

**Study on Novel Thermoresponsive Phase Behavior of
Copolymer Solutions**

2011

Zhenjie Liu

Acknowledgements

I am very grateful to the program of international program in Nagoya Institute of Technology funded by the Japanese government, which let me carry out my research whole-heartedly and experience many unforgettable things in life. Owing to this program, I could come to Japan to study my favorite science, make friends and experience a different life style and Japanese culture. It is very valuable for me to live and study in Japan in the past three years. All what had happened during my period of staying in Japan would be wonderful memories.

I show my sincerely heartfelt gratitude to Professor Katsuhiko Inomata, my supervisor, who always gave me advice and suggestion throughout my study. I thank Professor Katsuhiko Inomata very much for revising and submitting research papers. I am also very deeply grateful to Professor Katsuhiko Inomata for painstaking care in my life in Japan in past days.

Thank every student in the laboratory of Professor Katsuhiko Inomata very much for their help in past years. Thanks for helping to do some experiments and measurements. Thanks for caring and helping when I had troubles in my daily life.

Thanks Professor Eiji Nakanishi, Professor Masahito Suzuki, Professor Masahiro Higuchi and Professor Wan-tai Yang for reviewing the doctor thesis and giving some very useful suggestions.

Finally, I should show my great appreciation to my family for supporting and trusting me in the past so many years. I am also truly grateful to my friends for their listening, advising and encouraging in some tight corner.

Content

Chapter 1

Introduction	1
---------------------------	----------

Chapter 2

Reversible Thermoresponsive Behavior of Poly(2-chloroethyl vinyl ether-<i>alt</i>-maleic anhydride) in Organic Media under Mild Conditions	13
---	-----------

2-1 Introduction	13
------------------------	----

2-2 Experimental	14
------------------------	----

2-2-1 Materials	14
-----------------------	----

2-2-2 Synthesis of Polymer	14
----------------------------------	----

2-2-3 Nuclear Magnetic Resonance (NMR)	14
--	----

2-2-4 Fourier Transform Infrared Spectroscopy (FT-IR)	15
---	----

2-2-5 Gel Permeation Chromatograph (GPC)	15
--	----

2-2-6 Thermoresponsive Measurement of Polymer Solution	15
--	----

2-3 Results and Discussion	16
----------------------------------	----

2-3-1 Synthesis of Copolymer	16
------------------------------------	----

2-3-2 Reversible Thermoresponsive Behavior	18
--	----

2-4 Conclusion	22
----------------------	----

Chapter 3

Reversible Thermoresponsive Behavior of Poly(2-chloroethyl vinyl ether-<i>alt</i>-maleic anhydride) in Mixed Solvent of Tetrahydrofuran/Hexane	25
---	-----------

3-1 Introduction	25
------------------------	----

3-2 Experimental part	26
-----------------------------	----

3-2-1 Materials	26
-----------------------	----

3-2-2 Synthesis of polymers	26
-----------------------------------	----

3-2-3 Gel Permeation Chromatograph (GPC)	26
--	----

3-2-4 FT-IR measurement	27
-------------------------------	----

3-2-5 Sample preparation of polymer solution	27
--	----

3-2-6 Static light scattering (SLS) measurement	27
---	----

3-2-7 ¹ H NMR measurement	27
--	----

3-3 Results and Discussion	28
----------------------------------	----

3-3-1 Synthesis and chemical composition of copolymers	28
--	----

3-3-2 LCST-type phase behavior of polymer solution	28
--	----

3-3-3 Effect of polymer concentration and solvent composition on T _{cp}	29
--	----

3-3-4 NMR spectra of polymer solution	33
---	----

3-5 Conclusion	35
Chapter 4	
LCST-type Phase Behavior of Poly(2-chloroethyl vinyl ether-<i>alt</i>-maleic anhydride) in <i>n</i>-Butyl Acetate	40
4-1 Introduction	40
4-2 Experimental	41
4-2-1 Materials	41
4-2-2 Synthesis of Copolymer	41
4-2-3 Gel Permeation Chromatograph (GPC)	42
4-2-4 Preparation of Polymer Solutions	42
4-2-5 Light Scattering	42
4-3 Results and discussion	43
4-3-1 Synthesis of Copolymers	43
4-3-2 LCST-type Phase Behavior of Polymer Solution	44
4-3-3 Effect of Addition of Co-solvent on the T_{cp} of P(CVE-MA)/BuAc	50
4-4 Conclusion	55
Chapter 5	
Thermoreversible UCST-type Phase Behavior of Comb-like Poly(phenyl maleimide-<i>co-n</i>-octadecyl vinyl ether) Copolymer in Organic Media	60
5-1 Introduction	60
5-2 Experimental	61
5-2-1 Materials	61
5-2-2 Synthesis of polymers	62
5-2-3 Gel Permeation Chromatograph (GPC)	62
5-2-4 FT-IR measurement	62
5-2-5 ^1H NMR measurement	62
5-2-6 ^{13}C NMR measurement	63
5-2-7 Preparation of polymer solution	63
5-2-8 Static Light Scattering (SLS) Measurement	63
5-3 Results and discussion	63
5-3-1 Synthesis of copolymer	63
5-3-2 UCST-type thermoresponsive behavior of polymer solution	67
5-3-3 Effect of solvent and co-solvent on UCST-type thermoresponsive behavior	69
5-3-4 High resolution ^1H NMR spectra of copolymer in DMF- d_7 at different temperatures	73

5-4 Conclusion.....	75
Chapter 6	
Conclusion	80
Publications	82
Academic conferences	82

Chapter 1

Introduction

Stimuli-sensitive polymers are a kind of polymers which can change physical properties or chemical structure abruptly and abundantly responding to small changes of external stimuli in environment. Until now, many external stimuli can be employed to induce stimuli-sensitive behavior of polymer and these external stimuli can be temperature, light, magnetic or electric field, acoustic field, mechanical forces, pH value or ionic strength in aqueous media, or some additives in some proper media.¹

In the past great enthusiasm has been plunged into the research on stimuli-sensitive polymers and many kinds of stimuli-sensitive polymers have been developed. Light can be controlled conveniently without the limitation of time or space and the light irradiation processes can be tuned by switching on/off the light source or changing the light parameter such as the wavelength or the intensity, so a lot of light-sensitive polymers have been prepared²⁻⁴. Usually some photo-sensitive moieties such as azobenzene² or *o*-nitrobenzyl chromophores³ were incorporated into polymers and these light responsive polymers can be used in many fields such as drug delivery, holography, and nanoporous materials.⁴ As an electric field was imposed on some polymers, those polymer materials may bend, shrink or swell. Those polymers are called electro-responsive polymers which will change their properties in respond to external electro field. Electro-responsive polymers can change electrical energy into mechanical energy and can be used as smart materials which may be useful for sensing, artificial muscle actuation, energy transduction and controlled drug delivery.^{1, 5-15} As polymer chain was immobilized directly onto the surface of magnetic particles by covalent bond or polymer network entrapped magnetic particles, polymer system can respond to magnetic field.^{1, 16-19} Due to responding to external magnetic field, the magnetic-responsive polymers can be used for sensors, cancer therapy agents, switches, separation media, and drug delivery systems.^{1, 20} Some particular polymers which can be sensitive to some special agents especially to biological molecules also were synthesized and these stimuli-responsive polymers own the potentiality for biosensing/diagnostics, controlled drug delivery, smart films/matrices for tissue engineering. Polymers with disulfide bond can be reversibly converted to thiols expose to reducing agents or undergo disulfide exchange meeting other thiols and these polymers can be considered redox-/thiol-responsive polymers.^{1, 21} Because in many bio-processes transformation from thiol to disulfides is very important for proteins, so redox-/thiol-responsive polymers can be used for drug delivery.^{1, 22-24} Polymers

composed of enzyme-sensitive substrates are enzyme-responsive polymers which can lead to supramolecular architecture or macroscopic transition and these polymers can be used in some bio-engineering fields.^{1, 25-28} Polymer which can respond to glucose is another class of biological molecule-sensitive polymers owning great potential applications for glucose sensing or insulin delivery¹. The glucose-responsive polymer can be synthesized based on reversible reaction¹ between glucose and boronic acid,²⁹⁻³² reaction between glucose and oxygen catalyzed by glucose oxidase³³⁻³⁴ and competitive binding of glucose with glycopolymer-lectin complexes³⁵. The glucose-responsive polymer can be used for insulin delivery and so on.³⁶ The pH-responsive polymer is also a very important kind of stimuli-sensitive polymers and attracts research attention. The pH-responsive polymer can change their conformation according to the pH value of aqueous solution resulting in changes of solubility in water. Usually, the pH-responsive polymers bear weakly ionizable groups and will change the degree of ionization with the change of pH value¹. So the pH-responsive polymers are some polyacids or polybases.¹ Polyacids such as poly(acrylic acid)³⁷ and poly(methacrylic acid)³⁸ accept protons at low pH value and release protons at neutral and high pH value in water. When polyacids release protons at higher pH values polyelectrolyte will be formed and the electrostatic repulsion between polymer chain segments will reinforce the solubilization of polymer chains, however, when the pH value is low the polymer chain segments will be protonated and the electrostatic repulsion between polymer chains will disappear resulting in aggregation of polymer chain because of the dominance of hydrophobic effect between protonated polymer chain.^{1,37} Whereas polybases such as Poly(N,N-dimethyl aminoethyl methacrylate)³⁹, poly(N,N-diethyl aminoethyl methacrylate)⁴⁰, Poly(vinylpyridine)⁴¹ and Poly(vinyl imidazole)⁴² will be protonated at alkaline condition and positively ionized at low and neutral solution conditions.¹ The positively ionized polymer chains own reinforced solubilization because of electrostatic repulsion between ionized polymer chain segments. Usually, polybases with a pendent amine group accept protons at acidic solution conditions with a low pH value and release them at high pH value resulting in aggregation of polymer chains due to hydrophobic interactions between the polymer chains.^{1, 40} The pH-responsive polymer can be grafted onto a membrane and obtain a material with a pH-responsive surface.^{1,43, 44} The pH-responsive polymer also is used widely in some bio-related fields such as intelligent bioconjugate^{1, 45, 46} and drug delivery^{1, 47-49}.

Besides those stimuli-sensitive polymers mentioned above, because of conveniently control and easy application to some fields, temperature is a most common and popular stimulus in responsive-stimuli polymer systems. So thermoresponsive polymer is also a

very important kind of stimuli-sensitive polymers. Thermoresponsive polymer could abruptly change their some properties such as solubility and chain conformation responding to small changes of temperature. Usually, thermoresponsive polymer system exists as a solution state at which polymer solution owns a critical solution temperature depending on the polymer concentration, and according to the phase behavior with respond to temperature change thermoresponsive polymer can be divided into two classes. One owns an upper critical solution temperature (UCST) above which polymer solution is one phase, while below UCST the polymer solution is heterogeneous. The other has a lower critical solution temperature (LCST) and above LCST phase separation will occur.^{1, 50-51}

In the past several decades LCST polymers in water has provoked lots of interest and many LCST-related applications have been developed. Water soluble LCST polymers usually contain hydrophilic and hydrophobic moieties, and between macromolecule and water there exist some intermolecular forces such as hydrogen bonding or balance between hydrophilic and hydrophobic interaction.^{1,50-51} As the temperature is lower than LCST, because the hydrophilic interaction dominates or there exist a relatively strong hydrogen bonding between polymer chain and water the polymer can dissolve in water with a coil conformation.^{1, 50-51} As the temperature is above LCST, the hydrophobic interaction dominates or the hydrogen bonding between macromolecule and water is disrupted, and the polymer becomes insoluble in water resulting in phase separation.^{1, 50-51} At the temperature above LCST, the conformation of polymer chain will change from coil to globule. Until now many water soluble thermoresponsive polymers have been synthesized and studied.^{1,50-51} The water soluble thermoresponsive polymer can be grafted onto surfaces or interfaces and an intelligent surface or interface can be obtained, which can be used in some fields such as chromatograph and temperature modulated membrane.⁵²⁻⁵³ The water soluble thermoresponsive polymer can be conjugated to some bio-molecules and the activity of obtained bio-molecules can be controlled by the temperature. Based on the interaction or affinity between a certain bio-molecules and bio-conjugated thermoresponsive polymer, some intelligent applications in bio-related fields can be developed.^{1, 50-56} For example, bio-conjugated thermoresponsive polymers can be used for proteins separation, and some materials modified by the thermoresponsive polymer can also be used for cell manipulation.⁵⁴ A very important application of water soluble thermoresponsive is drug delivery, and based on the thermoresponsive polymers many controlled release systems have been developed.⁵⁵ Water soluble thermoresponsive polymers can also be made into hydrogel and hydrogels based on water soluble thermoresponsive polymers also own

some important applications such as drug delivery, shape memory materials and tissue engineering materials.⁵⁶

Thermoresponsive behavior of polymer in some nonaqueous media such as in ionic liquids or organic media also attracts much research interest. Researches on ionic liquid is booming because of some advantages such as chemical stability, nonflammability, and thermoresponsive polymer systems in ionic liquid have also been studied.⁵⁷⁻⁶⁰

Nowadays, due to academic interest and industrial applications thermoresponsive polymers in organic media have started to attract much attention. Though thermoresponsive polymers have been studied many decades ago, the conventional thermoresponsive polymer system such as UCST-type and LCST-type usually exhibits thermoresponsive behavior at some tough conditions such as at high temperature near or above the boiling point of solvent or in sealed cells.⁶¹⁻⁶⁷ It is not so convenient to study the conventional thermoresponsive polymer systems due to the need for tough conditions. Though the study on conventional organic thermoresponsive polymer system can help to understand polymer science and build some theory especially on polymer solution chemistry, applications based on organic thermoresponsive polymer systems were seldom developed with a comparison with aqueous thermoresponsive polymer systems. So it is necessary to discover new thermoresponsive organic polymer systems which can exhibit thermoresponsive behavior at mild conditions, and until now only very a few new organic thermoresponsive polymer systems have been developed.⁶⁸⁻⁷⁵

As for LCST-type thermoresponsive polymer systems, there usually exist two kinds of systems based on the driving force which causes phase separation with increasing temperature. One is polymer aggregation resulting from the hydrophobic interaction due to the collapse of hydrogen bonding or amphiphilic balance, and usually this kind of polymer systems is aqueous.^{1, 51} In aqueous polymer solution the interaction between polymer chain and water molecule is strong enough, which can be recognized by many kinds of measurements,⁷⁶ and the volume change of polymer usually is very large during phase separation. In the other LCST-type thermoresponsive polymer system, the phase separation with increasing temperature is because of the difference of expansivity or free volume between polymer and solvent, and usually this kind of thermoresponsive behavior happens at critical conditions of solvent, e.g., close to or higher than the boiling point of solvent.⁶¹⁻⁶⁷ The second LCST-type phase behavior of polymer solution usually occurs in organic media, of course, at critical conditions of solvent, and this kind of thermoresponsive behavior can be understood well by some classic free volume theories,⁷⁷ e.g. the solvent is much more expanded than the polymer and the this

difference can lead to the phase separation, so high molecular weight polymer usually incline to occur phase separation close to critical condition of the solvent such as near the boiling point of the solvent.⁷⁸ Nowadays, some attention is being paid to the research on novel LCST-type thermoresponsive polymer systems in organic media. These novel thermoresponsive polymer systems were different from conventional LCST-type polymer systems, and they can exhibit thermoresponsive behavior at mild conditions.⁶⁸⁻⁷⁰ Usually in these novel thermoresponsive polymer systems polymer owned unique chemical structure or there exist some unique interactions between polymer and organic solvent molecules, e.g., poly(vinyl ether) with ionic liquid pendants,⁷⁰ fluoroalkyl-end-capped polymer⁶⁸ and heat-set gel-like networks with metal complexes⁶⁹ can exhibit LCST characteristic behavior in organic media.

