added base is investigated as a possible preparation of a new series of water-soluble or stimuli-responsive copolymers. Under appropriate conditions, the polymerization allows the selective preparation of polymers with various shapes and different sequence distributions of monomer units, including stimuli-responsive block copolymers, gradient copolymers, poly(vinyl alcohol) graft copolymers, and star-shaped polymers. The stimuli-induced self-association of the diblock copolymers is also examined. An aqueous solution of the diblock copolymer with a thermosensitive segment undergoes rapid physical gelation upon warming to the critical temperature to give a transparent gel, and returns sensitively to the solution state upon cooling. The sharp transition of stimuli-responsive segments with highly controlled primary structure turns out to play an important role in the self-association. Small-angle neutron scattering, dynamic light scattering, and electron microscopy studies reveal that the physical gelation involves a thermosensitive micellization of diblock copolymers (core size: 18–20 nm) and subsequent micelle macrolattice formation (bcc symmetry). Based on the gelation mechanism, several stimuli-responsive gelation systems are achieved using other stimuli such as the addition of a selective solvent or compound, cooling, pH change, and irradiation with ultraviolet light.

Keywords: living cationic polymerization using an added base; macrolattice formation of the micelles; star-shaped polymers; stimuli-induced self-association; stimuli-responsive block copolymer

DOI: 10.1002/masy.200451113

Introduction

Recently, nano-organized self-assemblies using amphiphilic block copolymers or hydrophobically modified water-soluble polymers have attracted attention both academically and for possible practical applications.[1-3] A key to successful synthesis of more intelligent polymers would be the utilization of living polymerization, as the chemical structure, molecular weight, and hydrophobicity of the amphiphilic polymers are known to control the morphology of the self-aggregates. However, the development of such well-controlled amphiphilic block copolymers has been limited because of difficulties in the formation of a polar hydrophilic moiety by living polymerization. Recent progress in living polymerization, particularly in controlled/living radical polymerization, has led to the design and synthesis of novel well-defined amphiphilic block copolymers.

In the field of cationic polymerization, living polymerization has been achieved through the use of nucleophilic counteranions, externally added bases, or added salts. In the first two cases, the key point is the stabilization of propagating carbocation by the nucleophilic interaction. We are currently investigating the living cationic polymerization of polar monomers in the presence of an added base[4] toward preparation of living polymers with various properties. In particular, the production of stimuli-responsive polymers with a variety of functional groups would make it possible to prepare novel intelligent polymers.[5-10]

In this work, toward designing a new strategy for preparing such stimuli-responsive polymers (mainly diblock copolymers) by living cationic polymerization, the polymerization of monomers with polar functional groups was carried out, and the synthesis of polymers of various shapes was investigated. A new stimuli-induced self-association of the diblock copolymers was also examined.

Results and Discussion

1. Synthesis and Properties of Various Functional Polymers by Living Cationic Polymerization

Synthesis. As a typical example of living cationic polymerization of a monomer with a polar side group, homo- and block-copolymerizations of BMSiVE [2-(*tert*-butyldimethylsilyloxy)ethyl vinyl ether] were carried out using $Et_{1.5}AlCl_{1.5}$ in the presence of ethyl acetate in toluene at 0 °C.[9,11] As shown in Fig. 1(A), the polymer molecular weight increased in direct proportion to conversion. The polymers exhibited very narrow, nearly monodisperse molecular weight distributions (MWDs), as shown in Fig. 1(B). ^1H NMR structural analysis confirmed that the silyloxy pendants remained entirely intact. The MWD of the polymers by sequential block copolymerization is shown in Fig. 1(C). EOVE was polymerized first, and BMSiVE was added neat to the polymerization mixture when EOVE has been consumed almost quantitatively. The MWD clearly shifted toward higher molecular weighs, but still it remained very narrow ($M_w/M_n \leq 1.1$). The absence of tailing to lower molecular weights reflects the quantitative formation of block copolymers. These results demonstrate that the presence of an added base induces the living cationic polymerization of BMSiVE despite the presence of acid-sensitive silyloxy groups.

