Novel Thermosensitive Polyethers Prepared by Anionic Ring-Opening Polymerization of Glycidyl Ether Derivatives

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A new series of thermo-sensitive polyethers were prepared by anionic ring-opening polymerization of glycidyl ether derivatives: glycidyl methyl ether, ethyl glycidyl ether, and ethoxyethyl glycidyl ether. The prepared polymers have controllable molecular weight with narrow molecular weight distributions. These polymers exhibit a lower critical solution temperature (LCST) in water. The LCST is altered from 14.6 to 57.7 °C by decreasing the hydrophobicity of the side-chain units.

Stimuli-responsive polymers, which change reversibly from a water-soluble coil to a water-insoluble collapsed globule upon small changes in temperature, pH or light intensity, have attracted much attention in terms of possible applications including nano-organized self-assemblies of polymers,[1] intelligent hydrogels,[2,3] and smart polymer protein conjugates.[4] Amphiphilic polymers such as poly(*N*-isopropyl acrylamide),[5] poly(vinyl ether)s with side oxyethylene units and their block copolymers,[6,7] and poly(*N*-vinyl isobutylamide)[8] were found to exhibit thermally induced phase separation in water. These thermo-sensitive polymers have been prepared by radical[5,8] and cationic[6,7] polymerization methods. To widen the structural variety and to realize thermo-sensitive polymers with a controllable LCST, end-group functionality, and ability to afford block copolymers, new thermo-sensitive polymers by a suitable polymerization method have been desired.

Poly(ethylene oxide) (PEO) is a non-toxic, flexible, water-soluble polymer and reveals a LCST higher than 100 °C.[9] By introducing hydrophobic side-chain groups to PEO, we designed and prepared a new series of temperature-sensitive polymers with a controllable LCST. Because of the biocompatibility of PEO, the new polymers are expected to be useful for the modification of proteins and solid surfaces, which yields the stimuli-control of protein and biocompatible intelligent solid surfaces.

Figure 1 illustrates the preparation procedure and structure of polymers. Glycidyl methyl ether (GME) and ethyl glycidyl ether (EGE) were purchased from Tokyo Kasei Co. n-Butyl glycidyl ether (BGE) was a gift from Daiso Co. Ethoxyethyl glycidyl ether (EEGE) was synthesized by Williamson condensation reaction from epichlorohydrin and 2-ethoxyethanol. These monomer compounds were purified by repeated distillation until no trace of epichlorohydrin was detected by gas chromatography.

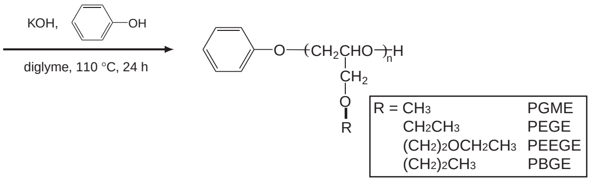

Figure 1. Preparation procedures and structures of polymers.

Phenol (6.7 mmol) was dissolved in dried ethylene glycol dimethyl ether (100 ml) and then dried potassium hydroxide (6.7 mmol) was added as a catalyst. After this mixture was introduced into an autoclave, the content was repeatedly evacuated and purged by N_2 at room temperature to yield potassium phenoxide. While N_2 gas was flowing, GME (220 mmol) was added to the mixture. The reaction mixture was stirred at 110 °C for 24 h under anhydrous conditions. The reaction mixture was neutralized by adding 1 wt% sulfuric acid until its pH became 5 to 6. To remove ionic impurities, the mixture was stirred with an acid-adsorbent for 30 min and with a base-adsorbent for 1 h, respectively, and then filtrated. The filtrate was evaporated to dryness at 100 °C for 1 h under reduced pressure, yielding PGME as a light-yellow viscous liquid. The other monomers were also polymerized by similar methods.

