

Effect of Salen-Metal Complexes on Thermosensitive Reversibility of Stimuli-Responsive Water-Soluble Poly(urethane amine)s

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ABSTRACT: The double stimuli responsive water-soluble poly(urethane amine)s are prepared under supercritical carbon dioxide (scCO₂) with renewable resources—carbon dioxide and natural α -amino acids—as the starting materials. The urethane content, which will decide on the thermosensitive behavior of poly(urethane amine)s, is regulated not only by the substituent on aziridine derivatives but also by the coordinated metallic ion of Salen-metal complexes as a catalyst. Interestingly, the thermosensitive reversibility is also changed through the application of Salen-metal complexes in the copolymerization reaction of CO₂ with aziridine derivatives. © 2013 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* 129: 3696–3703, 2013

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INTRODUCTION

The reversible substantial properties have attracted much attention in the recent decades due to their applications in intelligent control, biomaterials, switching materials, and so on.^{1,2} Especially, the controllable reversibility of material properties has become an extraordinary fascinating performance^{3–5} because this is a basic issue for intelligent devices, which are applied to a variety of the fields of national economy in high automation society.^{6,7} One of them, stimuli responsive polymers are one of excellent candidates widely being studied under external stimuli such as temperature, pH, solvent, light, electric or magnetic field, chemical triggers, etc.¹ Temperature/pH-responsive polymers are being much more considerably investigated due to their convenience, stimuli-responsive effectiveness and wide existence in nature. This enables them attractive for controlled drug delivery, microactuators, and gene-transfection agents.⁸ On the other hand, water-soluble polymer is another hot topic on account of friendly environmental consideration.² Therefore, stimuli responsive water-soluble polymers with a controllable reversibility are becoming an attractive and prospective class of intelligent materials.

It is known that stimuli-responsive water-soluble polymers have been widely studied not only in natural polymers but also in synthetic polymers such as block copolymers, graft copolymers, random copolymers, etc.^{1,2} A classic stimuli-responsive water-soluble polymer is poly(*N*-isopropylacrylamide) (PNIPAAm),^{9,10} which undergoes a sharp coil-to-globule transition at 32°C in

water from a hydrophilic state at lower temperature to a hydrophobic state at higher temperature. This behavior is called as inverse temperature-dependent solubility, i.e., stimuli-responsive water-soluble polymers are separated from the solution upon heating and dissolved upon cooling at a certain temperature. This phase transition temperature is usually defined as a lower critical solution temperature (LCST). Presently, synthetic polymers are generally prepared from petrochemical materials. Considering the increasing petroleum price, the environment pollution and the limitation of natural polymers in the variety and controllable properties, it has become a challenge to prepare synthetic stimuli responsive water-soluble polymers with a controllable reversibility completely from renewable resources.

The CO₂-based polymerization is the most attractive approach to synthesize polymers from renewable resources¹¹ because CO₂ is nontoxic, nonflammable, abundant, economical and recyclable. Especially, the copolymerization under supercritical carbon dioxide (scCO₂) is one exciting subject because CO₂ is utilized as not only starting material but also reaction media with the replacement of hazardous organic solvents.^{12,13} Simultaneously, the CO₂-based copolymerization is also propitious to the alleviation of environmental pollution and greenhouse effect by the consumption of CO₂ in effective chemical fixation.¹⁴ Besides, the synthesized polymers by the CO₂-based copolymerization will potentially bear biodegradability, for example, aliphatic polycarbonates from epoxides and CO₂.¹⁵ To the best of our knowledge, the polymers bearing amide groups is the largest group of

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stimuli responsive polymers due to the existence of hydrogen bonding, like the above-mentioned PNIPAAm.^{9,10} Such stimuli responsive water-soluble synthetic polymers, poly(urethane amine)s, have been prepared by the copolymerization of aziridine derivatives and CO₂.^{16–18} The polymers consist of hydrophobic urethane and hydrophilic amine and exhibit a good thermally induced reversible transition property in aqueous solution. As a main driving force, the hydrogen bonds between amino groups and water are advantageous to the polymeric dissolution in water. As the temperature is increased, the H-bond-assisted hydrophilicity is counterbalanced by the increased hydrophobicity owing to the fractional breakdown of hydrogen bonds, which will lead to a spontaneous macromolecular aggregation. These aliphatic poly(urethane amine)s might be biodegradable with the existence of urethane linkages and display excellent pH- and temperature- responsive properties in aqueous solution. Regrettably, the stimuli responsive reversibility was not investigated. Simultaneously, it is hard to regulate the LCST of poly(urethane amine)s by controlling the pressure and temperature of scCO₂. Therefore, the preparation of smart poly(urethane amine)s with a controllable thermoresponsive reversibility by the CO₂ copolymerization completely from renewable resources would be one significant and practical subject.

Herein, double stimuli responsive thermoresponsive water-soluble poly(urethane amine)s are synthesized by the CO₂ copolymerization with renewable resources— α -amino acids and CO₂—as the starting materials with the aim of green and sustainable methodology. The reason is that α -amino acids are the main component of natural peptides and proteins in animals and plants. They will become important environment-friendly and recyclable chemical resources with the strengthened environment problems and the potential exhaustion of petroleum resources. Additionally, the application of α -amino acids as starting materials for synthetic polymers also provides a possible precondition for polymeric biodegradability. Notably, the thermosensitive reversibility of poly(urethane amine)s synthesized in our laboratory is controlled by the catalyst selection while LCST of poly(urethane amine)s is tuned by the substituent of aziridine derivatives and by the pH value of aqueous solution.