Scheme 1 summarizes the properties of the living polymers obtained (water-soluble polyalcohols and polycarboxylic acid in the frame were obtained using a corresponding protected monomer). In these systems, the propagating carbocations were stabilized by nucleophilic interaction with the added base to prevent not only the conventional chain transfer and termination, but also acid-catalyzed side reactions.

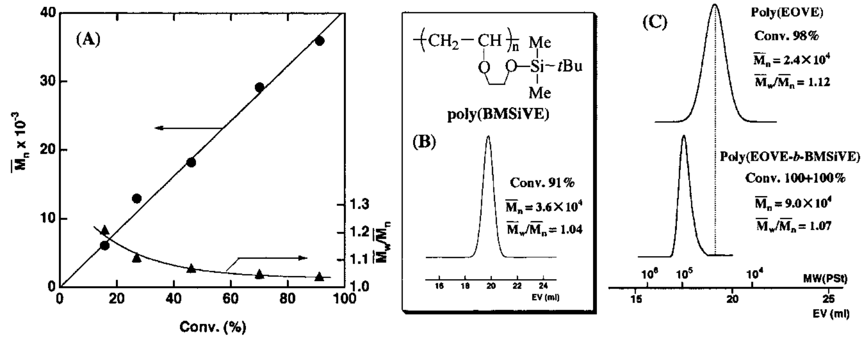
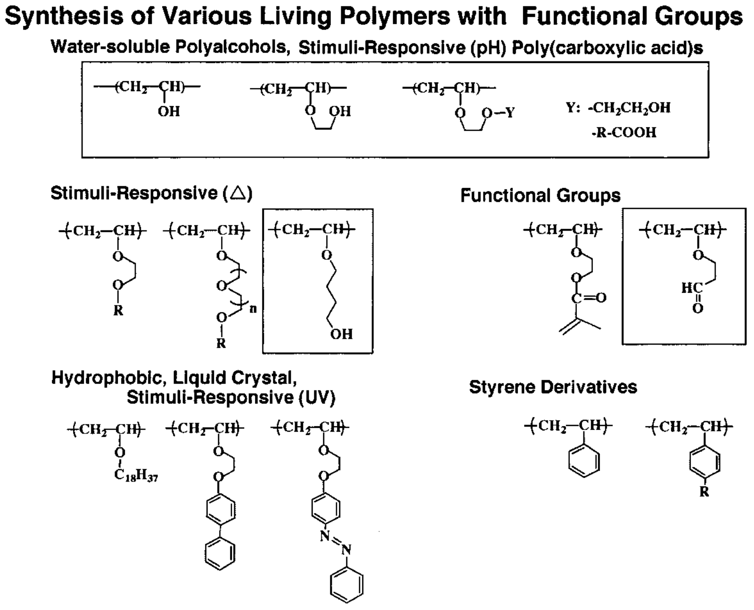
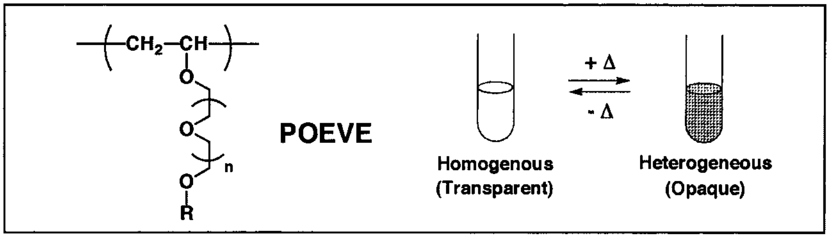


Figure 1. Relationships between conversion and M_n or M_w/M_n (A), MWDs of poly(BMSiVE) (B), and poly(EOVE-*b*-BMSiVE) (C) obtained with $1/Et_{1.5}AlCl_{1.5}$ in the presence of ethyl acetate in toluene at 0°C: $[BMSiVE]_0$=0.8M, $[1]_0$=4.0mM, $[Et_{1.5}AlCl_{1.5}]_0$=20mM, [ethyl acetate]=1.0 M; **1**: $CH_3CH(O\textit{i}Bu)OCOCH_3$, poly(EOVE): $-[CH_2CH(OCH_2CH_2OC_2H_5)]_n-$.