The number-average molecular weight and the molecular weight distribution of obtained polymers were characterized by ^{1}H NMR and gel permeation chromatography (GPC), respectively, as listed in Table 1. The molecular weight was calculated from the ratio of integrated signal intensities between phenolic protons and side-chain end methyl protons. All the polymers exhibited relatively narrow molecular weight distributions less than 1.2, and the M_n was determined by the feed ratio of monomer to phenol, suggesting that a living-like anionic polymerization proceeded. The narrow distribution of molecular weight may be advantageous for the sharp phase transition. Although the molecular weight of all polymers shown in Table 1 is around 3000, it was confirmed that higher molecular weights up to 8000 could be obtained by increasing the molar ratio of monomer to phenol in feed and by lengthening the reaction time.

Table 1. M_n and M_w/M_n of obtained polymers

Polymers	M_n[a)]	M_w/M_n[b)]
PGME	3000	1.19
PEGE	3100	1.20
PEEGE	2700	1.17
PBGE	2500	—

a) Number average molecular weight (M_n) determined by ^{1}H NMR, based on the ratio of integrated signal intensities between phenolic protons (6.9–7.3 ppm) and side-chain end methyl protons (1.2 ppm).
b) Ratio of weight average molecular weight to number average molecular weight (M_w/M_n) determined by GPC.

The LCSTs of 1 wt% aqueous polymer solutions were measured by monitoring the transmittance of a 500-nm light beam through a 1-cm quartz sample cell at a rate of 1 °C min^{-1} in heating and cooling scans, as shown in Figure 2. Since PBGE was not soluble in water even at 4 °C, the LCST could not be measured. For PEGE, a phase transition occurred around 15 °C, where the solubility of polymer sharply altered. The LCST of PEGE solution was obtained to be 14.6 °C from the temperature at 50% transmittance. The LCST values of PEEGE and PGME were determined to be 40.0 and 57.7 °C, respectively. The LCST value depends on the structure of the side chain as follows: $-CH_2OCH_3 > -CH_2OCH_2CH_2OCH_2CH_3 > -CH_2OCH_2CH_3$. Aoshima et al. reported that the same dependency of LCST on the side chain structure was observed for a series of poly(alkoxyethyl vinyl ether) and their LCST values increased with increasing the hydrophilicity of the alkoxy part.[6,7] Thus, it seems that less hydrophobic the side-chain groups are, the higher the LCST of the present polymer is. While the phase transition curve revealed no hysteresis between the heating and cooling scans for PEGE and PGME, a slight hysteresis was observed for PEEGE. The sharpness of the phase transition for PGME was inferior to those for other polymers. Since all the polymers have similar molecular weight distributions, the lower cohesive forces between PGME molecules originated from the less hydrophobic side-chain groups might be the reason for the dull phase transition.

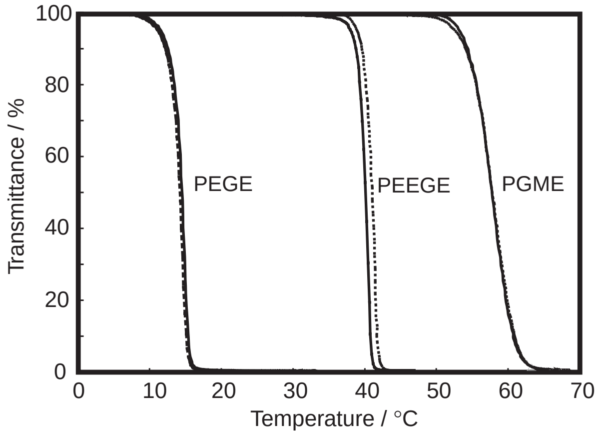

Figure 2. Temperature dependence of transmittance at 500 nm for 1 wt% aqueous polymer solutions. Heating scan: solid line, cooling scan: dotted line.

The development of well-controlled amphiphilic block copolymers and bioconjugates using the present thermo-sensitive polymers is underway.

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