EXPERIMENTAL

Chemicals and Reagents

α -amine acids were purchased from Ningbo Haishuo and Sichuan Biochem-ZX. Other reagents were purchased from Sinopharm Chemical Reagent. All the reagents were of analytical grade and used without further purification. CO₂ with a purity of 99.999% was purchased from Peking Haiwen Special Gases.

Instruments and Characterization

¹H-NMR spectra were recorded on a Bruker DPX-400 spectrometer with Me₄Si as an internal standard. The urethane content was calculated from elemental analysis under the assumption of copolymer structures containing urethane and amine moieties or the integral area of urethane in ¹H-NMR spectra. The transmittance spectra of aqueous solution were measured by a HITACHI U-3010 UV-Vis spectrometer with a Julabo temperature controller. The phase transition temperature

was defined as the onset of the transmittance curve measured from the heating process. Molecular weight was determined at 40°C by GPC using a dual-detector system consisting of a MALLS device (DAWN-EOS Model, Wyatt) and a refractive index detector (Optilab rEX dn/dc, Wyatt) with a polymer concentration of 10 mg/mL at a flow rate of 1.0 mL/min. The eluent was respectively water for Entries 1 and 5 through 7 and THF for Entries 2 through 4.

Synthesis of Aziridine Derivatives

The synthetic procedure of 2-*iso*-propylaziridine was given as an example. L-Valine (23 g, 0.2 mol) was added to a stirred suspension of NaBH₄ (19 g, 0.5 mol) in THF (100 mL). The flask was immersed in an ice-water bath. A solution of concentrated H₂SO₄ (21 g, 0.21 mol) in diethyl ether (40 mL) was added dropwise to maintain the reaction mixture below 10°C. The reaction was continued under stirring at room temperature for 12 h. Methanol (40 mL) was added carefully to destroy excess NaBH₄. The resulting mixture was stirred for 3 h at room temperature and then concentrated. The solution of NaOH (20 wt %, 200 mL) was added and the mixture was distilled to remove the solvents. The residue was heated and refluxed for 3 h, then cooled and filtered through a thin pad of celite. The filtrate was extracted with CH₂Cl₂ (three times, 150 mL) and dried over anhydrous MgSO₄. The extract was rectified to give a crude product which was further purified via distillation under a reduced pressure. The pure L-Valinol was obtained in 84.5% yield.^{19,20} The product was directly used in the next synthetic procedure without any characterization.

A solution of sulfuric acid (0.4 mol) in water (40 mL) was added slowly to a stirred, cooled (5°C) solution of L-Valinol (0.38 mol) in water (38 mL). After the addition was completed, the reaction mixture continued to be stirred for 1 h, then condensed to remove water under reduced pressure. The residue was heated to 135°C under vacuum for 12 h; a solid matter was gradually formed, indicating that the conversion of hydroxyl compound to the sulfate ester. Upon cooling to room temperature, 135 mL of sodium hydroxide solution (30%) was added and then heated to 110°C for 3 h. The mixture was subjected to steam distillation and the distillate was extracted with diethyl ether (three times, 40 mL). The organic layer was separated and dried over sodium hydroxide pellets (10 g). After filtered, the solvent was removed under reduced pressure. Pure 2-*iso*-propylaziridine was obtained by distillation over sodium hydroxide pellets as a colorless liquid in 80% yield.^{21–23} The pure aziridine was stored over sodium hydroxide pellets as a preservative in refrigerator and freshly distilled from sodium prior to copolymerization. Other aziridine derivatives were synthesized via the same procedure. ¹H-NMR (400Hz, CDCl₃, δ), Compound **2a**: 1.50 (3H, CH₃), 1.25 (1H, CH₂), 1.75 (1H, CH₂), 2.0 (1H, CH); Compound **2b**: 1.00 (3H, CH₃), 1.34 (1H, CH₂), 1.40 (2H, CH₂), 1.70 (1H, CH₂), 1.90 (1H, CH); Compound **2c**: 0.6 (1H, NH), 1.0 (3H, CH₃), 1.1 (3H, CH₃), 1.20 (1H, CH), 1.35 (1H, CH₂), 1.70 (1H, CH), 1.75 (1H, CH₂); Compound **3d**: 0.2 (1H, NH), 0.96 (3H, CH₃), 1.26 (1H, CH₂), 1.30 (2H, CH₂), 1.40 (1H, CH₂), 1.70 (1H, CH₂), 1.90 (1H, CH). ¹H-NMR spectra of 2-methylaziridine, 2-ethylaziridine, 2-*iso*-propylaziridine

and 2-*n*-propylaziridine were shown in Figures S1–S4 of the Supporting Information.