Scheme 1. Synthesis and properties of various living polymers obtained with an added base.

Properties. Heating a transparent aqueous solution of the polymer with oxyethylene chains and a ω-alkyl group (POEVE) caused the solution to become cloudy at a certain critical temperature.[5-7] As shown in Fig. 2, the phase separation was quite sensitive and reversible on heating and cooling. The suggested mechanism of phase separation is as follows. At low temperature, the polymers are soluble in water by hydration. When the temperature reaches the critical point, dehydration occurs, giving rise to aggregation (phase separation) by hydrophobic interaction. POEVEs are the only living polymers to date that exhibit such a sharp phase separation, and the effects of molecular weight, MWD, and sequence distribution on the critical temperature T_{ps} have been investigated extensively. The sequence distributions have been shown to affect the phase separation behavior remarkably, and represents a means of preparing novel thermo-sensitive gelation systems.[5,7]



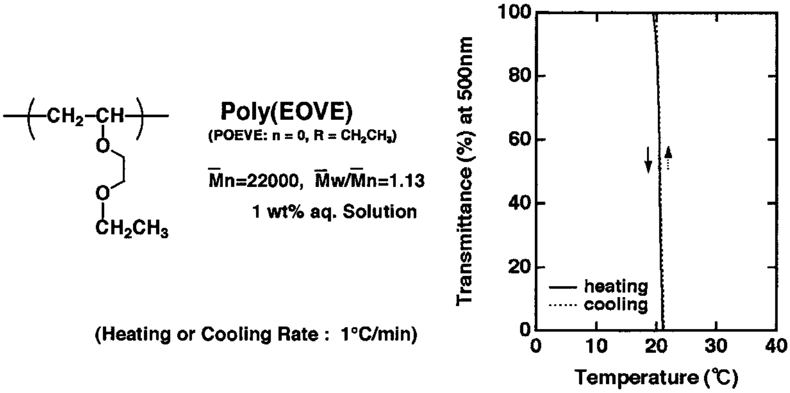
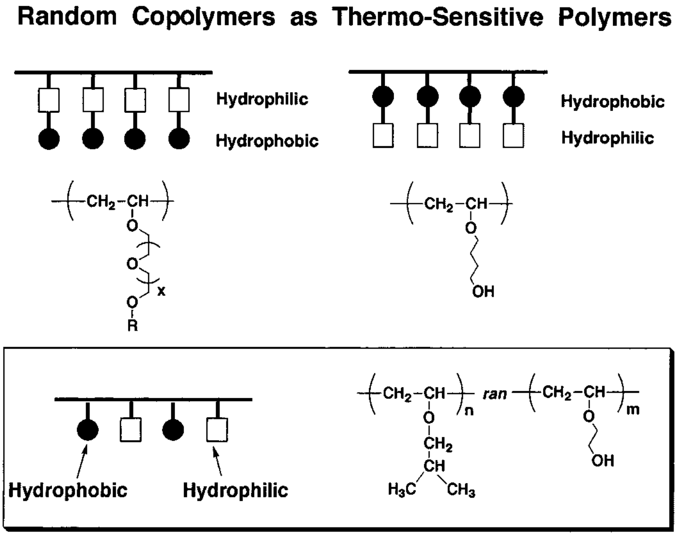


Figure 2. A typical phase diagram, traced by the transmittance at 500nm, of 1 wt% aqueous poly(EOVE) solution.