In our study, we discovered a novel organic polymer solution which can exhibit LCST characteristic behavior at mild conditions and the cloud point of polymer solution can be tuned conveniently. Because the discovered polymer systems exhibit LCST characteristic behavior at mild condition not at solvent critical, the possibility for the reason why phase separation happens is the difference of free volume between polymer and solvent is small. In another hand because polymer exhibited LCST-type thermoresponsive behavior in some weak polar organic solvent at mild conditions, so there could exist no strong interaction between polymer and organic solvent. So the reason why our discovered polymer system can exhibit LCST-type behavior may be that there exist a unique interaction between our synthesized polymer and used solvent, and this interaction may change with temperature changes resulting in phase separation in a critical point.

As for UCST-type thermoresponsive organic polymer solution, it is very important and useful to discover a tunable UCST-type thermoresponsive organic polymer solution though it is common that polymer can exhibit UCST-type thermoresponsive behavior. Until now only very a few tunable UCST-type organic polymer solution system were obtained.⁷¹⁻⁷⁴ These tunable UCST-type organic polymer systems especially at mild conditions own some useful applications. As polymer chains were grafted onto the surface of some colloid particles, based on the UCST-type thermoresponsive behavior in organic media the aggregation of related colloidal particles can be controlled by temperature, e.g., temperature-induced aggregation of magnetic nanoparticles grafted by poly(2-methoxyethyl methacrylate) in methanol⁷⁹ or polystyrene in cyclohexane⁸⁰.

In our study on UCST-type thermoresponsive polymer solutions, a novel tunable organic copolymer solution was discovered. The discovered organic polymer system can exhibit UCST characteristic behavior at mild conditions, and it is distinct that the

cloud point of organic polymer solution can be tuned conveniently in a wide temperature range.

If the organic thermoresponsive polymer system owns a well tunable ability to switch with the temperature change, there is a possibility that some smart or intelligent materials can be designed based on that thermo switch. For example, based on the LCST or UCST thermo moieties, the thermo switchable self-assembly micellar system can be designed, which is useful for some applications such as sensor or nano-reactor in organic media.

The study in this thesis focuses on discovering novel organic thermoresponsive polymer systems at mild conditions, investigating the thermoresponsive behavior of those thermoresponsive systems and trying to comprehending the possible related theories.

REFERENCE

- 1 Gil, E.S. & Hudson, S.M. Stimuli-responsive polymers and their bioconjugates. *Prog. Polym. Sci.* **29**, 1173–1222 (2004).
- 2 Kumar, G. S. Photochemistry of Azobenzene-Containing Polymers. *Chem. Rev.* **89**, 1915-1925 (1989).
- 3 Schumers, J-M., Fustin, C-A., Can, A., Hoogenboom, R., Schubert, U.S. & Gohy, J-F. Are o-Nitrobenzyl (Meth)acrylate Monomers Polymerizable by Controlled-Radical Polymerization. *J. Polym. Sci., Part A: Polym. Chem.* 2009, **47**, 6504-6513.
- 4 Schumers, J-M., Fustin, C-A. & Gohy, J-F. Light-responsive block copolymers. *Macromol. Rapid Commun.* **31**, 1588-1607 (2010).
- 5 Yao, L. & Krause S. Electromechanical responses of strong acid polymer gels in DC electric fields. *Macromolecules* **36**, 2055-2065(2003).
- 6 Kim, S.J., Yoon, S.G., Lee, Y.H. & Kim, S.I. Bending behavior of hydrogels composed of poly(methacrylic acid) and alginate by electrical stimulus. *Polym. Int.* **53**, 1456–1460 (2004).
- 7 Kim, S.Y., Shin, H. S., Lee, Y.M. & Jeong, C. N. Properties of electroresponsive poly(vinyl alcohol)/poly(acrylic acid) IPN hydrogels under an electric stimulus. *J. Appl. Polym. Sci.* **73**, 1675–1683 (1999).
- 8 Homma, M., Seida, Y. & Nakano, Y. Evaluation of optimum condition for designing high-performance electro-driven polymer hydrogel systems. *J. Appl. Polym. Sci.* **75**, 111–118 (2000).
- 9 Kim, S. J., Park, S.J., Kim, I.Y., Shin, M-S. & Kim, S.I. Electric stimuli responses to poly(vinyl alcohol)/chitosan interpenetrating polymer network hydrogel in NaCl solutions. *J. Appl. Polym. Sci.* **86**, 2285–2289 (2002).

- 10 Kim, S.J., Park, S.J., Shin, M-S. & Kim, S.I. Characteristics of electrical responsive chitosan/polyallylamine interpenetrating polymer network hydrogel. *J. Appl. Polym. Sci.* **86**, 2290–2295 (2002).
- 11 Kim, S.J., Park, S.J., Lee, S.M., Lee, Y.M., Kim, H.C. & Kim, S.I. Electroactive characteristics of interpenetrating polymer network hydrogels composed of poly(vinyl alcohol) and poly(n-isopropylacrylamide). *J. Appl. Polym. Sci.* **89**, 890–894 (2003).
- 12 Kim, S.J., Shin, S.R., Lee, J.H., Lee, S.H. & Kim, S. I. Electrical response characterization of chitosan/polyacrylonitrile hydrogel in NaCl solutions. *J. Appl. Polym. Sci.* **90**, 91–96 (2003).
- 13 Kim, S.J., Yoon, S.G., Lee, S.M., Lee, S.H. & Kim, S.I. Electrical sensitivity behavior of a hydrogel composed of poly(methacrylic acid)/poly(vinyl alcohol). *J. Appl. Polym. Sci.* **91**, 3613–3617 (2004).
- 14 Kim, S.J., Kim, H.I., Shin, S.R. & Kim, S.I. Electrical behavior of chitosan and poly(hydroxyethyl methacrylate) hydrogel in the contact system. *J. Appl. Polym. Sci.* **92**, 915–919 (2004).
- 15 Gao, Y., Xu, S., Wu, R., Wang, J. & Wei, J. Preparation and characteristic of electric stimuli responsive hydrogel composed of polyvinyl alcohol/poly (sodium maleate-co-sodium acrylate). *J. Appl. Polym. Sci.* **107**, 391–395 (2008).
- 16 Szabó, D., Szeghy, G. & Zrínyi, M. Shape transition of magnetic field sensitive polymer gels. *Macromolecules* **31**, 6541–6548 (1998).
- 17 Wang, G., Tian, W.J. & Huang, J. P. Response of ferrogels subjected to an AC magnetic field. *J. Phys. Chem. B* **110**, 10738–10745 (2006).
- 18 Zhang, J., Xu, S. & Kumacheva, E. Polymer microgels: reactors for semiconductor, metal, and magnetic nanoparticles. *J. Am. Chem. Soc.* **126**, 7908–7914 (2004).
- 19 Suzuki, D. & Kawaguchi, H. Stimuli-sensitive core/shell template particles for immobilizing inorganic nanoparticles in the core. *Colloid Polym. Sci.* **284**, 1443–1451 (2006).
- 20 Oh, J.K. & Park, J.M. Iron oxide-based superparamagnetic polymeric nanomaterials: Design, preparation, and biomedical application. *Prog. Polym. Sci.* **36**, 168–189 (2011).
- 21 Oh, J.K., Siegwart, D.J., Lee, H-i., Sherwood, G., Peteanu, L., Hollinger, J.O., Kataoka, K. & Matyjaszewski, K. Biodegradable nanogels prepared by atom transfer radical polymerization as potential drug delivery carriers: synthesis, biodegradation, in vitro release, and bioconjugation. *J. Am. Chem. Soc.* **129**, 5939–5945 (2007).

- 22 You, Y-Z., Zhou, Q-H., Manickam, D.S., Wan, L., Mao, G-Z. & Oupicky, D. Dually responsive multiblock copolymers via reversible addition-fragmentation chain transfer polymerization: synthesis of temperature- and redox-responsive copolymers of poly(*n*-isopropylacrylamide) and poly(2-(dimethylamino)ethyl methacrylate). *Macromolecules* **40**: 8617–8624 (2007).
- 23 Sun K.H., Sohn Y.S. & Jeong B. Thermogelling poly(ethylene oxide-*b*-propylene oxide-*b*-ethylene oxide) disulfide multiblock copolymer as a thiol-sensitive degradable polymer. *Biomacromolecules* **7**, 2871–2877(2006).
- 24 Zelikin, A.N., Quinn, J.F. & Caruso F. Disulfide cross-linked polymer capsules: en route to biodeconstructible systems. *Biomacromolecules* **7**, 27–30 (2006).
- 25 Thornton, P. D., McConnell, G. & Ulijn, R.V. Enzyme responsive polymer hydrogel beads. *Chem. Commun.* **47**, 5913–5915 (2005).
- 26 Ulijn, R.V. Enzyme-responsive materials: a new class of smart biomaterials. *J. Mater. Chem.* **16**, 2217–2225 (2006).
- 27 Sperinde, J. J. & Griffith, L.G. Synthesis and characterization of enzymatically cross-linked poly(ethylene glycol) hydrogels. *Macromolecules* **30**, 5255–5264 (1997).
- 28 Sperinde, J. J.; Griffith, L.G. Control and prediction of gelation kinetics in enzymatically cross-linked poly(ethylene glycol) hydrogels. *Macromolecules* **33**, 5476–5480 (2000).
- 29 Matsumoto, A., Kurata, T., Shiino, D. & Kataoka, K. Swelling and shrinking kinetics of totally synthetic, glucose-responsive polymer gel bearing phenylborate derivative as a glucose-sensing moiety. *Macromolecules* **37**, 1502–1510 (2004).
- 30 Zhang, Y.; Guan, Y. Zhou, S. Synthesis and volume phase transitions of glucose-sensitive microgels. *Biomacromolecules* **7**, 3196–3201 (2006).
- 31 Lapeyre, V., Gosse, I., Chevreux, S. & Ravaine, V. Monodispersed glucose-responsive microgels operating at physiological salinity. *Biomacromolecules* **7**, 3356–3363 (2006).
- 32 Hoare, T. & Pelton, R. Charge-switching, amphoteric glucoseresponsive microgels with physiological swelling activity. *Biomacromolecules* **9**, 733–740 (2008).
- 33 Hassan, C.M.; Doyle I I I, F.J.; Peppas, N.A. Dynamic behavior of glucoseresponsive poly(methacrylic acid-*g*-ethylene glycol) hydrogels. *Macromolecules* **30**, 6166–6173 (1997).
- 34 Podual, K., Doyle III, F.J. & Peppas, N. A. Preparation and dynamic response of cationic copolymer hydrogels containing glucose oxidase. *Polymer* **41**, 3975–3983 (2000).

- 35 Liu, F., Song, S.C., Mix, D., Baudy, M. & Kim, S.W. Glucose-induced release of glycosylpoly(ethylene glycol) insulin bound to a soluble conjugate of concanavalin A. *Bioconjugate Chem.* **8**, 664–672(1997).
- 36 Kataoka, K., Miyazaki, H., Bunya, M., Okano, T. & Sakurai Y. Totally synthetic polymer gels responding to external glucose concentration: their preparation and application to on-off regulation of insulin release. *J. Am. Chem. Soc.* **120**, 12694–12695 (1998).
- 37 Philippova, O.E., Hourdet, D., Audebert, R. & Khokhlov, A.R. pH-responsive gels of hydrophobically modified poly(acrylic acid). *Macromolecules* **30**, 8278–8285 (1997).
- 38 Torres-Lugo, M. & Peppas, N.A. Molecular design and in vitro studies of novel pH-sensitive hydrogels for the oral delivery of calcitonin. *Macromolecules* **32**: 6646–6651 (1999).
- 39 Okubo, M., Ahmad, H. & Suzuki, T. Synthesis of temperaturesensitive micron-sized monodispersed composite polymer particles and its application as a carrier for biomolecules. *Colloid. Polym. Sci.* **276**, 470–475 (1998).
- 40 Lee, A.S., Bütün, V., Vamvakaki, M., Armes, S.P., Pople, J.A. & Gast, A.P. Structure of pH-dependent block copolymer micelles: charge and ionic strength dependence. *Macromolecules* **35**, 8540–8551 (2002).
- 41 Gohy, J-F., Lohmeijer, B. G.G., Varshney, S.K., Décamps, B., Leroy, E., Boileau, S. & Schubert, U. S. Stimuli-responsive aqueous micelles from an ABC metallo-supramolecular triblock copolymer. *Macromolecules* **35**, 9748–9755 (2002).
- 42 Sutton, R. C., Thai, L., Hewitt, J. M., Voycheckand, C. L. & Tan, J. S. Microdomain characterization of styrene–imidazole copolymers. *Macromolecules* **21**, 2432–2439 (1988).
- 43 Iwata, H., Hirata, I. & Ikada, Y. Atomic force microscopic analysis of a porous membrane with pH-sensitive molecular valves. *Macromolecules* **31**, 3671–3678 (1998).
- 44 Ying, L., Wang, P., Kang, E. T. & Neoh, K. G. Synthesis and characterization of poly(acrylic acid)-graft-poly(vinylidene fluoride) copolymers and pH-sensitive membranes. *Macromolecules* **35**, 673–679 (2002).
- 45 Asayama, S., Maruyama, A., Cho, C. & Akaike, T. Design of comb-type polyamine copolymers for a novel pH-sensitive DNA carrier. *Bioconjugate Chem.* **8**, 833–838 (1997).