Synthesis of Salen-Metal Complexes

Salicylaldehyde (40 mmol) and ethylene diamine (20 mmol) were respectively dissolved in methanol (10 mL). Then, the solution of ethylene diamine was dropped into that of salicylaldehyde under stirring in the iced-water bath. A number of yellow precipitate was produced immediately. While the addition of ethylene diamine was finished, the precipitate was filtrated out and dried. Finally, compound **3**, salicylaldehydoethylenediamine, was obtained as a yellow slice-like crystal in 71% yield, which will be applied as a Salen ligand. ¹H-NMR (400Hz, CDCl₃, δ), 3.95 (4H, CH₂), 6.83 (2H, ArH), 6.91 (2H, ArH), 7.24 (4H, ArH), 8.36 (2H, =CH), 13.22 (2H, OH).

The synthetic procedure of Salen-Zn complex was given as an example. Compound **3** (2.5 mmol) was dissolved in toluene (20 mL). The solution of ZnCl₂ (2.5 mmol) in methanol (20 mL) was dropped within 10 min. The precipitate was gradually produced and refluxed for 2 h. Then, the precipitate was filtrated out and washed with methanol for several times until the filtrate become colorless. Compound **4a**, the Salen-Zn complex, was obtained as a yellow powder after dried in vacuum. It will directly be applied to the copolymerization of aziridines and CO₂ as a catalyst without any further purification. Compounds **4b** and **4c**, the Salen-Co and Salen-Cr complexes, were prepared using the same synthetic procedure as the Salen-Zn complex.

Copolymerization of Aziridines and CO₂

The synthetic procedure of the copolymerization reaction between 2-methylaziridine and CO₂ was given as an example. The copolymerization reaction was carried out in a 100 mL stainless steel autoclave. The autoclave was filled with N₂ after Salen-metal catalyst (0.05 g) was added. Then, 2-methylaziridine (5 mL) was introduced with a syringe. At this time, the reactor was pressurized to 10.0 MPa by CO₂. After stirring at 100°C for 24 h, the reaction was stopped by cooling the autoclave in an iced-water bath, followed by the slow release of CO₂.^{16–18} The polymeric product was purified by precipitation from methanol/ether to remove low-molecular-weight product and finally dried *in vacuo*. ¹H-NMR (400Hz, D₂O, δ), 0.70–1.40 (CH₃), 2.10–3.20 (CH₂ and CHNH), 3.40–3.90 (CHNC=O). Elemental Analysis: Entry 1, C, 54.00; H, 9.646; N, 18.59. Entry 2, C, 58.34; H, 9.708; N, 14.72. Entry 3, C, 62.31; H, 11.50; N, 13.60. Entry 4, C, 59.48; H, 9.764; N, 12.26. Entry 5, C, 49.33; H, 8.804; N, 16.11. Entry 6, C, 52.15; H, 9.736; N, 18.08. Entry 7, C, 53.24; H, 9.521; N, 18.26. ¹H-NMR spectra of copolymers from 2-methylaziridine were assigned in Figure S5 of the Supporting Information.

RESULTS AND DISCUSSION

All the intermediates, the catalysts and the polymers were synthesized according to the synthetic route in Scheme 1. First of all, four natural α-amino acids, DL-analine, L-2-aminobutyric acid, L-norvaline, L-valine, are reduced with NaBH₄–H₂SO₄ as a reduction reagent^{19,20} in order to prepare Compounds **1a–1d** such as DL-2-aminopropanol, L-2-aminobutynol, L-*n*-valinol, and L-valinol. These 2-amino alcohols are then cyclized via Wenker

reaction under the action of H₂SO₄ and NaOH in turn.^{21–23} In the cyclization process, the treatment of 2-amino alcohols with H₂SO₄ first results in a intermediate of sulfate ester, which is sequentially cyclized under NaOH. Finally, a series of aziridine derivatives, Compounds **2a–2d** such as 2-methylaziridine, 2-ethylaziridine, 2-*n*-propylaziridine and 2-*iso*-propylaziridine, are obtained as the polymerization monomers. Compounds **2a–2d** was identified by the measurement of ¹H-NMR spectra. The results are in accord with the chemical structures in Scheme 1.

Compounds **4a–4c**, Salen-metal complexes such as Salen-Co, Salen-Cr and Salen-Zn, which have been proved to be an efficient catalyst for the copolymerization of epoxides with CO₂,^{24–26} are synthesized by a two-step reaction according to the literature procedures.²⁷ First, Compound **3**, salicylaldehydoethylenediamine, is obtained as a Salen ligand in yellow lamellar crystals by the reaction of salicylaldehyde with ethylene diamine in methanol. The identification result of ¹H-NMR spectra is in accord with the chemical structure in Scheme 1. Subsequently, Salen ligand is coordinated with metallic ion provided by metal chlorides, such as cobaltous chloride (CoCl₂), chromic chloride (CrCl₃) and zinc chloride (ZnCl₂), affording three Salen complexes as the catalyst of CO₂ copolymerization reaction. These metal complexes will directly be used as a catalyst without any further purification. In general, four metallic coordination positions are occupied by Salen ligand and the coordination positions in the axial direction are vacated for the catalytic effect in the copolymerization reaction.