As another possibility for thermosensitive phase separation, more generalized methods have recently been examined. That is, instead of thermo-sensitive homopolymers with an appropriate hydrophilic/hydrophobic balance (the upper two polymers in Scheme 2), [5-11] thermo-sensitive random copolymers of hydrophilic and hydrophobic monomers were synthesized via living cationic copolymerization (Scheme 2).[12] On heating, an aqueous solution of a random copolymer undergoes thermally induced phase separation at a critical temperature (Fig. 3). This phase separation is quite sensitive and reversible on heating and cooling. Interestingly, the randomness of the sequence distribution is indispensable to realizing such highly sensitive phase separation.



Scheme 2. Thermo-sensitive homopolymers with an appropriate hydrophilic/hydrophobic balance and random copolymers of hydrophilic and hydrophobic monomers.

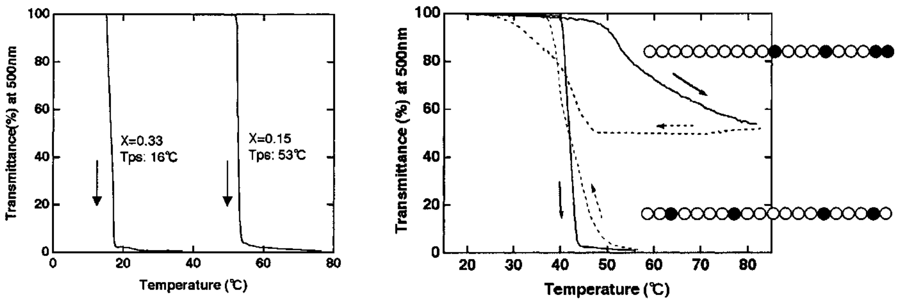
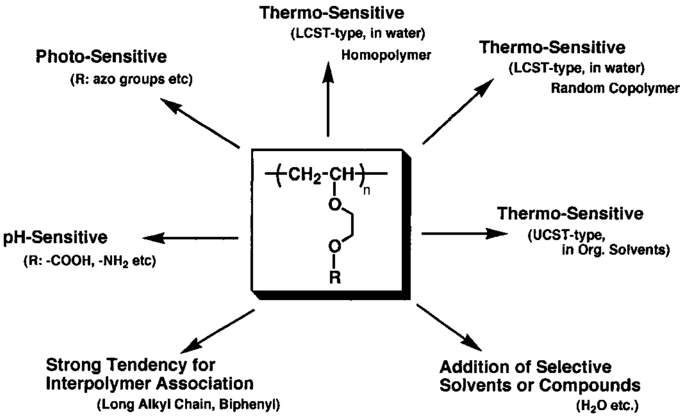


Figure 3. Temperature dependence of the transmittance at 500 nm of 1.0 wt% aqueous solutions of random copolymers (IBVE$_x$-*ran*-HOVE$_{1-x}$)$_{200}$ (x = 0.33 and 0.15; $M_w/M_n \leq 1.05$) and the effects of sequence distribution on phase separation behavior (x = 0.20): heating rate 1.0 °C/min; poly(HOVE): -[CH$_2$CH(OCH$_2$CH$_2$OH)]$_n$-.



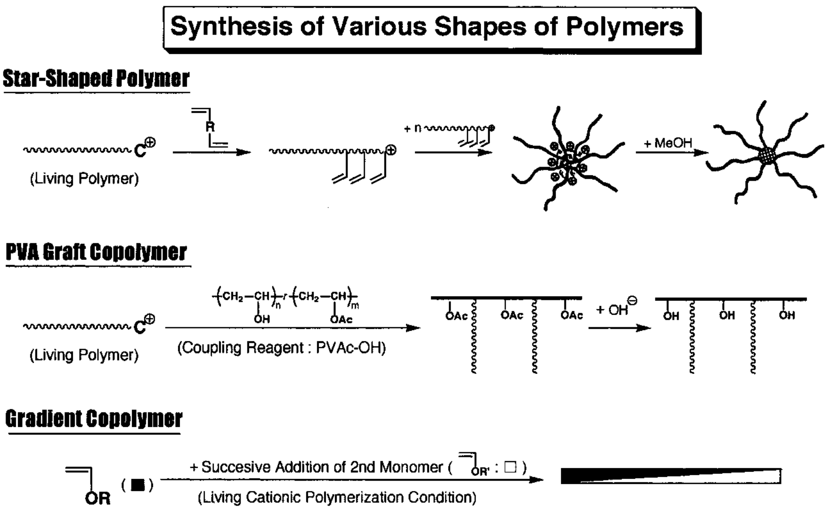
Scheme 3. Synthesis of sensitive stimuli-responsive polymers with various stimuli.