- 46 Cheung, C.Y., Murthy, N., Stayton, P.S. & Hoffman, A. S. A pH sensitive polymer that enhances cationic lipid-mediated gene transfer. *Bioconjugate Chem.* **12**, 906–910 (2001).
- 47 Risbud, M.V., Hardikar, A.A., Bhat, S.V. & Bhonde, R. R. pH sensitive freeze-dried chitosan–polyvinyl pyrrolidone hydrogels as controlled release system for antibiotic delivery. *J. Control. Release* **68**, 23–30 (2000).
- 48 Brown, C.D., Kreilgaard, L., Nakakura, M., Caram-Lelham, N., Pettit, D.K., Gombotz, W.R. & Hoffman, A. S. Release of PEGylated granulocyte-macrophage colony-stimulating factor from chitosan/glycerol films. *J. Control. Release* **72**, 35–46 (2001).
- 49 Kakoulides, E.P., Smart, J.D. & Tsibouklis, J. Azocross-linked poly(acrylic acid) for colonic delivery and adhesion specificity: synthesis and characterization. *J. Control. Release* **52**, 291–300 (1998).
- 50 Liu, F. & Urban MW. Recent advances and challenges in designing stimuli-responsive polymers. *Prog. Polym. Sci.* **35**, 3-23 (2010).
- 51 Liu, R., Fraylich, M. & Saunders, B. R. Thermoresponsive copolymers: from fundamental studies to applications. *Colloid. Polym. Sci.* **287**, 627–643 (2009).
- 52 Park, Y.S., Ito, Y. & Imansish, Y. Permeation control through porous membranes immobilized with thermosensitive polymer. *Langmuir* **14**, 910–914 (1998).
- 53 Ma, C.S., Zhang, W. & Ciszowska, M. Transport of ions and electrostatic interactions in thermoresponsive poly(*N*-isopropylacrylamide-co-acrylic acid) hydrogels: electroanalytical studies. *J. Phys. Chem. B* **105**, 10446–10452(2001).
- 54 Jeong, B. & Gutowska, A. Lessons from nature: stimuli-responsive polymers and their biomedical applications. *Trends Biotechnol.* **20**, 305-311 (2002).
- 55 Bajpai, A.K., Shukla, S.K., Bhanu, S. & Kankane, S. Responsive polymers in controlled drug delivery. *Prog. Polym. Sci.* **33**, 1088–1118 (2008).
- 56 Ahn, S-k., Kasi, R.M., Kim, S-C., Sharma, N. & Zhou, Y. Stimuli-responsive polymer gels. *Soft Matter* **4**, 1151–1157 (2008).
- 57 Ueki, T. & Watanabe, M. Macromolecules in ionic liquids: progress, challenges, and opportunities. *Macromolecules* **41**, 3739-3749 (2008).
- 58 Kodama, K., Nanashima, H., Ueki, T., Kokubo, H. & Watanabe, M. Lower critical solution temperature phase behavior of linear polymers in imidazolium-based ionic liquids: effects of structural modifications. *Langmuir* **25**, 3820-3824 (2009).

- 59 Ueki, T., Karino, T., Kobayashi, Y., Shibayama, M. & Watanabe, M. Difference in lower critical solution temperature behavior between random copolymers and a homopolymer having solvophilic and solvophobic structures in an ionic liquid. *J. Phys. Chem. B* **111**, 4750-4754 (2007).
- 60 Ueki, T. & Watanabe, M. lower critical solution temperature behavior of linear polymers in ionic liquids and the corresponding volume phase transition of polymer gels. *Langmuir* **23**, 988-990 (2007).
- 61 Siow, K. S., Delmas, G. & Patterson, D. Cloud-point curves in polymer solutions with adjacent upper and lower critical solution temperatures. *Macromolecules* **5**, 29-34 (1972).
- 62 Konno, S., Saeki, S., Kuwahara, N., Nakata, M. & Kaneko, M. Upper and lower critical solution temperatures in polystyrene solutions. IV. Role of configurational heat capacity. *Macromolecules* **8**, 799-804 (1975).
- 63 Bae, Y. C., Lambert, S. M., Soane, D. S. & Prausnitz, J. M. Cloud-point curves of polymer solutions from thermo-optical measurements. *Macromolecules* **24**, 4403-4407 (1991).
- 64 Patterson, D., Delmas, G. & Somcynsky, T. A Comparison of Lower Critical Solution Temperatures of Some Polymer Solutions. *Polymer* **8**, 503-516 (1967).
- 65 Burchard, W. Thermodynamic Solution Properties of Three Polymers Exhibiting Lower Critical Solution Temperature. *Polymer* **10**, 467-475 (1969).
- 66 Cowie, J. M. G. & Swinyard, B. Location of three critical phase boundaries in poly(acrylic acid)-dioxane solutions. *Polymer* **31**, 1507-1513 (1990).
- 67 Cowie, J. M. G., Maconnachie, A. & Ranson, R. J. Phase equilibria in cellulose acetate-acetone solutions. The effect of the degree of substitution and molecular weight on upper and lower critical solution temperatures. *Macromolecules* **4**, 57-61 (1971).
- 68 Migisawa, M., Ohnishi, K. & Sawada, H. Preparation of novel fluoroalkyl-end-capped 2-acrylamido-2-methylpropanesulfonic acid cooligomeric nanoparticles containing adamantane units possessing a lower critical solution temperature characteristic in organic media. *Langmuir* **23**, 5848-5851 (2007).
- 69 Kuroiwa, K., Shibata, T., Takada, A., Nemoto, N. & Kimizuka, N. Heat-set gel-like networks of lipophilic Co(II) triazole complexes in organic media and their thermochromic structural transitions. *J. AM. Chem. Soc.* **126**, 2016-2021 (2004).
- 70 Seno, K-I., Kanaoka, S. & Aoshima, S. Synthesis and LCST-type phase separation behavior in organic solvents of poly(vinyl ethers) with pendant imidazolium or pyridinium salts. *J. Polym. Sci. part A: Polym Chem.* **46**, 5724-5733 (2008).

- 71 Roth, P. J., Jochum, F. D. & Theato, P. UCST-type behavior of poly[oligo(ethylene glycol) methyl ether methacrylate] (POEGMA) in aliphatic alcohols: solvent, co-solvent, molecular weight, and group dependences. *Soft matter*, **7**, 2484-2492 (2011).
- 72 Yoshida, T., Seno, K-I., Knanoka, S. & Aoshima, S. Stimuli-responsive reversible physical networks. I. Synthesis and physical network properties of amphiphilic block and random copolymers with long alkyl chains by living cationic polymerization. *J. Polym. Sci. part A: Polym Chem.* **43**, 1155-1165 (2005).
- 73 Seno, K-I., Date, A., Kanaoka, S. & Aoshima, S. Synthesis and solution properties of poly(vinyl ether)s with long alkyl chain, biphenyl, and cholesteryl pendants. *J. Polym. Sci. part A: Polym Chem.* **46**, 4392-4406 (2008).
- 74 Koyama, M., Hirano, T., Ohno, K. & Katsumoto, Y. Molecular understanding of the UCST-Type phase separation behavior of a stereocontrolled poly(*N*-isopropylacrylamide) in bis(2-methoxyethyl) ether. *J. Phys. Chem. B* **2008**, *112*, 10854–10860.
- 75 Yadav, P. J. P., Aswal, V. K., Sastry, P. U., Patra, A. K. & Maiti, P. Thermoreversible gelation of poly(vinylidene fluoride-co-hexafluoro propylene) in phthalates. *J. Phys. Chem. B* **113**, 13516–13525 (2009).
- 76 Schlid, H. G. Poly(*N*-isopropylacrylamide): experiment, theory and application. *Prog. Polym. Sci.* **17**, 163-249. (1992)
- 77 Patterson, D. Free volume and polymer solubility. a qualitative view. *Macromolecules* **2**, 672-677. (1969)
- 78 Tong, Z., Zeng, F. Zheng, X. & Sato, T. Inverse molecular weight dependence of cloud points for aqueous poly(*N*-isopropylacrylamide) solutions. *Macromolecules* **32**, 4488-4490. (1999)
- 79 Gelbrich, T., Feyen, M. & Schmidt, A. M. Magnetic Thermoresponsive Core–Shell Nanoparticles. *Macromolecules* **39**, 3469–3472. (2006)
- 80 Kaiser, A. & Schmidt, A. M. Phase behavior of polystyrene-brush-coated nanoparticles in cyclohexane. *J. Phys. Chem. B* **112**, 1894-1898. (2008)

Chapter 2

Reversible Thermoresponsive Behavior of Poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in Organic Media under Mild Conditions

2-1 Introduction

The thermoresponsive behavior of the lower critical solution temperature (LCST) in an aqueous polymer solution is common and has been studied widely. However, it is rare that a polymer exhibits a sensitive LCST characteristic in organic media. As a result of academic interest and industry applications, much attention has been drawn to thermoresponsive polymers in organic media. In the past, a few studies¹⁻⁸ investigated the LCST-type phase separation in organic solvents under tough conditions such as at a high pressure above the boiling point of the solvent in a sealed cell. While the temperature increases, the difference in the size or expansion coefficient between the polymer and solvent increases and causes phase separation at a certain critical temperature, as explained by the theory of free volume.⁹ Although some theories and models⁹⁻¹⁴ have tried to elucidate and predict the phase behavior of polymer/organic solvent systems, until now novel LCST-type systems of the polymers in organic media have seldom been identified especially in mild conditions.¹⁵⁻¹⁷

In this paper, experimental observations of unique phase behavior in a poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) (P(CVE-MA)) solution are reported. In some organic solvents, the polymer presents LCST-type thermoresponsive phase behavior under mild conditions. The clouding temperature of the polymer solution can be tuned easily in a wide range with different media. In some organic media, the polymer solution can form a relatively stable dispersion system above a certain temperature. This dispersion system can recover to become a dilute polymer solution as the temperature of the system falls below the clouding temperature. This kind of process is reversible and very similar to the behavior of poly(*N*-isopropyl acrylamide) aqueous solutions.

2-2 Experimental

2-2-1 Materials

Sodium hydroxide (NaOH; Nacalai tesque; 97%), anhydrous sodium sulfate (Na_2SO_4 ; Nacalai tesque; 97%), calcium hydride (CaH_2 ; Nacalai tesque; EP), and 2,2'-azobisisobutyronitrile (AIBN; Wako; >98%) were used as received. 2-Chloroethyl vinyl ether (TCI; >97.0%) was washed three times with equal volume of water made slight alkaline with NaOH, dried with Na_2SO_4 and refluxed in the presence of CaH_2 for 2h and distilled under reduced vacuum. Maleic anhydride (TCI, >99.0%) was recrystallized in benzene. Methyl ethyl ketone (MEK; TCI; >99.0%) was refluxed in the presence of CaH_2 for 2h, distilled under reduced pressure and kept in the presence of molecular sieve. Propyl acetate (TCI; >98.0%), ethyl acetate (TCI; >98.0%), butyl acetate (Aldrich; ACS reagent, $\geq 99.5\%$), octane (TCI; >97.0%), decane (TCI; >99.0%), dodecane (TCI; >99.0%), 1,2-dichloroethane (Wako; >99.5%), and tetrahydrofuran (THF; Wako; >99.5%) were used without further purification.

2-2-2 Synthesis of Polymer

Copolymerization of maleic anhydride and 2-chloroethyl vinyl ether was carried out by free-radical solution polymerization. Typically, maleic anhydride (1.225 g), 2-chloroethyl vinyl ether (1.332 g), AIBN (0.006 g), and methyl ethyl ketone (5 g) were added into a 50 mL three-neck flask equipped with a condenser and an inlet of nitrogen gas. The reaction solution was stirred for 2h at the 70 °C. The resultant polymer was precipitated in diethyl ether and dried in vacuum at 100 °C for at least 8h.

2-2-3 Nuclear Magnetic Resonance (NMR)

The structure of the alternating copolymer was characterized by ^{13}C NMR and ^1H NMR spectra using BRUKER AVANCE 600 (600 MHz) spectrometer and acetone- d_6 as the solvent.

2-2-4 Fourier Transform Infrared Spectroscopy (FT-IR)

Infrared spectrum of copolymer was recorded in a Nicolet AVATAR 320S FT-IR spectrophotometer in KBr pellet.

2-2-5 Gel Permeation Chromatograph (GPC)

Molecular weight of the prepared copolymer were determined by GPC using 2 columns of TSKgel GMH_{XL} and one column of TSKgel G2000H_{XL} connected to integrated HLC-8020 system (TOSOH) at a 1.0 mL/min flow rate of THF. Polystyrene standards were used for calibration.

2-2-6 Thermoresponsive Measurement of Polymer Solution

1) Sample Preparation

5mg polymer was dissolved in 5g solvent. The composition of the used solvents was different from one to another. The sample was sealed and kept in a refrigerator at about 3 °C overnight before the measurements were done.