The copolymerization reaction is cautiously carried out in a 100 mL stainless steel autoclave due to the utilization of high gas pressure. First of all, four aziridine derivatives with different substituent are copolymerized under supercritical condition with CO₂ without any catalyst at 10 MPa and 100°C for 24 h. Poly(urethane amine)s (Entries 1–4) are obtained by the precipitation from the precipitating agents, such as the component solvent of methanol and ether. The polymeric products were characterized by ¹H-NMR, elemental analysis and GPC that employs a dual-detector system consisting of a MALLS device and a refractive index detector (GPC-MALLS). The ¹H-NMR spectra of Entry 1 was illustrated in Figure 1. Its urethane content is calculated from the data of elemental analysis or the ratio of the peak areas from the proton signals of CH₃ and CHNC=O, which are respectively located around δ1.10 and δ3.70 as shown in Figure 1. The urethane content of other polymers was obtained by a similar approach. All the relative data are summarized in Table I. The data of elemental analysis for the copolymers were inserted in Table S1 of the Supporting Information. It is evidently that products from Entries 1–4 have a similar chemical structure except for the difference in R-group and urethane content as shown in Scheme 1. The weight molecular weight (*M_w*) of Entries 1–4 in Table I indicated that Entries 1–3 have a similar *M_w* of ~1×10⁴, which is much less than 5.9×10⁴ of Entry 4. Obviously, the excellent solvation ability of 2-*iso*-propyl substituent with a branched structure would be beneficial to the molecular weight increase by enhancing the polymeric solubility in scCO₂, which is an apolar solvent because of the barycentre superposition of positive and negative charges in its linear molecular structure (O–C–O).

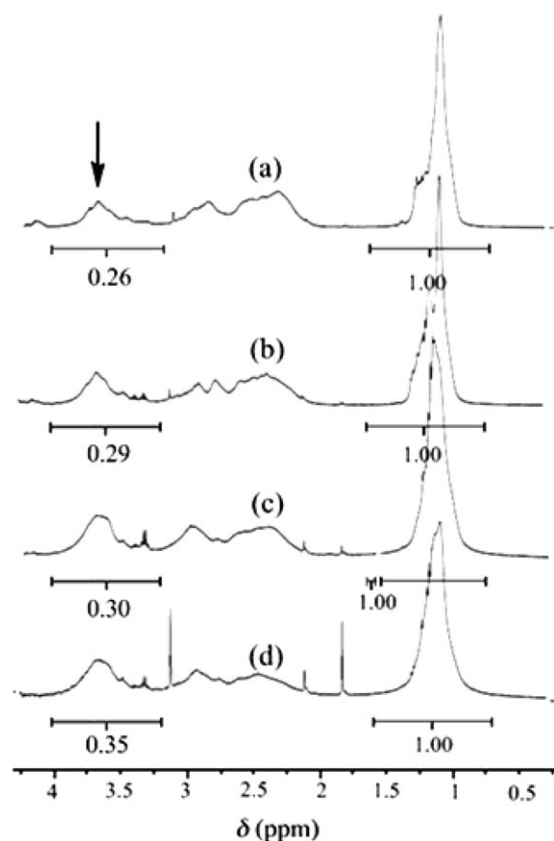
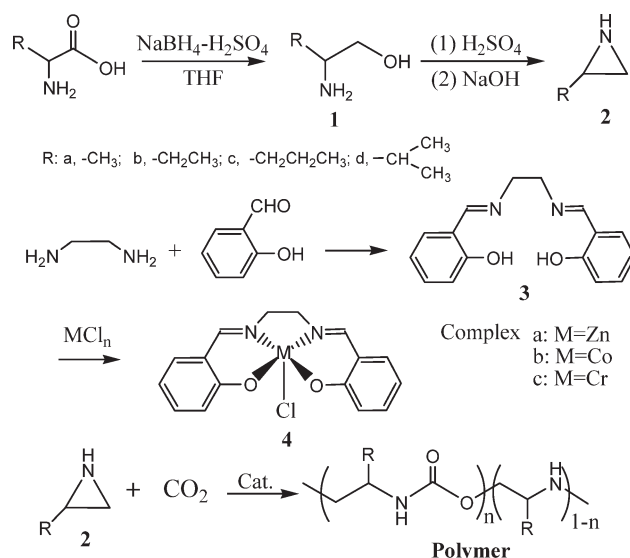


Figure 1. $^1\text{H-NMR}$ spectra in D_2O of the copolymer from 2-methylaziridine and CO_2 with different catalysts: (a) Entry 6 from Salen-Cr, (b) Entry 1 without any catalyst, (c) Entry 7 from Salen-Zn, (d) Entry 5 from Salen-Co.

Simultaneously, the urethane content is increased from 41.9% of Entry 1, 50.1% of Entry 2 and 41.4% of Entry 3 to 65.9% of Entry 4. It can be assumed that such a urethane content increase would be resulted from the improvement of polymerization probability of CO_2 by increasing the solubility of not only the monomer and the resulting polymer but also the intermediate species in the process of copolymerization reaction.



Scheme 1. Synthetic routes of aziridine derivatives, Salen-metal complexes and poly(urethane amine)s.