More recently, we have investigated the synthesis of stimuli-responsive polymers, sensitive to other stimuli, as shown in Scheme 3.

2. Synthesis of Various Shapes of Polymers

Scheme 4 summarizes the selective preparation of polymers with various shapes and different sequence distributions of monomer units by living cationic polymerization with an added base: (i) star-shaped polymers, (ii) PVA graft copolymers, and (iii) gradient copolymers.

Star-shaped polymers of vinyl ethers were prepared through linking reactions of linear living polymers with a small amount of a bifunctional vinyl ether by living cationic polymerization. Under optimum conditions, as shown in Fig. 4, quantitative conversion of living poly(IBVE)s (arms) was achieved to give star-shaped polymers with a very narrow MWD ($M_w/M_n = 1.11$). Multiangle laser light scattering (MALLS) and dynamic light scattering (DLS) analyses revealed that the M_w and size of the star-shaped polymer obtained with living poly(IBVE) ($M_n = 1.64 \times 10^4$, $M_w/M_n = 1.07$) were 19.5×10^4 (f (the number of arms per molecule) = 11) and 9.5 nm (diameter), respectively.



Scheme 4. Selective syntheses of polymers with various shapes and different sequence distributions by living cationic polymerization.

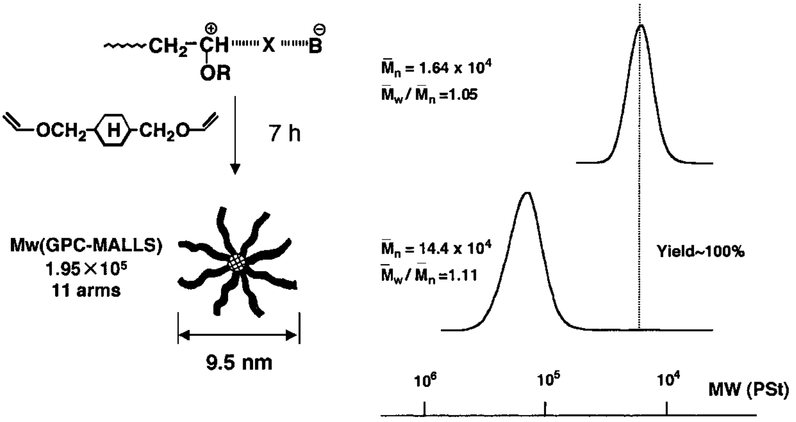


Figure 4. Synthesis of a star-shaped polymer of IBVE with 1/$EtAlCl_2$ in the presence of ethyl acetate in hexane at 0°C; DP_n(arm)~160; [divinyl compd.]$_0$/[1]$_0$=10.0; Living poly(IBVE), [IBVE]$_0$=1.5M , [$CH_3COOC_2H_5$]=1.0M, [1]$_0$/[$EtAlCl_2$]$_0$=10.0/20.0, mM.

Poly(vinyl alcohol) (PVA) graft copolymers were also prepared, consisting of a PVA main-chain and poly(vinyl ether) branches.[13,14] The synthetic route involves the quantitative coupling reaction of living poly(vinyl ether) cationic chains with partially saponified PVAc (PVAc-OH). The latter (PVAc-OH) is soluble in several organic solvents such as toluene, and no side reactions occurred in the course of coupling. The polymer main-chain could be readily converted to PVA by conventional saponification after the coupling reactions. Using this method, various types of grafts, such as two different grafts and diblock grafts, were prepared and the difference in phase separation behavior was examined.