2) Static Light Scattering (SLS) Measurement

The thermoresponsive phase behavior of the polymer solution was characterized by the scattered light intensity at different temperatures at a fixed angle of 90°. Static light scattering was measured by a laboratory-made apparatus equipped with an ALV/SO-SIPD detector using He-Ne laser (the wavelength $\lambda_0 = 633 \text{ nm}$).² Sample solutions were optically purified by a Millipore filter of nominal pore size of 1.0 μm and transferred into optical tube. The heating and cooling rate of the system is about 0.2 °C/min. The scattered light intensity of the polymer solution was measured immediately as the temperature of the system reached the desired temperature.

2-3 Results and Discussion

2-3-1 Synthesis of Copolymer

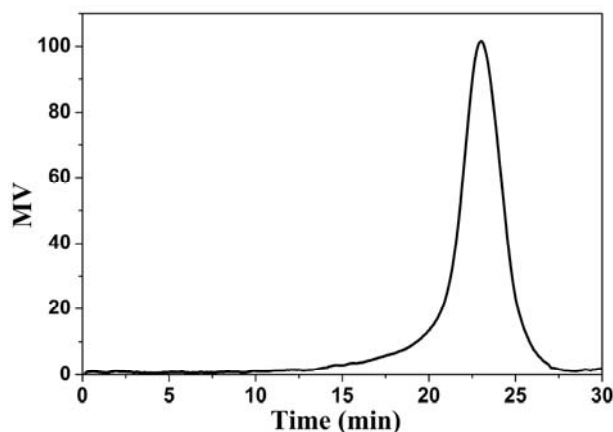


Fig. 2-1. GPC chromatogram of the synthesized copolymer

The GPC chromatogram of synthesized copolymer is shown in Fig. 2-1 and the weight-averaged molecular weight of the resultant polymer is 66,000 g/mol with the molecular weight distribution of 3.14.

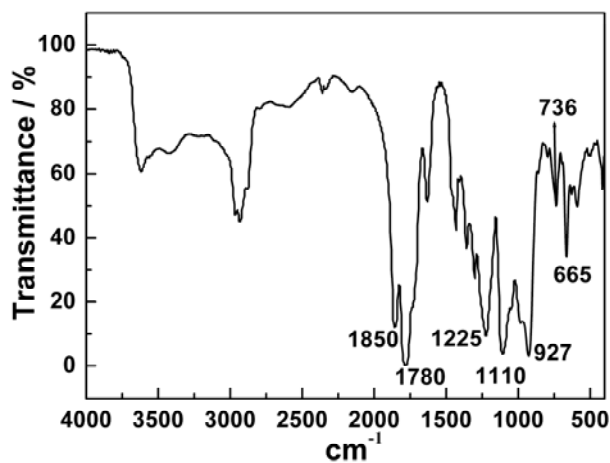


Fig. 2-2. FT-IR spectrum of P(CVE-MA)

The FT-IR spectrum of P(CVE-MA) is shown in Fig. 2-2. Peaks at 1850 and 1780 cm^{-1} correspond to the asymmetric and symmetric C=O stretch. Peaks at 1225 and 927 cm^{-1} are due to ring stretching vibrations of a saturated cyclic five-membered anhydride. Peaks at 1110, 736 and 665 cm^{-1} are the characteristic adsorption of groups of

2-chloroethyl vinyl ether repeating unit. It is concluded that the resultant polymer is a copolymer of maleic anhydride and 2-chloroethyl vinyl ether.

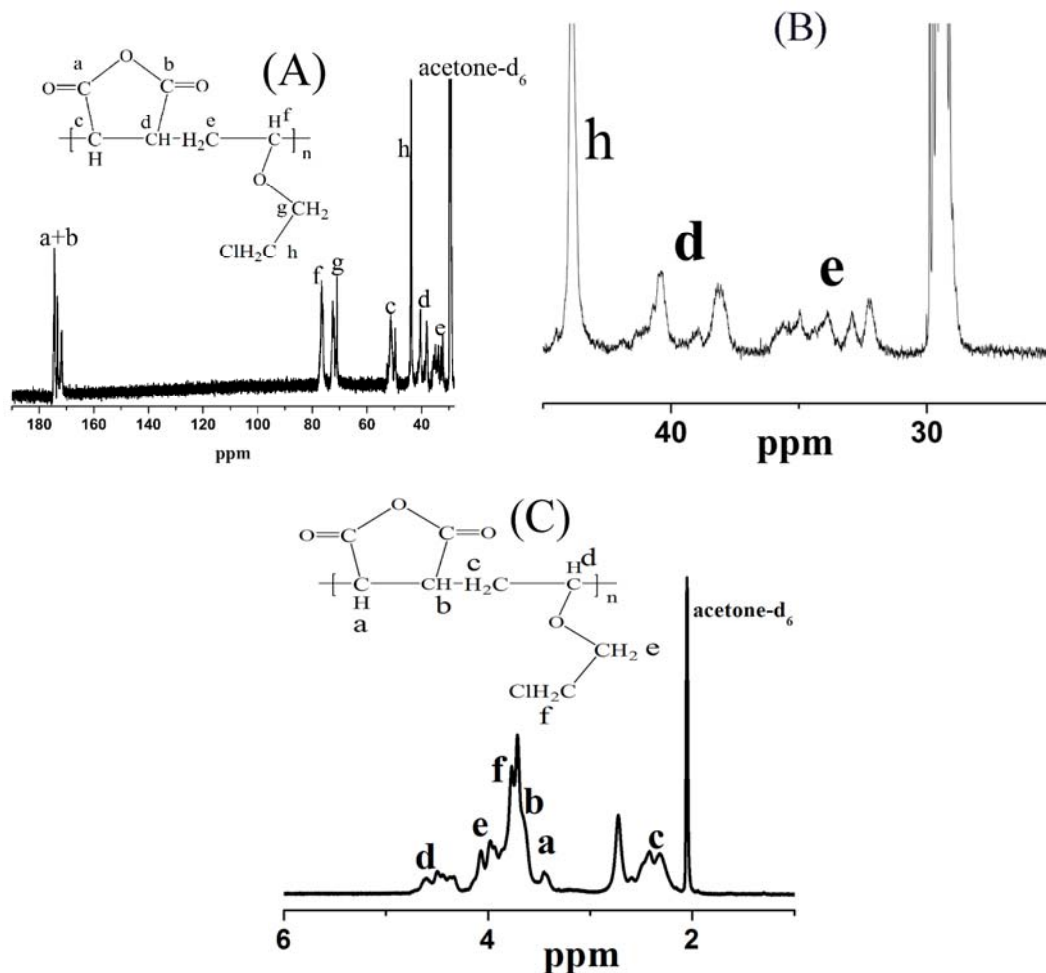


Fig. 2-3. NMR spectrum of the copolymer in acetone- d_6 : (A) ^{13}C NMR, (B) ^{13}C NMR resonance for the alternating structure, (C) ^1H NMR.

It is well known that vinyl ethers and maleic anhydride can form alternating copolymers with 1:1 overall composition by free radical polymerization.¹⁸ The structure of the alternating copolymer was characterized by ^{13}C and ^1H NMR spectra using BRUKER AVANCE 600 (600 MHz) spectrometer and acetone- d_6 as the solvent. The spectrum of ^{13}C NMR measured at 35 °C is shown in Fig. 2-3 (A) and (B) in which the resonance for main chain methylene carbon (e) at 37-32 ppm for alternating structure exists, and it can be concluded that the copolymer of 2-chloroethyl vinyl ether and maleic anhydride is an alternating polymer.¹⁸ ^1H NMR spectrum of copolymer is also shown in Fig. 2-3 (C), and the integrated area ratio of 3.3-4.0 ppm (protons a, b, e and f)

to 4.2-4.8ppm (proton d) approaches to 6 which indicates that the mole fraction of 2-chloroethyl vinyl ether and maleic anhydride group is 1:1.

2-3-2 Reversible Thermoresponsive Behavior

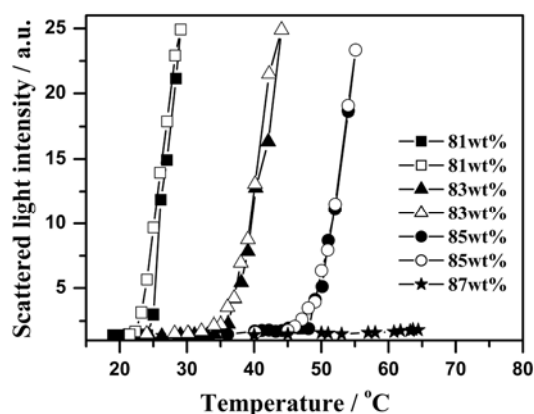


Fig. 2-4. Temperature dependence of scattered light intensity for the poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) solutions in mixed solvents of THF and hexane. The weight percentage of THF is indicated in the graph, and the polymer concentration in the solution is about 0.1wt%. The solid and hollow symbols represent heating and cooling process, respectively.

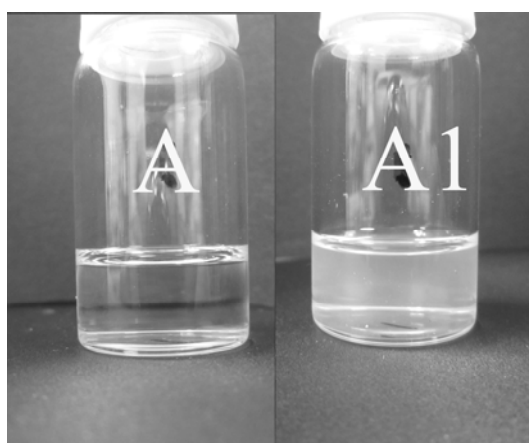


Fig. 2-5. Photograph of the polymer solution in THF/hexane with 81wt% THF at different temperatures: A, 20°C; A1, 40°C.

In THF/hexane mixed solvent with proper composition, the dilute solution of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) exhibited abrupt increase in the

scattered light intensity at a certain temperature (Fig. 2-4). At a higher temperature, the polymer solution became turbid as shown in Fig. 2-5. This turbid solution became transparent again as the system cooled down. That is to say, the polymer became insoluble above a critical temperature, and phase separation was observable by eyes in the final stage. In other words, poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) presents LCST-type thermoresponsive phase behavior in organic media such as THF/hexane under relatively mild conditions, i.e., much lower than the boiling point of the solvent. With the increase of THF in the mixed solvent, the clouding temperature of the polymer solution increased. Because the concentration of the polymer in the solvent was low (about 0.1 wt%), the cloud point temperature observed by eyes to be higher than the critical solution temperature, as measured by SLS. For example, in the mixed solvent with 81wt% THF shown in Fig. 2-5, the visually observed clouding temperature is about 40°C, which is higher than the critical temperature of 25°C measured by SLS. It can also be seen from Fig.2-4 that there exists a discrepancy in the temperature dependence of the scattered light intensity comparing the cooling curve with heating curve at a lower weight percentage of THF in the mixed solvent.

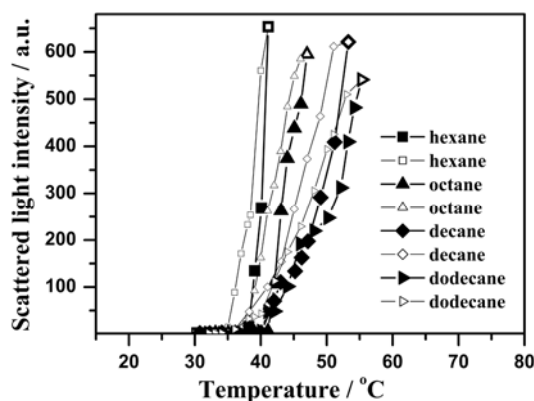


Fig. 2-6. Temperature dependence of scattered light intensity for the polymer solution in mixed solvents of propyl acetate and various *n*-alkanes with 83wt% of propyl acetate.

The solid and hollow symbols represent heating and cooling process, respectively.

The thermoresponsive behavior of polymer in the mixed solvent of propyl acetate and various *n*-alkane was also observed and reversible (Fig. 2-6). It can be seen from Fig. 2-6 that the slope of the curves becomes low with the size increase of *n*-alkane, i.e., the sensitivity to the temperature for solution turbidity becomes weaker and weaker with the size increase of *n*-alkane. It is obvious that the increasing rate of scattered light intensity of polymer solution in the mixed solvent of propyl acetate and *n*-dodecane and *n*-decane (about 52 a.u. / °C) is slower than that in other mixed solvents containing

shorter *n*-alkanes (at least 60 a.u. / °C), and this tendency also exists during cooling processing. There also exists discrepancy between curves for heating and cooling processes in these mixed solvent to some extent.

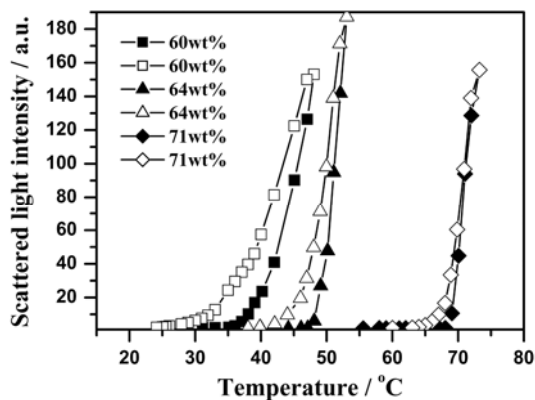


Fig. 2-7. Temperature dependence of scattered light intensity for the polymer solutions in mixed solvents of propyl acetate and 1,2-dichloroethane. The weight percentage of propyl acetate in the mixed solvents is indicated in the graph. The solid and hollow symbols represent heating and cooling process, respectively.

The clouding temperature of the polymer solution decreases with the weight increase of 1,2-dichloroethane in the mixed solvent of propyl acetate/1,2-dichloroethane (Fig.2-7). The discrepancy between heating and cooling processes becomes remarkable as the weight percentage of propyl acetate in the mixed solvent decreases.