Notably, Entry 2 has a higher urethane content than Entries 1 and 3 in despite of a similar molecular weight. The lower urethane content of Entry 1 might be derived from the poor polymeric solubility in scCO_2 , which is induced by the short length of methyl aliphatic chain. The lower urethane content of Entry 3 may come from the steric hindrance of *n*-propyl group in the copolymerization. In other words, the higher urethane content of Entry 2 is resulted from the better polymeric solubility than Entry 1 and the lower steric hindrance of ethyl group than *n*-propyl group. Consequently, the urethane content of poly(urethane amine)s can be enhanced by increasing aliphatic substituent length of aziridine derivatives, except for the existence of steric hindrance from the aliphatic substituent. Therefore, we may have a conclusion that the substituent of aziridine derivatives can efficiently affect on both the molecular weight and the urethane content of poly(urethane amine)s.

The copolymerization of 2-methylaziridine with CO_2 was also performed under supercritical condition with different Salen-

Table I. Relative Data of the Copolymers from CO_2 and Aziridine Derivatives

Entry	Aziridines ^a	Catalyst	Yield (%) ^b	Urethane content (%) ^c	$M_w (\times 10^{-3})^d$	PDI ^d	LCST ($^{\circ}\text{C}$) ^e
1	2-Methylaziridine	-	35	41.9	12	1.67	50
2	2-Ethylaziridine	-	31	50.1	10	1.73	-
3	2- <i>n</i> -Propylaziridine	-	43	41.4	10	1.74	-
4	2- <i>iso</i> -Propylaziridine	-	47	65.9	59	2.03	-
5	2-Methylaziridine	Salen-Co	28	71.1	4.1	1.26	50
6	2-Methylaziridine	Salen-Cr	50	49.2	4.3	1.60	70
7	2-Methylaziridine	Salen-Zn	40	45.8	10	1.42	45

^a5 mL of aziridine, 0.05 g of catalyst, CO_2 pressure of 10 MPa, 100°C , 24 h.

^bEntries 1, 5, 6, and 7 were purified by reprecipitation from methanol/ether; Entries 2, 3, and 4 were purified via alumina column chromatography using dichloromethane as eluent.

^cCalculated from elemental analyses or $^1\text{H-NMR}$ spectra.

^dDetermined by GPC using a dual-detector system consisting of a MALLS device and a refractive index detector.

^eMeasured by a temperature-variable UV-vis spectrometer.

Table II. Solubility of Entries 2–4 in Aqueous Solution at Different pH Value

Entry	Aziridine	pH = 0.5	pH = 1.0	pH = 1.5	pH = 2.0
2	2-Ethylaziridine	+	+	+	–
3	2- <i>n</i> -Propylaziridine	+	–	–	–
4	2- <i>iso</i> -Propylaziridine	–	–	–	–

Tested at ambient temperature with the polymer concentration of 10 mg mL⁻¹; Solubility: +, soluble; –, insoluble.

metal complexes, including Salen-Co, Salen-Cr, and Salen-Zn, as a catalyst aiming to enhance the copolymerization ability of CO₂ and to regulate the urethane content of poly(urethane amine)s by the selection of metallic coordination ability of different metal ions, such as cobalt ion (Co²⁺), chromium ion (Cr³⁺) and zinc ion (Zn²⁺). The data in Table I indicated that the urethane content is increased from 41.9% of Entry 1 to 71.7% of Entry 5, 49.2% of Entry 6, and 45.8% of Entry 7. This suggested that the application of Salen-Co, Salen-Cr, and Salen-Zn as a catalyst can efficiently tune the urethane content of poly(urethane amine)s in the process of the copolymerization of aziridine derivatives with CO₂. It was presumed that the increase in urethane content should be realized by enhancing the polymerization ability of CO₂ under the catalytic effect of Salen-metal complexes, i.e., the application of Salen-metal catalysts can activate CO₂ to a certain extent and allow it efficiently to take part in the copolymerization reaction. However, the molecular weight of Entries 5 and 6 is respectively decreased to 4.1 × 10³ and 4.3 × 10³ while that of Entry 7 almost has no change compared with Entry 1. It was deemed that the large atomic weight of Co²⁺ and Cr³⁺ decreases the solubility of intermediate species in scCO₂. Therefore, the molecular weight of poly(urethane amine)s is decreased although the urethane content is increased. These points need a more precise investigation about the action of Salen-metal complexes for the copolymerization of aziridine derivatives with CO₂.

For the thermoresponsive characteristics of stimuli-responsive poly(urethane amine)s, the polymer solubility is an important issue because this will decide on the parameters of phase transition behavior, such as temperature, pH value, etc. With the aim of biomedical application, only the water solubility of poly(urethane amine)s is herein studied by the polymer aqueous solution with a concentration of 10 mg mL⁻¹. The polymeric water solubility is able dramatically to be changed by a little chemical modification on the substituent of aziridine derivatives. Poly(urethane-amine)s from 2-methylaziridine (Entries 1, 5, through 7) are easily soluble in water while those from 2-ethyl, 2-*n*-propyl, and 2-*iso*-propyl aziridines (Entries 2 through 4) are not sufficiently soluble in water at ambient temperature. However, the water solubility of Entries 2 and 3 take on an excellent pH-sensitivity in strong acid solution as shown in Table II. A pH-induced phase separation is produced from pH 1.5 to pH 2.0 in an aqueous solution of Entry 2 and caused from pH 0.5 to pH 1.0 in an aqueous solution of Entry 3. Visually, it is easy to observe the sharp phase transition between a transparent and cloudy solution as the pH value is changed. Additionally, Entry 4 is insoluble even in a strong acid solution. The solubility tuned by the solution acidity is attributed to the electrostatic

repulsion of the inter- and intra-molecule in the polymers. The amine groups in poly(urethane amine)s are capable of donating or accepting protons upon the change of pH value in the solution, which accompanies a reversible conformational transformation between the hydrophobic and hydrophilic states.²⁸ The polymeric pH-responsive property in strong acidic surroundings would attract a great deal of attention as a small variation in the pH value can induce some significant physical changes of the polymers. In addition, the solubility change of different entries might be primarily attributed to the different hydrophobicity of the substituent and the difference of urethane content regardless of the molecular weight of the polymers.