Gradient copolymers have a very characteristic sequence distribution, in which the instantaneous composition changes continuously along the main chain.[15] During living polymerization of the first monomer in the presence of an added base, a second monomer was successively added, and the polymerization proceeded in a living fashion to give narrow-MWD polymers with compositional change along the polymer chain.[16]

3. __Stimuli-Induced Self-Association of Diblock Copolymers__

The rapid formation of a physical gel occurred on warming an aqueous solution of a diblock copolymer having a water-soluble polyalcohol segment and a thermoresponsive segment, $-[CH_2CH(OCH_2CH_2OH)]_m$-*block*-$[CH_2CH(OCH_2CH_2OC_2H_5)]_n-$, to the lower critical solution temperature (LCST) of phase separation for the thermoresponsive segment.[9,17-19] The viscosity change was quite abrupt and reversible on heating and cooling. Figure 5 shows a temperature scan of G' and G''. Around 20 °C, G' changes by more than 4 orders of magnitude within the temperature range of less than 1 °C.

On the basis of dynamic viscoelasticity, small-angle neutron scattering (SANS), transmission electron microscopy (TEM), and DLS measurements, the mechanism of physical gelation was deduced to begin with the formation of micelles with well-controlled size and structure, followed by close packing of the micelles (bcc macrolattice formation) or weak interaction between the micelles. [17-19]

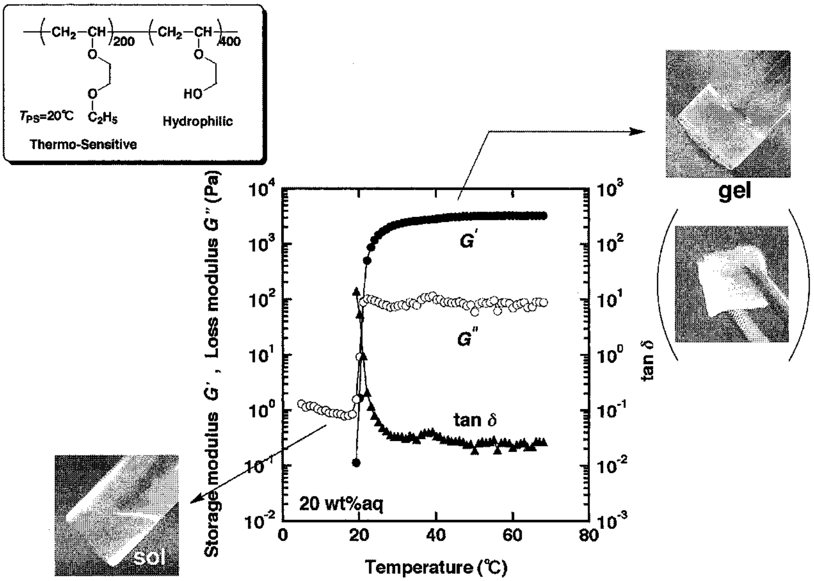
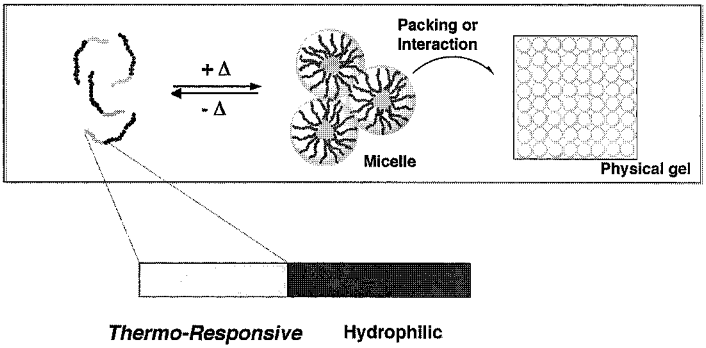
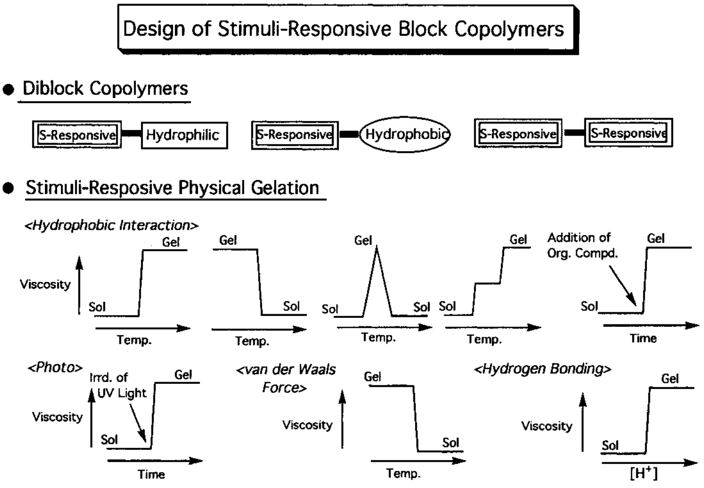