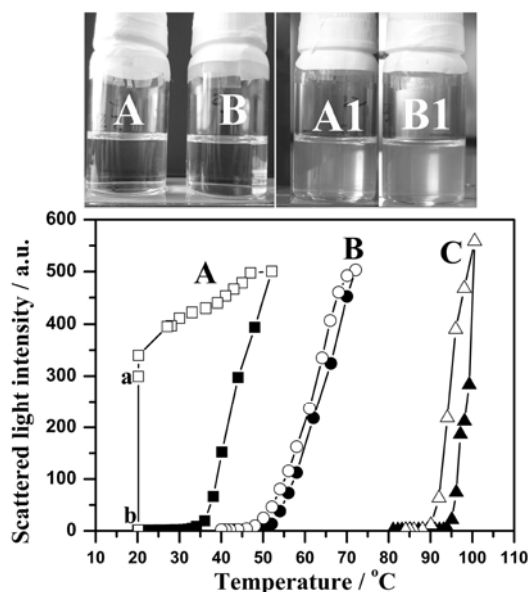


Fig. 2-8. Temperature dependence of scattered light intensity for polymer solutions in different organic media: (A) heating (solid square) and cooling (hollow square) process in the mixed solvent of butyl acetate and *n*-octane with 83wt% of butyl acetate. The data points a and b represents the results for 1h and 3h after finishing the cooling process, respectively; (B) heating (solid circle) and cooling (hollow circle) process in the mixed solvent of ethyl acetate and *n*-octane with 83wt% of ethyl acetate; (C) heating (solid triangle) and cooling (hollow triangle) process in butyl acetate. In the upper photograph, the bottles A and B represent the polymer solutions of butyl acetate/*n*-octane and ethyl acetate/*n*-octane, respectively, at 20°C. These solutions become turbid after heating to 70°C as shown by A1 and B1.

For poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride), THF and propyl acetate are good solvent and *n*-alkane and 1,2-dichloroethane are nonsolvent. As the nature of the media becomes poor, i.e., with increase of nonsolvent, the clouding temperature of the polymer solution decreases and the discrepancy between heating and cooling scans becomes remarkable. A much more remarkable discrepancy during cooling is observed in the mixed solvent of butyl acetate/*n*-octane and a much long time is needed to recover to the original transparent state (Fig.2-8, a → b). It can be concluded that the butyl acetate is not a very good solvent especially at a higher temperature though the polymer can be dissolved in it. So the measurement of SLS only in the butyl acetate was done and the LCST-type phase behavior was observed as shown in curve C in Figure 5. The clouding temperature of the polymer in the butyl acetate is high (about 95°C) but enough below its boiling temperature (124-126 °C) and not so much more remarkable

discrepancy is observed.

One of reasons why alternating copolymers of 2-chloroethyl vinyl ether and maleic anhydride exhibit LCST-type behavior may be attributed to that there exist unique interaction between polymer and solvent duo to the unique chemical composition of this polymers. In our preliminary experiments, some polymers with similar chemical structure did not exhibit LCST behavior in some related organic media, i.e., poly(ethyl vinyl ethr-*alt*-maleic anhydride) did not exhibit any LCST behavior at same conditions. Unfortunately, it is difficulty to prepare random copolymers of 2-chloroethyl vinyl ether and maleic anhydride, so the influence of the monomer sequence can not be evaluated. In this kind of thermoreversible system, the conformation of polymer in the solvent, the morphology and stability of the dispersed particles change during the phase separation, which could help us to understand the polymer solution chemistry much more deeply. Furthermore, this kind of polymer with the groups of carboxylic anhydride and alkyl chloride can be made modification conveniently. Therefore basing on the novel LCST thermosensitivity of this polymer, self-assembly of polymer with different composition or topology could be studied and some novel sensors or smart materials are expected to be developed.

2-4 Conclusion

The reversible LCST-type phase behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) can be obtained in some proper organic media under mild conditions, and the clouding temperature of the polymer solution can be tuned conveniently in a wide range

REFERENCES

- 1 Patterson, D., Delmas, G., & Somecynsky, T. A Comparison of Lower Critical Solution Temperature of Some Polymer Solutions. *Polymer* **8**, 503-516 (1967).
- 2 Burchard, W. Thermodynamic Solution Properties of Three Polymers Exhibiting Lower Critical Solution Temperature. *Polymer* **10**, 467-475 (1969).
- 3 Cowie, J. M. G., Maconnachie, A., & Ranson, R. J. Phase Equilibria in Cellulose Acetate-Acetone Solutions. The Effect of the Degree of Substitution and Molecular Weight on Upper and Lower Critical Solution Temperatures. *Macromolecules* **4**, 57-61 (1971).

- 4 Siow, K. S., Delmas, G., & Patterson, D. Cloud-Point Curves in Polymer Solutions with Adjacent Upper and Lower Critical Solution Temperatures. *Macromolecules* **5**, 29-34 (1972).
- 5 Saeki, S., Kuwahara, N., Konno, S., & Kaneko, M. Upper and Lower Critical Solution Temperatures in Polystyrene Solutions. *Macromolecules* **6**, 246-250 (1973).
- 6 Konno, S., Saeki, S., Kuwahara, N., Nakata, M., & Kaneko, M. Upper and Lower Critical Solution Temperatures in Polystyrene Solutions. IV. Role of Configurational Heat Capacity. *Macromolecules* **8**, 799-804 (1975).
- 7 Cowie, J. M. G. & Swinyard, B. Location of Three Critical Phase Boundaries in Poly(acrylic acid)-Dioxane Solutions. *Polymer* **31**, 1507-1513 (1990).
- 8 Bae, Y. C., Lambert, S. M., Soane, D. S., & Prausnitz, J. M. Cloud-Point Curves of Polymer Solutions from Thermo-optical Measurements. *Macromolecules* **24**, 4403-4407 (1991).
- 9 Patterson, D. Free Volume and Polymer Solubility. *Macromolecules* **2**, 672-677 (1969).
- 10 Ho, C. B., & Chan, B.Y. Liquid-Liquid Equilibria of Binary Polymer Solutions with Specific Interactions. *Polymer* **39**, 6449-6454 (1998).
- 11 Wang, F., Saeki, S., & Yamaguchi, T. Absolute Prediction of Upper and Lower Critical Solution Temperatures in Polymer/Solvent Systems Based on Corresponding State Theory. *Polymer* **40**, 2779-2785 (1999).
- 12 Jang, J. G. & Bae, Y. C. Phase Behavior of Binary Polymer Solutions: The Extended Lattice Fluid Model. *J. Appl. Polym. Sci.* **70**, 1143-1150 (1998).
- 13 Liu, H. & Zhong, C. Modeling of The θ (Lower Critical Solution Temperature) in Polymer Solutions Using Molecular Connectivity Indices. *Eur. Polym. J.* **41**, 139-147 (2005).
- 14 Nies, E., Stroeks, A., Simha, R., & Jain, R. K. LCST Phase Behavior According to the Simha-Somcynsky Theory: Application to the *n*-Hexane Polyethylene System. *Colloid Polym. Sci.* **268**, 731-743 (1990).
- 15 Seno, K.-I., Kanaoka, S., & Aoshima, S. Synthesis and LCST-type Phase Separation Behavior in Organic Solvents of Poly(vinyl ethers) with Pendant Imidazolium or Pyridinium Salts. *J. Polym. Sci. Part A: Polym. Chem.* **46**, 5724-5733 (2008).
- 16 Mugisawa, M., Ohnishi, K., & Sawada, H. Preparation of Novel Fluoroalkyl-End-Capped 2-Acrylamido-2-methylpropanesulfonic Acid Cooligomeric Nanoparticles Containing Adamantane Units Possessing a Lower

- Critical Solution Temperature Characteristic in Organic Media. *Langmuir* **23**, 5848-5851 (2007).
- 17 Kuroiwa, K., Shibata, T., Takada, A., Nemoto, N., & Kimizuka, N. Heat-Set Gel-like Networks of Lipophilic Co(II) Triazole Complexes in Organic Media and Their Thermochromic Structural Transitions. *J. Am. Chem. Soc.* **126**, 2016-2021 (2004).
 - 18 Ha, N. T. H., Fujimori, K., Henry, P. C., & Tucker, D. J. Assignment of ^{13}C NMR chemical shift and microstructure of copolymers of 2-chloroethyl vinyl ether-maleic anhydride and n-butyl vinyl ether-maleic anhydride. *Polym. Bull.* **43**, 81-85 (1999).
 - 19 Inomata, K., Kasuya, M., Sugimoto, H., & Nakanishi, E. Effect of Helix-Coil Transition on Association Behavior of Both-ends Hydrophobically-modified Water-soluble Polypeptide. *Polymer* **46**, 10035-10044 (2005).

Chapter 3

Reversible Thermoresponsive Behavior of Poly(2-chloroethyl vinyl ether-alt-maleic anhydride) in Mixed Solvent of Tetrahydrofuran/Hexane

3-1 Introduction

Thermoresponsive polymers can undergo relatively large and abrupt physical or chemical property changes in response to small external changes of temperature in the environment, and those polymers generally have a lower critical solution temperature (LCST) or upper critical solution temperature (UCST). Most interest is related to LCST-type polymers, and based on this kind of polymers many applications have also been developed.¹⁻³

As for LCST-type phase behavior of polymers in water some theories have been developed in order to predict the thermoresponsive behavior and discover new polymers which can exhibit LCST-type phase behavior⁴⁻⁶, and water-soluble thermoresponsive polymers have been used in many fields^{1, 6, 7-9} such as controlled drug delivery⁷, thermoresponsive stabilizers⁸ and bioconjugates¹. However, in the past LCST-type phase behavior of polymers in organic media did not attract so much attention, and one of reasons may be that LCST of conventional polymer systems in organic media occurs at some tough conditions such as near or above boiling point of solvent, so it is not convenient to study this kind of phenomena¹⁰⁻¹⁷. Nowadays LCST-type phase behavior in organic media at mild conditions has started to attract some interest, but only a few novel examples have been reported¹⁸⁻²⁰, for example, polymers capped by fluoroalkyl groups¹⁸, heat-set gel-like networks of lipophilic Co(II) triazole complexes¹⁹ and polymers with ionic liquid pendants²⁰.

Here we report an organic polymer solution system which can exhibit LCST-type phase behavior at mild conditions. In chapter 2 we simply reported the phenomenon that alternating copolymer of 2-chloroethyl vinyl ether and maleic anhydride (P(CVE-MA)) can present LCST-type phase behavior in proper organic media²¹. It is commonly reported that some polymers can exhibit LCST-type phase behavior in mixed solvent of water and organic media²²⁻³¹. However, it is novel that organic polymer solution exhibits LCST-type phase behavior by changing the quality of mixed solvent at mild conditions, and studying this kind of thermoresponsive phase behavior can help us to understand

the polymer solution properties deeply. Herein we study LCST-type behavior of P(CVE-MA) in mixed THF/hexane solvent in detail and try to comprehend the mechanism of reversible thermoresponsive behavior

3-2 Experimental part

3-2-1 Materials

Sodium hydroxide (NaOH; Nacalai tesque; 97%), anhydrous sodium sulfate (Na₂SO₄; Nacalai tesque; 97%), calcium hydride (CaH₂; Nacalai tesque; EP), and 2,2'-azobisisobutyronitrile (AIBN; Wako; >98%), hexane (Kishida Chemical; 96%) were used as received. 2-Chloroethyl vinyl ether (CVE; TCI; >97.0%) was washed three times with equal volume of water made slight alkaline with NaOH, dried with Na₂SO₄ and refluxed in the presence of CaH₂ for 2 hours and distilled under reduced vacuum. Maleic anhydride (MA; TCI; >99.0%) was recrystallized in benzene. Methyl ethyl ketone (MEK; TCI; >99.0%) was refluxed in the presence of CaH₂ for 2 hours, distilled under reduced pressure and kept in the presence of molecular sieve. Tetrahydrofuran (THF; Wako; >99.5%) was distilled before using. THF-*d*₈ (Nacalai tesque) was used as received.

3-2-2 Synthesis of polymers

Copolymerization of MA and CVE was carried out by free-radical solution polymerization: i.e. , MA (1.225 g), CVE (1.332 g), AIBN (0.006 g), and MEK (5 g) were added into a 50 mL three-neck flask equipped with a condenser and an inlet of nitrogen gas. The polymerization solution was stirred for 2 hours at the 70°C. The resultant polymer was precipitated in diethyl ether and dried under vacuum at 100°C for at least 8 hours. In order for polymerization of lower molecular weight polymer, MA (1.225 g), CVE (1.332 g), AIBN (0.01 g), and THF (10 g) were also reacted in the same system at 60°C for 6 hours.

3-2-3 Gel Permeation Chromatograph (GPC)

Molecular weight of the prepared copolymer were determined by GPC using 2 columns of TSKgel GMH_{XL} and one column of TSKgel G2000H_{XL} connected to

integrated HLC-8020 system (TOSOH) at a 1.0 mL/min flow rate of THF. Polystyrene standards were used for molecular weight calibration.

3-2-4 FT-IR measurement

Infrared spectrum of copolymer was recorded in a Nicolet AVATAR 320S FT-IR spectrophotometer in KBr pellet.

3-2-5 Sample preparation of polymer solution

Certain amount of polymer was dissolved in the mixed solvent of THF and hexane. The composition of the used solvents was different from one to another. The sample was sealed and kept in a refrigerator at about 3 °C overnight before the measurements were done.

3-2-6 Static light scattering (SLS) measurement

Thermoresponsive phase behavior of the polymer solution was characterized by the scattered light intensity (I_s) at different temperatures at a fixed angle of 90°. I_s was measured by a laboratory-made apparatus equipped with an ALV/SO-SIPD detector using He-Ne laser (the wavelength $\lambda_0 = 633 \text{ nm}$)³². Sample solutions were optically purified by a Millipore filter of nominal pore size of 1.0 μm and transferred into optical tube. The heating and cooling rate of the system is about 0.2 °C/min. I_s of the polymer solution was measured immediately as the temperature of the system reached the desired temperature.