It is well known that the thermoresponsive property should be well controlled for practical applications as a smart material. In this work, the LCST will be regulated in a subtle balance between hydrophilic and hydrophobic moieties inside the polymers, which is realized by controlling the hydrophobic urethane content of poly(urethane amine)s. As was mentioned above, the urethane content of poly(urethane amine)s has been successfully tuned not only by changing the aliphatic substituent of aziridine derivatives as a comonomer but also by applying different Salen-metal complexes as a catalyst in the process of copolymerization reaction. In succession, the thermosensitive property of the resulting poly(urethane amine)s was estimated by the transparency measurement from the polymeric aqueous solution of 2.0 wt % at 500nm using a temperature-variable UV-vis spectrometer with a Julabo temperature controller. The

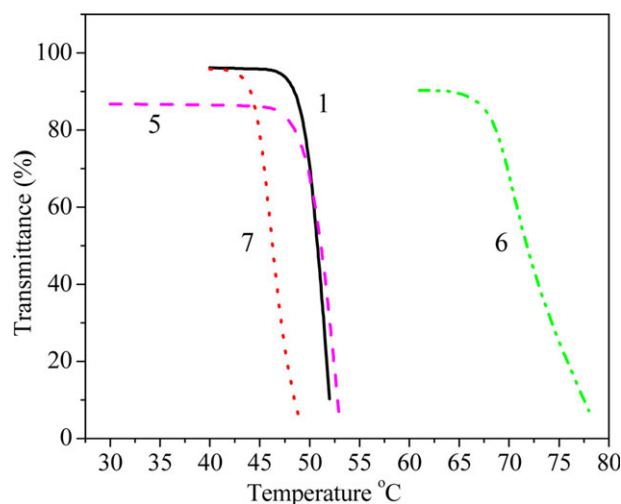


Figure 2. Light transmittances of 2.0 wt % aqueous solutions of Entries 1 and 5 through 7. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

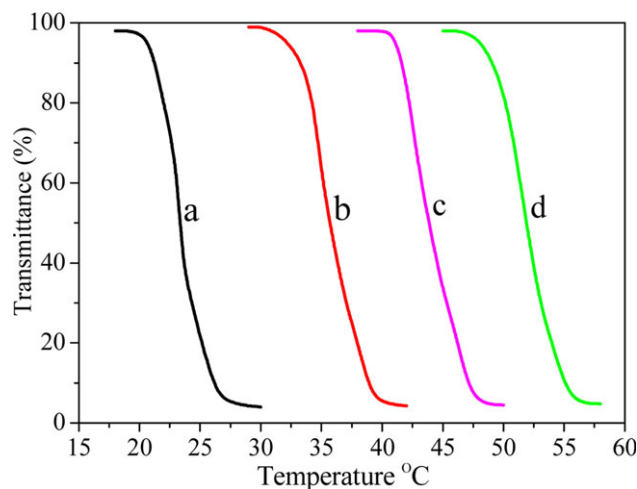


Figure 3. Light transmittances of 0.80 wt % solution of the product from Entry 7 adjusted to various pH: (a) pH 13.0, (b) pH 10.0, (c) pH 7.4, (d) pH 5.0. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

results indicated that Entries 1 and 5 through 7 take on an evident inverse temperature dependent solubility. Their light transmittance curves with the increase in temperature are shown in Figure 2. The LCST is defined as the onset point in the absorbance curve during the heating process. All the data are summarized in Table I.

From the data in Table I, only Entry 1 from 2-methylaziridine has a LCST of 50°C in the neutral solution for Entries 1 through 4 synthesized in the absence of Salen-metal complexes, although their urethane content has been successfully regulated by the replacement of aliphatic chain on aziridine derivatives. When the methyl substituent of Entry 1 is replaced by ethyl, *n*-propyl and *iso*-propyl substituent, there is no transmittance change between 30°C and 80°C in the aqueous solution of Entries 2-4. This is attributed to the decrease of water solubility derived from the high hydrophobic ability of long aliphatic chains, such as ethyl, *n*-propyl, *iso*-propyl groups. However, Entries 2 and 3 bear an evident pH-responsive behavior of water solubility in strong acidic environment as shown in Table II. Considering that the amino group of poly(urethane amine)s could be protonated with the decrease in pH value, the electrostatic repulsion between intra- and inter- molecule would influence the hydrophilicity and hydrophobicity by changing the equilibrium between amine and ammonium. Therefore, the hydrophobic/electrostatic balance is varied with different density of charges at different pH medium in the aqueous solution of poly(urethane amine)s. Simultaneously, the water solubility of poly(urethane amine)s is also increased with the enhancement of aqueous solution acidity, especially in strong acidic solution. This phenomenon allows us to believe that LCST can also be regulated by the change of pH value in polymeric aqueous solutions, which will be further proved and discussed by the following transmittance measurement of Entry 7 shown in Figure 3.