Figure 5. Temperature dependence of storage modulus G', loss modulus G'', and tan δ for 20wt% $EOVE_{200}$-*b*-$HOVE_{400}$ aqueous solution (frequency=1Hz).



Scheme 5. Schematic representation of thermally-induced physical gelation of diblock copolymers.

Based on the gelation mechanism, several systems with various patterns for physical gelation behavior (sol-gel, gel-sol, or sol-gel-sol) have been developed, which are responsive to other stimuli such as the addition of a selective solvent[20] or compound, cooling, pH change, and irradiation with ultraviolet light. Scheme 6 illustrates the physical gelation behavior for a series of block copolymers.



Scheme 6. Various stimuli-responsive physical gelation behavior with diblock copolymers.

Experimental

Materials. Si-containing vinyl ethers and OEVEs were prepared from a corresponding hydroxyalkyl vinyl ether or 2-chloroethyl vinyl ether as reported previously. The cationogen $CH_3CH(O\textit{i}Bu)OCOCH_3$ (**1**) was prepared from IBVE (isobutyl vinyl ether) and acetic acid.

Polymerization Procedure. Polymerization was carried out at 0 °C under a dry nitrogen atmosphere in a glass tube equipped with a three-way stopcock. The reaction was initiated by the addition of $Et_{1.5}AlCl_{1.5}$ toluene solution to a mixture of a monomer, an added base, and the cationogen in toluene or hexane at 0 °C. After a certain period, the polymerization was quenched with prechilled methanol containing a small amount of aqueous ammonia solution. The product polymer was recovered from the organic layer by evaporation and vacuum-dried overnight. The conversion of a monomer was determined by gravimetry. Desilylation of the product polymers was carried out with the addition of 3.0 N aqueous HCl-EtOH to a purified polymer in THF-EtOH at 0 °C.

Characterization. The MWD of the polymers was measured by size exclusion chromatography (SEC) in chloroform at 40 °C on three polystyrene gel columns. The number-average molecular weight (M_n) and M_w/M_n were calculated from SEC curves in reference to polystyrene calibration. The M_w of the star-shaped polymers was also determined by MALLS in chloroform at 40 °C on a Dawn E instrument (Ga-As laser, $\lambda = 690$ nm). The size of the star-shaped polymers was determined from the R_h by DLS in chloroform at 30 °C.

Aqueous solutions of the polymers were prepared by dissolving the polymer in Mill-Q water (18 MΩ cm). The phase-separation temperatures of the polymer solutions were determined from the transmittance at 500 nm, monitored at a rate of 1 °C /min on heating and cooling scans. A high-sensitivity differential scanning calorimeter was used to study the endothermic enthalpy. The (apparent) viscosity based on flow properties and the dynamic viscoelasticity of the polymer solutions were measured using a stress-controlled rheometer with a cone-plate of 4 cm diameter and angle of 2°. Dynamic viscoelastic measurement was carried out at various temperatures at an angular frequency of 6.283 rad/s (1.0 Hz). SANS, small-angle x-ray scattering (SAXS), and freeze-fracture TEM measurements were performed as described in detail elsewhere. [17,19]

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