3-2-7 ¹H NMR measurement

About 0.088 g polymer was dissolved in 0.52g THF- d_8 in a NMR tube with an outer diameter of 5 mm, and ¹H NMR spectra in THF- d_8 at different temperature were measured using BRUKER AVANCE 600 (600 MHz) spectrometer. Weight percentage of polymer in THF- d_8 was about 15wt%. After ¹H NMR spectra at different temperatures in THF- d_8 , about 0.02 g polymer (to keep the same polymer concentration) and 0.105g hexane was added into the former polymer solution, and ¹H NMR spectra at different temperatures were also measured in the mixed solvent. The weight percentage

of polymer was about 15wt% in mixed THF- d_8 /hexane solvent, and the weight percentage of THF- d_8 in the mixed solvent was about 83.2wt%. Scanning times was 128 and receiver gain was kept constant in all NMR measuring experiments.

3-3 Results and Discussion

3-3-1 Synthesis and chemical composition of copolymers

The GPC graph of synthesized copolymer is shown in Fig. 3-1. P(CVE-MA)-H, with a weight-averaged molecular weight (M_w) of 66000 g/mol, was synthesized in MEK (Fig. 3-1 a), and another copolymer P(CVE-MA)-L with M_w of 6000 g/mol was prepared in THF (Fig. 3-1 b). P(CVE-MA)-H owns a broad molecular weight distribution and the ratio of M_w and number-averaged molecular weight (M_n) was 3.14, while P(CVE-MA)-L owns M_w/M_n of 1.89.

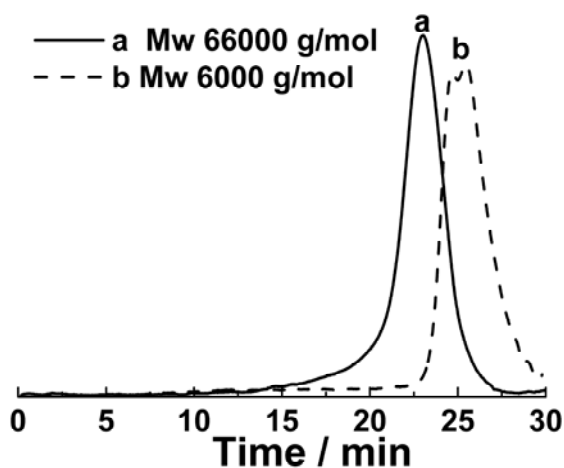


Fig. 3-1. GPC graph of prepared polymers.

3-3-2 LCST-type phase behavior of polymer solution

The solution of P(CVE-MA) in the mixed solvent of THF/hexane can exhibit reversible thermoresponsive behavior. In SLS measurements, I_s of polymer solution increased substantially above a certain critical temperature (Fig. 3-2). Visually, the polymer solution would become turbid as the temperature increased to a certain temperature, means phase separation occurred at higher temperature region. The turbid system can recover to the original state of clear polymer solution as the temperature became lower than the critical temperature, and this kind of process was reversible. The temperature at

which the polymer solution becomes turbid depends on the polymer concentration in the solution at a certain solvent composition. Especially at lower polymer concentrations, the temperature at which I_s increased sharply was lower than the temperature at which the polymer solution became turbid visually²¹. Here, the former temperature is considered as the cloud point (T_{cp}) of the polymer solution. T_{cp} is defined from the curve of I_s versus temperature, i.e., the temperature at the intersection point of the tangent of two part curves with different increase ratio, as indicated by point A in Fig.3-2.

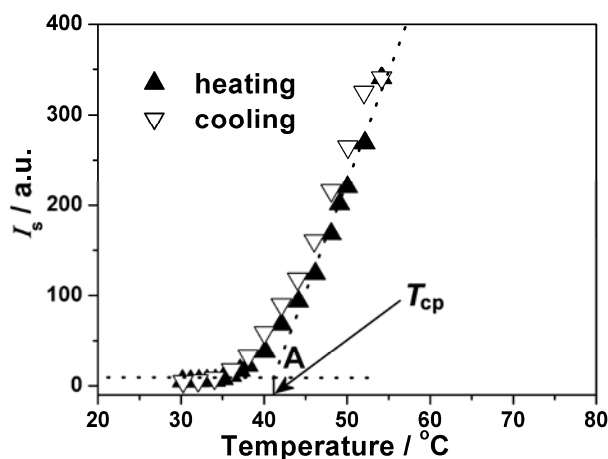


Fig. 3-2. Temperature dependence of I_s for P(CVE-MA)-H solution in the mixed solvent of THF and hexane. The weight percentage of THF in the mixed solvent is 83 wt%, and concentration of P(CVE-MA)-H is 0.4 wt%.

3-3-3 Effect of polymer concentration and solvent composition on T_{cp}

P(CVE-MA) solution can occur phase separation at desired temperature by tuning the solvent composition of mixed solvent of THF and hexane. First we investigated the thermoresponsive behavior of P(CVE-MA)-H ($M_w = 66,000$ g/mol). As the polymer concentration was above 0.1 wt% and the weight percentage of THF in the mixed solvent was enough low (usually, < 79 wt%), T_{cp} of polymer solution was below 0 °C (observed by naked eyes in refrigerator). As the weight percentage of THF was far high (usually, > 88 wt%) and polymer concentration was below 2 wt% , the polymer solution maintained clear state below boiling point of THF and hexane. So in order to characterize thermoresponsive behavior, the weight percentage of THF in mixed solvent ranged from 81 to 85 wt% in this paper. Temperature dependence of I_s of polymer solutions in different solvent compositions is shown in Fig. 3-3. It can be seen from Fig. 3-3 that I_s increases abruptly at a certain T_{cp} , which indicates thermoresponsive behavior of polymer solution.

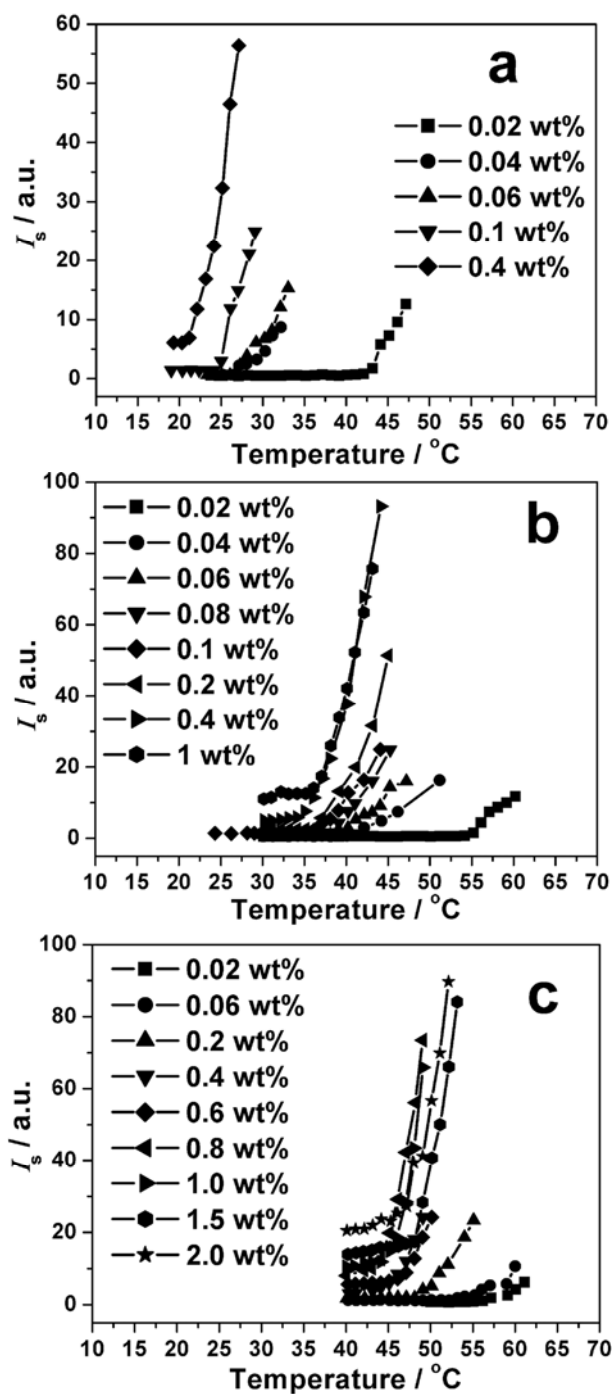


Fig. 3-3. Temperature dependence of I_s of P(CVE-MA)-H solutions at different weight percentage of THF (a) 81 wt%, (b) 83 wt%, and (c) 85 wt%. The weight percentage of polymer in solution is indicated in the graph.

As shown in Fig. 3-3 the increasing behavior of I_s with temperature depends on polymer concentration. At higher concentrations, I_s increased much more abruptly and

its temperature dependence after phase separation was much steeper than those of lower polymer concentration.

It can be seen from Fig. 3-3 that T_{cp} of polymer solution is relied on polymer concentration and solvent compositions to a certain extent. T_{cp} as a function of polymer concentration can be obtained from Fig. 3-3 and plotted in Fig. 3-4. It can be seen from Fig. 3-4 that P(CVE-MA)-H presents LCST-type phase behavior in the mixed solvent of THF/hexane with proper weight percentage of THF. In low concentration region, T_{cp} decreased as the increase in polymer concentration, and then approached to a certain constant value. This phenomenon is often observed in various LCST-type thermoresponsive polymer solution³³⁻³⁶ and also observed in P(CVE-MA)/n-butyl acetate solutions in chapter 4³⁷. THF is a good solvent for P(CVE-MA) and hexane is nonsolvent, so with increase in THF in the mixed solvent, the homogeneous one-phase region below the T_{cp} curve in Fig. 3-4 became wider. Similar result was also observed in mixed aqueous solution of poly(*N*-isopropyl acrylamide)²².

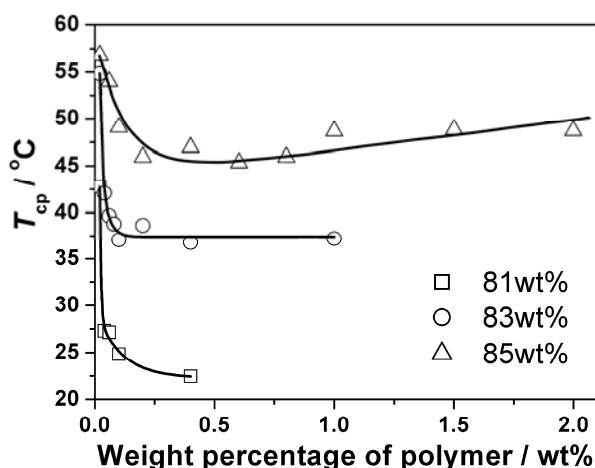


Fig. 3-4. T_{cp} of polymer solution at different polymer concentrations for P(CVE-MA)-H. The weight percentage of THF in mixed solvent is indicated in the graph.

Thermoresponsive behavior of P(CVE-MA)-L with lower M_w (6,000 g/mol) was also investigated in the mixed solvent of THF and hexane as shown in Fig. 3-5. In the mixed solvent with THF weight percentage of 81 wt%, LCST-type thermoresponsive behavior was observed at the polymer concentration ranging from 1 wt% to 10 wt%, and T_{cp} decreased with increase of polymer concentration (Fig. 3-5a). When the THF weight percentage was 83 wt%, the abrupt increase in I_s was not observed at the polymer concentration of 1 wt%, and LCST-type thermoresponsive behavior was recognized above 1.5 wt% (Fig. 3-5b). By further increase in THF weight percentage to

85 wt% (Fig. 3-5c), there was no thermoresponsive behavior even at high polymer concentrations of 10 wt%.

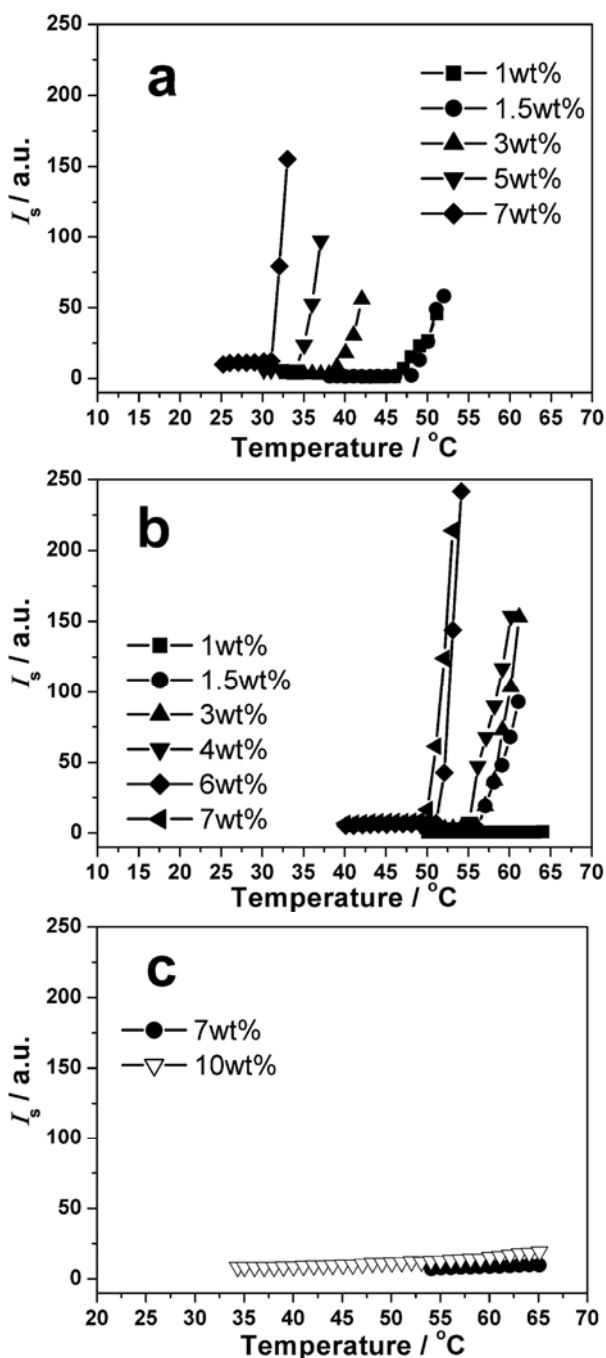


Fig. 3-5. Temperature dependence of I_s of P(CVE-MA)-L solutions at different weight percentage of THF (a) 81 wt%, (b) 83 wt%, and (c) 85 wt%. The weight percentage of polymer in solution is indicated in the graph.