In addition, it has been known that the polymers synthesized with different Salen-metal complexes as a catalyst bear different

urethane content, which is an key issue to affect the hydrophilicity and hydrophobicity of poly(urethane amine)s. It is obviously that LCST is decreased from 50°C of Entry 1 to 45°C of Entry 7 due to the application of Salen-Zn in the copolymerization reaction. On account of their similar molecular weight, we believe that this LCST decrease is mainly derived from the increase in urethane content from 41.5% of Entry 1 to 45.8% of Entry 7. Therefore, we may draw a conclusion that a high urethane content will result in the decrease of LCST value of poly(urethane-amine)s due to the hydrophobicity of urethane segment. Notably, although the urethane contents of Entries 5 and 6 are respectively increased to 71.1% and 49.2%, their LCSTs are not decreased as Entry 7 owing to the lowering of molecular weight. Contrarily, LCST of Entry 6 is increased to 70°C and LCST of Entry 5 has no change compared with that of Entry 1. This result suggested that the molecular weight of the polymers is also another key issue to affect the LCST value of poly(urethane amine)s as proved in literature.^{29,30} In other words, the decrease in molecular weight will increase the LCST value of poly(urethane amine)s. For Entry 5, no LCST change comes from the impact counterbalance between the increase of urethane content and the decrease of molecular weight on the hydrophilicity and hydrophobicity of poly(urethane amine)s. Consequently, it was believed that the cloud point of thermoresponsive poly(urethane amine)s could be tuned not only by its composition but also by the degree of polymerization. These results also suggested that the phase transition behavior might be controlled through the proper selection and design of catalysts.

The light transmittance with the change of pH value was investigated in detail using the aqueous solution of Entry 7 with a concentration of 0.80 wt % by adjusting the pH value of aqueous solution from strong alkaline region (pH = 13.0) to weak acid region (pH = 5.0). In this case, the pH value will change the LCST by affecting the hydrophilicity and hydrophobicity of poly(urethane amine)s. The temperature is applied as an external stimulus, which tunes the more elaborate phase transition. The transmittance in different pH values was measured with the temperature increase as illustrated in Figure 3. The results indicated that the aqueous solutions of Entry 7 show a remarkable different phase transition in response to both temperature and pH value, indicating a potential double stimuli-responsive behavior. As we expected, the LCST value is gradually decreased from 49°C (pH = 5.0) to 21°C (pH = 13.0) with the increase of pH value in aqueous solution. This suggested that the thermoresponsive property in the aqueous solution of poly(urethane-amine)s is tunable within a wide temperature range, depending on the change of pH value from alkalinity to acidity.

The cyclic turbidity curves of thermosensitive poly(urethane amine)s, i. e., the phase transition with the controlled heating and cooling, indicated that the thermosensitive polymers undergo reversible conformational or phase changes in response to the temperature variation. This is involved in an elaborate free-energy balance of hydrophobic, hydrophilic and H-bridge-mediated intermolecular or intramolecular interaction,^{2,31} which determine the water solubility of poly(urethane amine)s. As expected, the most of the turbidity curves take on a temperature

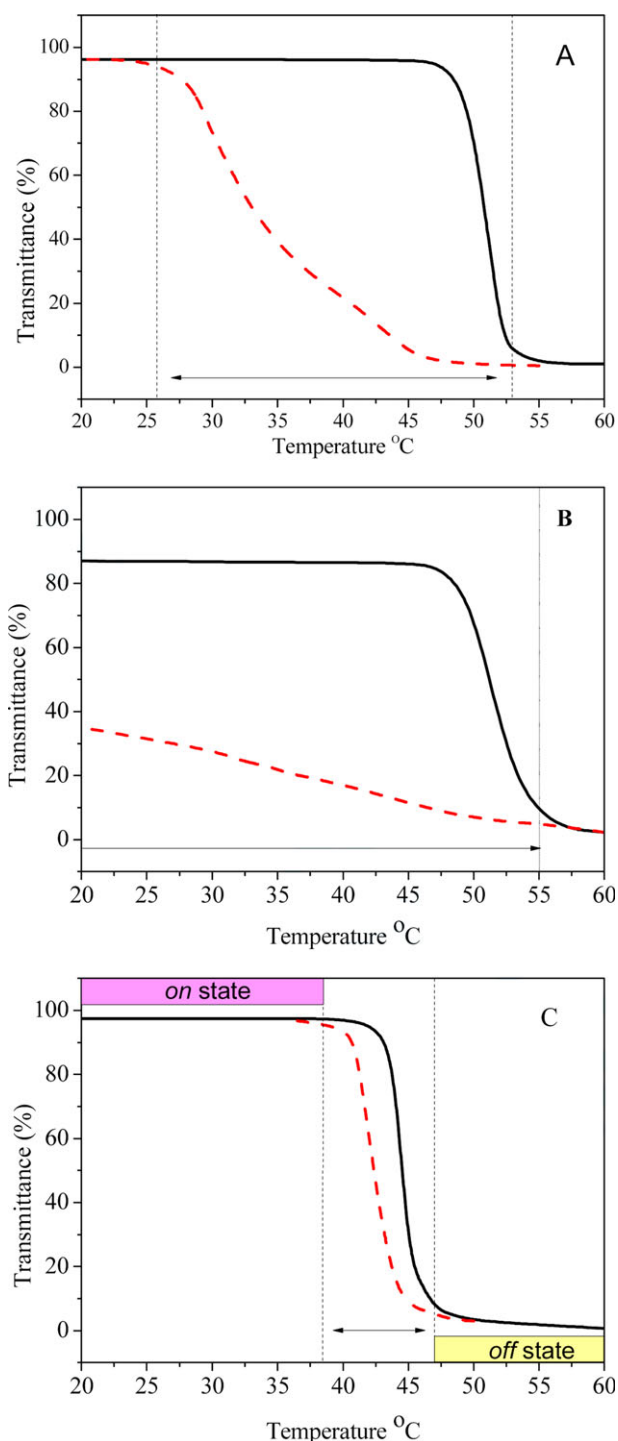


Figure 4. Plots of transmittance as a functional of temperature measured for aqueous solution (2.0 wt %) of (A) Entry 1, (B) Entry 5, (C) Entry 7; solid line, heating cycle; dash line, cooling cycle. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

hysteresis. The cyclic turbidity curves of Entries 1, 5 and 7 were showed in Figure 4. The results suggested that Entries 1 and 7 have a reversible phase transition as shown in Figure 4(a,b). However, Entry 1 exhibits an evident hysteresis in the cooling process while Entry 7 shows a sharp phase transition at LCST

not only in the heating process but also in the cooling process, indicating that no remarkable hysteresis exists when cooled. Notably, Entry 5 shown in Figure 4(b) has a quite serious hysteresis so that we deemed that it is an irreversible process. The aqueous solution of Entry 1 is changed to the turbidity state at $\sim 48^\circ\text{C}$, forming the solid precipitate. The degree of turbidity is not affected even if the temperature is increased above 53°C . In cooling, the turbidity starts to decrease close to 45°C and the solution becomes transparent at lower temperature although an evident hysteresis is revealed. This was previously observed in PNIPAAm with a narrow molecular weight distribution, which is related with an irreversible coil-to-globule transition from four distinct thermodynamically stable states.³²

At present, the reversible pH- and thermo-double responsive behavior of Entry 1 has been successfully applied to drug release as one component of alginate/polyacrylic acid (PAA)/poly(urethane amine)/ CaCO_3 due to the potential biodegradability and the absence of Salen-metal complexes in the synthetic process. Interestingly, the interaction between PAA and poly(urethane-amine) contributes the formation of alginate/ CaCO_3 hybrid beads with a unique morphology, in which the beads are covered with a compact inorganic layer.³³ Additionally, the sharp reversible thermoresponsive behavior of Entry 7 affords a potential application in photoswitching and sensor as shown in Figure 4(c).

The hysteresis between heating and cooling cycles likely arises from inter-/intra-chain hydrogen bonding at insoluble status as suggested in literature reports.³⁴ The most of thermoresponsive macromolecules possessing both H-bond donors and acceptors should theoretically exhibit a significant hysteresis. Below the critical temperature, the coil structure is favored as this allows the maximum interaction between the polymer and water. When strong hydrogen bonding is possible, the polymer has a low free energy of dissolution. However, the hydrogen-bonding effect is weakened above LCST. Concomitantly, the entropy-controlled “hydrophobic effect” increases. Hence, the polymer chains become partially dehydrated globules. In this collapsed state, the amines of poly(urethane-amine)s lead to the formation of intramolecular and intermolecular $\text{NH}\dots\text{O}=\text{C}$ hydrogen bonds that act as the “cross-linking points” to allow the chain aggregation. Therefore, the chain dissociation occurs only when the temperature is much lower than LCST, which is one main reason for the observed hysteresis.^{35,36} In addition, we deemed that the difference in thermoresponsive hysteresis is mainly derived from the minor subtly difference of chemical structure in the main chain of poly(urethane-amine)s, which was induced by different Salen-metal complexes as a catalyst in the copolymerization process. Basically, their thermosensitive hysteresis behaviors in aqueous solution is involved in a tailored elaborate balance between hydrophobic and hydrophilic segments in poly(urethane-amine)s. The specific relationship between hysteresis tunability and chemical structure is carefully being investigated in our laboratory.

CONCLUSIONS

The double stimuli responsive water-soluble poly(urethane amine)s with a reversible thermosensitive behavior were

synthesized in scCO₂ with/without Salen-metal complexes as a catalyst with renewable recourse as the starting materials. The LCST and phase transition behavior of poly(urethane amine)s are tuned by the selection of the substituent on the aziridine derivatives and the Salen-metal complexes used as a catalyst in the copolymerization process of aziridine derivatives and CO₂. Notably, the hysteresis behavior of reversible stimuli responsive thermosensitive behavior of poly(urethane amine)s is able to be changed via Salen-metal catalysts with different metal ions.

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