T_{cp} as the function of polymer concentration for P(CVE-MA)-L is shown in Fig. 3-6. It can be seen that polymer concentration owns less influence on T_{cp} in solutions with higher THF weight percentage. As similarly observed in Fig. 3-4, T_{cp} line for 83 wt% THF solution located at high temperature region than those for 81 wt% THF solution.

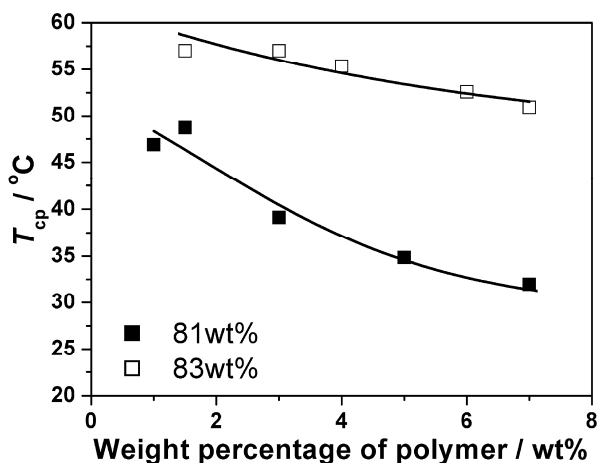


Fig. 3-6. T_{cp} of polymer solution at different polymer concentrations for P(CVE-MA)-L. The weight percentage of THF is indicated in the graph.

From comparison between Fig.3-4 and Fig.3-6, it can be concluded that T_{cp} of P(CVE-MA)-H solution is lower than that of P(CVE-MA)-L solution under same solvent conditions. Similar results was also observed in P(CVE-MA)/*n*-butyl acetate system in chapter 4³⁷.

3-3-4 NMR spectra of polymer solution

NMR spectroscopy can be used for studying thermoresponsive phase behavior of polymer solution and can help to understand the phase transition in molecular level³⁸⁻⁴³. High resolution ¹H NMR spectra of different protons of P(CVE-MA)-H in pure THF-*d*₈ measured at different temperature and their assignments are shown in Fig. 3-7a. In pure THF-*d*₈ all the protons of the polymer revealed a fine spectrum. The spectrum was almost identical in the range of 25 °C - 60 °C, indicates the almost same chemical environment for all protons within this temperature region.

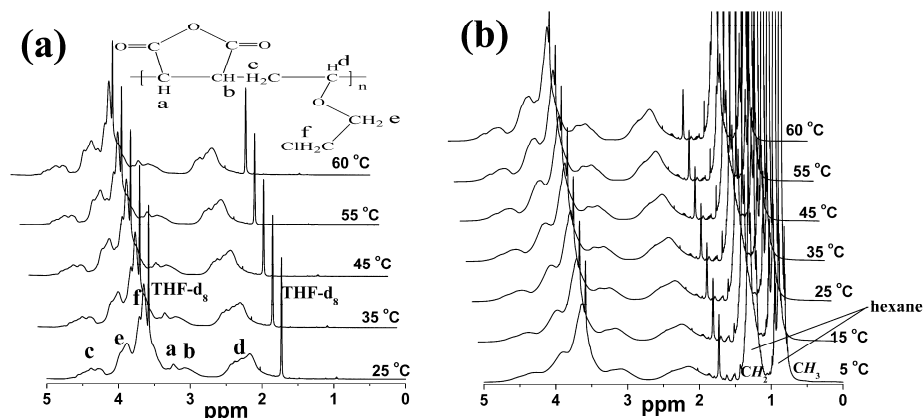


Fig. 3-7. ^1H NMR spectra of P(CVE-MA) at different temperatures. (a) In pure THF- d_8 , and (b) in THF- d_8 /hexane mixed solvent.

^1H NMR spectra of P(CVE-MA)-H in mixed THF- d_8 /hexane solvent measured at different temperatures are shown in Fig. 3-7b. It should be noted that no phase separation happened visually below 25 °C, and the solution in NMR tube became turbid above 35 °C. Comparing to the ^1H NMR spectrum in pure THF- d_8 , line shape for polymer protons broadened and splitting of the resonance disappeared. This indicates that the mobility of polymer chains was restricted with addition of hexane. We can also point out that the spectrum became sharper with the increase of temperature, which is in contrast to the spectrum in pure THF- d_8 , suggesting that the chemical environment or mobility of the polymer chain are strongly influenced by temperature in solution around T_{cp} . However, any discontinuous changes in the spectra at 25 °C and 35 °C, between which the phase separation occurred, could not be recognized. In usual LCST or UCST systems, NMR signals will be broadened and decreased in intensity by the phase separation because of the decrease in mobility of the polymer chain. Therefore, the results in Fig 3-7b seems strange because the peak intensity continued to increase even after the phase separation occurred above 35 °C.

One possible explanation of the above results is as follows. For P(CVE-MA), THF is good solvent and hexane is non-solvent. So in the THF/hexane mixed solvent, the polymer should be solvated by more THF molecules than hexane, presumably because of some specific interaction between THF and polymer. As the result, the solution can be recognized as the system of THF-solvated polymers dissolved in THF/hexane. If the amount of the solvated THF will be reduced with increasing temperature, the mixed solvent THF/hexane will become worse for the solvated polymer, and the polymer start to aggregate resulting into phase separated state. Even after the

phase separation into polymer-rich and polymer-poor phases, chain mobility in the former phase will be enough high because of the solvated THF, that is why any changes in ^1H NMR spectrum was not recognized by the phase separation and only the peak sharpening with increasing temperature was observed.

In order to inspect the above speculation, further researches for understanding this LCST behavior in molecular level much more deeply and accurately, such as vibrational spectroscopies, should be necessary, and will be conducted in future.

3-5 Conclusion

Alternating copolymer P(CVE-MA) with higher or lower molecular weight exhibited LCST-type phase behavior in mixed THF/hexane solvent. Cloud point of copolymer solution can be tuned by changing the solvent composition of mixed solvent or copolymer concentrations. Higher molecular weight polymer revealed lower T_{cp} than lower molecular weight polymer. As the weight percentage of THF increased in mixed THF/hexane solvent, T_{cp} was increased and effect of polymer concentration on T_{cp} became smaller. ^1H NMR spectra suggested that addition of hexane into polymer solution in THF may create proper medium condition in which temperature change can induce variation of polymer chain's environment or mobility largely. However, any discontinuous changes in NMR signals around T_{cp} could not be observed.

REFERENCES

1. Gil, E. S. & Hudson S. M. Stimuli-responsive polymers and their bioconjugates. *Prog. Polym. Sci.* **29**, 1173–1222(2004).
2. Aoshima, S. & Kanaoka, S. A renaissance in living cationic polymerization. *Chem. Rev.* **109**, 5245–5287 (2009).
3. Liu, F. & Urban, M.W. Recent advances and challenges in designing stimuli-responsive polymers. *Prog. Polym. Sci.* **35**, 3-23 (2010).
4. Maresov, E. A. & Semenov, A. N. Mesoglobule morphologies of amphiphilic polymers. *Macromolecules* **41**, 9439-9457 (2008).
5. Dimitrov, I., Trzebicka, B., Müller, A. H. E., Dworak, A., & Tsvetanov, C. B. Thermosensitive water-soluble copolymers with doubly responsive reversibly interacting entities. *Prog. Polym. Sci.* **32**, 1275–1343 (2007).
6. Schild, H. G. Poly(N-isopropylacrylamide): experiment, theory and application. *Prog. Polym. Sci.* **17**, 163-249 (1992).
7. Bajpai, A. K., Shukla, S. K., Bhanu, S. & Kankane, S. Responsive polymers in controlled drug delivery. *Prog. Polym. Sci.* **33**, 1088–1118 (2008).
8. Liu, R., Fraylich, M. & Saunders, B. R. Thermoresponsive copolymers: from fundamental studies to applications. *Colloid. Polym. Sci.* **287**, 627–643 (2009).
9. Jeong, B. & Gutowska, A. Lessons from nature: stimuli-responsive polymers and their biomedical applications. *Trends Biotechnol* **20**,305-311 (2002).
10. Siow, K. S., Delmas, G. & Patterson, D. Cloud-point curves in polymer solutions with adjacent upper and lower critical solution temperatures. *Macromolecules* **5**, 29-34 (1972).
11. Konno, S., Saeki, S., Kuwahara, N., Nakata, M. & Kaneko, M. Upper and Lower Critical Solution Temperatures in Polystyrene Solutions. IV. Role of Configurational Heat Capacity. *Macromolecules* **8**, 799-804 (1975).
12. Bae, Y. C., Lambert, S.M., Soane, D.S. & Prausnitz, J. M. Cloud-point curves of polymer solutions from thermo-optical measurements. *Macromolecules* **24**, 4403-4407 (1991).
13. Patterson, D., Delmas, G. & Somcynsky, T. A comparison of lower critical solution temperatures of some polymer solutions. *Polymer* **8**, 503-516 (1967).
14. Burchard, W. Thermodynamic solution properties of three polymers exhibiting lower critical solution temperature. *Polymer* **10**, 467-475 (1969).
15. Cowie, J. M. G. & Swinyard, B. Location of three critical phase boundaries in poly(acrylic acid)-dioxane solutions. *Polymer* **31**, 1507-1513 (1990).
16. Cowie, J. M. G., Maconnachie, A. & Ranson, R. J. Phase Equilibria in

- Cellulose Acetate-Acetone Solutions. The Effect of the Degree of Substitution and Molecular Weight on Upper and Lower Critical Solution Temperatures. *Macromolecules* **4**, 57-61 (1971).
17. Nies, E., Stroeks, A., Simha, R. & Jain, R. K. LCST phase behavior according to the Simha-Somcynsky theory: application to the n-hexane polyethylene system. *Colloid Polym. Sci.* 268:731-743 (1990).
 18. Migisawa, M., Ohnishi, K. & Sawada, H. Preparation of Novel Fluoroalkyl-End-Capped 2-Acrylamido-2-methylpropanesulfonic Acid Cooligomeric Nanoparticles Containing Adamantane Units Possessing a Lower Critical Solution Temperature Characteristic in Organic Media. *Langmuir* **23**, 5848-5851 (2007).
 19. Kuroiwa, K., Shibata, T., Takada, A., Nemoto, N. & Kimizuka, N. Heat-Set Gel-like Networks of Lipophilic Co(II) Triazole Complexes in Organic Media and Their Thermochromic Structural Transitions. *J. Am. Chem. Soc.* **126**, 2016-2021 (2004).
 20. Seno, K-I., Kanaoka, S. & Aoshima, S. Synthesis and LCST-type phase separation behavior in organic solvents of poly(vinyl ethers) with pendant imidazolium or pyridinium salts. *J. Polym. Sci. part A: Polym. Chem.* **46**, 5724-5733 (2008).
 21. Liu, Z., Guo, Y. & Inomata, K. lower critical solution temperature behavior of poly(2-chloroethyl vinyl ether-alt-maleic anhydride) in organic media. *Polym. J.* 42, 901-904 (2010).
 22. Schild, H. G., Muthukumar, M. & Tirrell, D. A. Cononsolvency in mixed aqueous solutions of poly(N-isopropylacrylamide). *Macromolecules* **24**, 948-952 (1991).
 23. Winnik, F. M., Ottaviani, M. F., Bossmann, S.H., Garibay-Garcia, M. & Turro, N. J. Consolvency of poly(N-isopropylacrylamide) in mixed water-methanol solutions: a look at spin-labeled polymers. *Macromolecules* **25**, 6007-6017 (1992).
 24. Winnik, F. M., Ottaviani, M. F., Boßmann, S. H., Wenseng, P., Garibay-Garcia, M. & Turro, N. J. Cononsolvency of poly(N-isopropylacrylamide): a look at spin-labeled polymers in mixtures of water and tetrahydrofuran. *Macromolecules* **26**, 4577-4588 (1993).
 25. Dalkas, G., Pagonis, K. & Bokias, G. Control of the lower critical solution temperature-type cononsolvency properties of poly(N-isopropylacrylamide) in water-dioxane mixtures through copolymerisation with acrylamide. *Polymer* **47**,

- 243–248 (2006).
26. Costa, R. O. R., Freitas, R. F. S. Phase behavior of poly(N-isopropylacrylamide) in binary aqueous solutions. *Polymer* **43**, 5879–5885 (2002).
 27. Tanaka, F., Koga, T., Kojima, H. & Winnik, F. M. Temperature- and Tension-Induced Coil–Globule Transition of Poly(N-isopropylacrylamide) Chains in Water and Mixed Solvent of Water/Methanol. *Macromolecules* **42**, 1321–1330 (2009).
 28. Zhang, G. & Wu, C. The Water/Methanol Complexation Induced Reentrant Coil-to-Globule-to-Coil Transition of Individual Homopolymer Chains in Extremely Dilute Solution. *J. Am. Chem. Soc.* **123**, 1376–1380 (2001).
 29. Yamauchi, H. & Maeda, Y. LCST and UCST Behavior of Poly(N-isopropylacrylamide) in DMSO/Water Mixed Solvents Studied by IR and Micro-Raman Spectroscopy. *J. Phys. Chem. B* **111**, 12964–12968 (2007).
 30. Kouřilová, H., Hanyková, L. & Spěvácěk, J. NMR study of phase separation in D₂O/ethanol solutions of poly(N-isopropylmethacrylamide) induced by solvent composition and temperature. *Eur. Polym. J.* **45**, 2935–2941 (2009).
 31. Liu, M., Bian, F. & Sheng, F. FTIR study on molecular structure of poly(N-isopropylacrylamide) in mixed solvent of methanol and water. *Eur. Polym. J.* **41**, 283–291 (2005).
 32. Inomata, K., Kasuya, M., Sugimoto, H., & Nakanishi, E. Effect of helix-coil transition on association behavior of both-ends hydrophobically-modified water-soluble. *Polymer* **46**, 10035–10044 (2005).
 33. Gao, J., Zhai, G., Song, Y. & Jiang, B. Multidimensionally stimuli-responsive phase transition of aqueous solutions of poly((N,N-dimethylamino)ethyl methacrylate) and poly(N,N-dimethyl-N-(methacryloyl)ethyl ammonium butane sulfonate. *J. Appl. Polym. Sci.* **107**, 3548–3556 (2008).
 34. Yamamoto, K., Serizawa, T. & Akashi, M. Synthesis and Thermosensitive Properties of Poly[(N-vinylamide)-co-(vinyl acetate)]s and Their Hydrogels. *Macromol. Chem. Phys.* **204**, 1027–1033 (2003).
 35. Mori, T., Shiota, Y., Minagawa, K. & Tanaka, M. Alternative approach to the design of thermosensitive polymers: The addition of hydrophobic groups to the ends of hydrophilic polyether. *J. Polym. Sci. part A: Polym. Chem.* **43**, 1007–1013 (2005).
 36. Hua, F., Jiang, X., Li, D. & Zhao, B. Well-defined thermosensitive, water-soluble polyacrylates and polystyrenics with short pendant

- oligo(ethylene glycol) groups synthesized by nitroxide-mediated radical polymerization. *J. Polym. Sci. part A: Polym. Chem.* **44**, 2454–2467 (2006).
37. Liu, Z., Guo, Y. & Inomata, K. LCST-type phase behavior of poly(2-chloroethyl vinyl ether-alt-maleic anhydride) in *n*-butyl acetate. In press
 38. Starovoytova, L. & Spěváček, J. Effect of time on the hydration and temperature-induced phase separation in aqueous polymer solutions. ¹H NMR study. *Polymer* **47**, 7329-7334 (2006).
 39. Starovoytova, L., Spěváček, J., Hanyková, L. & Ilavský, M. ¹H NMR study of thermotropic phase transitions in D₂O solutions of poly(N-isopropylmethacrylamide)/poly(vinyl methyl ether) mixtures. *Polymer* **45**, 5905–5911 (2004).
 40. Starovoytova, L., Spěváček, J. & Ilavský, M. ¹H NMR study of temperature-induced phase transitions in D₂O solutions of poly(N-isopropylmethacrylamide)/poly(N-isopropylacrylamide) mixtures and random copolymers. *Polymer* **46**, 677–683 (2005).
 41. Spěváček, J., Hanyková, L. & Ilavský, M. Phase Separation in Poly(N,N-diethylacrylamide)/D₂O Solutions and Physical Gels as Studied by ¹H NMR Spectroscopy. *Macromol. Chem. Phys.* **202**, 1122–1129 (2001).
 42. Starovoytova, L., Spěváček, J. & Trchová, M. ¹H NMR and IR study of temperature-induced phase transition of negatively charged poly(N-isopropylmethacrylamide-co-sodium methacrylate) copolymers in aqueous solutions. *Eur. Polym. J.* **43**, 5001–5009 (2007).
 43. Spěváček, J. NMR investigations of phase transition in aqueous polymer solutions and gels. *Curr. Opin. Colloid Interface Sci.* **14**, 184-191 (2009).

Chapter 4

LCST-type Phase Behavior of Poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in *n*-Butyl Acetate

4-1 Introduction

Much attention to lower critical solution temperature (LCST)-type phase behavior of polymer solution has been attracted. Polymers with LCST are kind of stimuli-sensitive polymers which are soluble at the temperature below LCST and become insoluble above LCST. A lot of LCST-type phase behaviors of aqueous polymer solution have been studied, and many theories and applications have been developed in the past.¹⁻³ Nowadays LCST-type phase behavior of polymer in some other nonaqueous media is also coming into study in order to research and develop some smart materials. For example, LCST polymer solutions of thermoresponsive polymer/ionic liquid systems have been reported.⁴⁻⁷

In conventional LCST polymer solutions in organic media, the critical temperature is usually higher than the boiling point (BP) of solvent.⁸⁻¹⁴ These reported systems can exhibit LCST-type phase behavior at some tough conditions such as in sealed high-pressure cells above the BP of solvent or with considerably high molecular weight polymers. Some theories have been tried to explain or predict this kind of LCST-type phase behavior.¹⁵⁻¹⁷ In free-volume theories, the difference of density or expansion coefficient between polymer and solvent above BP is proposed to lead to phase separation at elevated temperatures.¹⁷ Because these conditions is not convenient to research, a novel solution system of polymer/organic media which can present LCST at some mild conditions is expected to be discovered. Recently, very a few these novel polymer solution systems in organic media have been reported,¹⁸⁻²⁰ for example, polymers with some unique structure or chemical composition can exhibit LCST-type phase behavior. Fluoroalkyl-end-capped polymer presented LCST behavior which may be mainly related to the oleophilic-oleophobic balance corresponding to the oleophilic character from adamantyl segments and the oleophobic character from fluoroalkyl groups.¹⁸ Thermally reversible, heat-set gel-like networks with LCST characteristic in organic media were developed by combining the elements of the one-dimensional metal complexes and mesoscopic supramolecular assemblies.¹⁹ Poly(vinyl ether) with ionic liquid pendants of imidazolium or pyridinium salt can also undergo sensitive LCST-type phase separation in organic media.²⁰

Herein we report a novel polymer solution system in common organic media which can present LCST behavior at mild conditions. As reported in chapter 2,²¹ alternating copolymer of 2-chloroethyl vinyl ether (CVE) and maleic anhydride (MA), poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride), P(CVE-MA), can occur LCST-type phase separation in *n*-butyl acetate (BuAc), while the critical temperature was enough lower than BP of BuAc. In this paper, detailed phase behavior of BuAc solutions of P(CVE-MA) with various molecular weight will be described, and effect of addition of various co-solvents on LCST behavior will also presented.

4-2 Experimental

4-2-1 Materials

Benzene (Nacalai tesque; 99.5%), toluene (Nacalai tesque; 99.5%), cyclohexane (Nacalai tesque; 99.5%), dimethylsulfoxide (DMSO; Kishida Chemical Co. LTD; 99%), 2-hexanone (TCI; > 98.0%), sodium hydroxide (NaOH; Nacalai tesque; 97%), anhydrous sodium sulfate (Na₂SO₄; Nacalai tesque; 97%), calcium hydride (CaH₂; Nacalai tesque; EP), and 2,2'-azobisisobutyronitrile (AIBN; Wako; > 98%) were used as received. 2-Chloroethyl vinyl ether (CVE; TCI; > 97.0%) was washed three times with equal volume of water made slight alkaline with NaOH, dried with Na₂SO₄ and refluxed in the presence of CaH₂ for 2 hours and distilled under reduced pressure. Maleic anhydride (MA; TCI; > 99.0%) was recrystallized in benzene. Methyl ethyl ketone (MEK; TCI; > 99.0%) was refluxed in the presence of CaH₂ for 2 hours, distilled under reduced pressure and kept in the presence of molecular sieve. Propyl acetate (TCI; > 98.0%), *n*-butyl acetate (BuAc; Aldrich; ACS reagent; ≥ 99.5%), 1,2-dichloroethane (Wako; > 99.5%), and tetrahydrofuran (THF; Wako; > 99.5%) were distilled before using.

4-2-2 Synthesis of Copolymer

Copolymerization of MA and CVE was carried out by free-radical solution polymerization. Typically, certain amounts of MA, CVE, AIBN, and solvent were added into a 50 mL three-neck flask equipped with a condenser and an inlet of nitrogen gas. The reaction solution was stirred for certain hours at a certain temperature. The resultant polymer was precipitated in diethyl ether and dried in vacuum at 100 °C for at least 8

hours.

4-2-3 Gel Permeation Chromatograph (GPC)

Molecular weight of the prepared copolymer was determined by GPC using 2 columns of TSKgel α -3000 and α -5000 connected to SD-8022 system (Tosoh) at a 1.0 mL/min flow rate of *N,N*-dimethylformamide/lithium bromide (the concentration of lithium bromide was 15 mg/L). Polystyrene standards were used for molecular weight calibration.

4-2-4 Preparation of Polymer Solutions

Polymer solutions in BuAc were prepared by direct dissolution of certain amounts of polymer in BuAc. The bottle containing polymer and BuAc was placed in an oven at 60 °C for about 8 hours in order to dissolve the polymer. Then the bottle containing the polymer solution was kept in a refrigerator at about 3 °C before measurements.

Polymer solutions in BuAc/co-solvent were prepared as follows: firstly, certain amount of polymer was added into BuAc and then the bottle was kept in an oven at 60 °C for about 8 hours, and secondly certain amount of co-solvent was added into the prepared polymer solution. The bottle containing polymer solution in BuAc/co-solvent was kept in a refrigerator at about 3 °C before measurements.

Polymers for measurements were used immediately after polymerization in order to avoid degradation, oxidation, or water absorption.

4-2-5 Light Scattering

The thermoresponsive phase behavior of the polymer solution was characterized by using light scattering technique. The scattered light intensity (I_s) at different temperatures at a fixed angle of 90° was measured by a laboratory-made apparatus equipped with an ALV/SO-SIPD detector using He-Ne laser (the wavelength $\lambda_0 = 633$ nm).²² Sample solutions were optically purified by a Millipore filter of nominal pore size of 1.0 μm and transferred into optical tube. The heating and cooling rate of the system were about 0.2 °C/min. I_s of the polymer solution was measured immediately as the temperature of the system reached the desired temperature.

4-3 Results and discussion

4-3-1 Synthesis of Copolymers

CVE has electron-releasing alkoxy group and is usually used in the cationic polymerization,²³⁻²⁷ while MA contains electron-withdrawing group of carboxylic anhydride. They can form charge transfer complexes of donor-acceptor monomer systems, in which MA and CVE act as acceptor monomer and donor monomer, respectively.²⁸ It is well known that an alternating copolymers of vinyl ether and MA can be formed in free-radical polymerization.²⁹⁻³² As pointed out in chapter 2,²¹ the molar composition of MA and CVE in the formed copolymer evaluated from ¹H NMR was 1:1, and these monomers were alternately polymerized as suggested by ¹³C NMR spectrum.

Table 1 Polymerization condition of P(CVE-MA) with different molecular weight.

condition	P(CVE-M A)-1	P(CVE-M A)-2	P(CVE-M A)-3	P(CVE-M A)-4	P(CVE-M A)-5
solvent	MEK	MEK	MEK	THF	THF
MA / g	4.9	4.9	2.452	4.9	2.452
CVE / g	5.3	5.3	2.615	5.3	2.615
AIBN / g	0.0200	0.0248	0.04	0.04	0.4
solvent / g	40	20	55	40	100
reaction temp. / °C	60	70	70	60	60
reaction time / hour	6	2	2	6	6
M_w / g/mol	77,200	92,200	36,400	17,500	7,700
M_w/M_n	1.87	1.90	1.42	2.77	1.48
conversion / %	57.8	58.8	52.5	90.7	40.5

Copolymers with different weight-averaged molecular weight (M_w) were synthesized. Their reaction conditions and M_w evaluated from the GPC are listed in Table 1, and they are designated as P(CVE-MA)-1, -2, -3, -4 and -5. Higher molecular weight polymers ($M_w = 36,400, 77,200$ and $92,200$ g/mol) were synthesized

in MEK, and polymer with lower M_w (7,700 and 17,500 g/mol) was synthesized in THF with much more added amounts of initiator.

4-3-2 LCST-type Phase Behavior of Polymer Solution

Temperature-sensitive behavior of polymer solution can be studied by various methods such as turbidity, differential scanning calorimetry, light scattering measurement, viscometry, fluorescence and so on.³ In our research, the temperature-sensitive behavior was characterized by scattered light intensity I_s at a fixed 90° angle. It can be seen in Fig. 4-1 that I_s of polymer solution increased abruptly at a certain temperature in heating process. Above a certain polymer concentration (> 0.1 wt%), the polymer solution became turbid visually, means the phase separation occurred above a certain temperature, and this is called cloud point temperature (T_{cp}). In other words, polymer is soluble below T_{cp} and insoluble above T_{cp} , which is the character of LCST-type phase behavior of polymer solution. In our experiment, the T_{cp} is defined from the temperature dependence of I_s in Fig. 4-1, i.e., the temperature at the intersection point of the tangent derived from the plots for upper and lower temperature region around T_{cp} (the points A, B, C and D for different polymer solutions in Fig. 4-1).

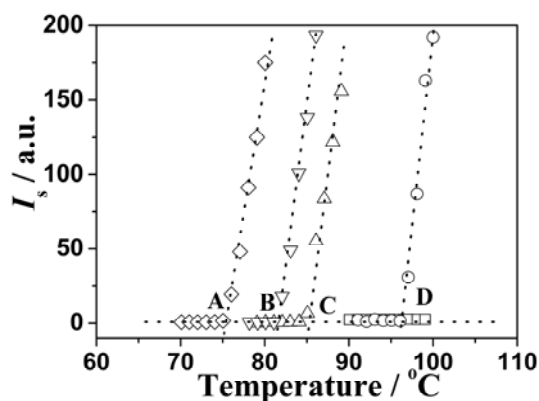


Fig. 4-1. Temperature dependence of scattered light intensity (I_s) of polymer solutions in BuAc with different weight-averaged molecular weight. (\diamond) 0.05wt% solution of P(CVE-MA)-2 ($M_w = 92,200$), (∇) 0.05 wt% solution of P(CVE-MA)-1 ($M_w = 77,200$), (\triangle) 0.05 wt% solution of P(CVE-MA)-3 ($M_w = 36,400$), (\circ) 1 wt% solution of P(CVE-MA)-4 ($M_w = 17,500$), and (\square) 10 wt% solution of P(CVE-MA)-5 ($M_w = 7,700$). The points A, B, C and D indicate T_{cp} for each solution, and the broken lines are tangent lines in order to evaluate T_{cp} .

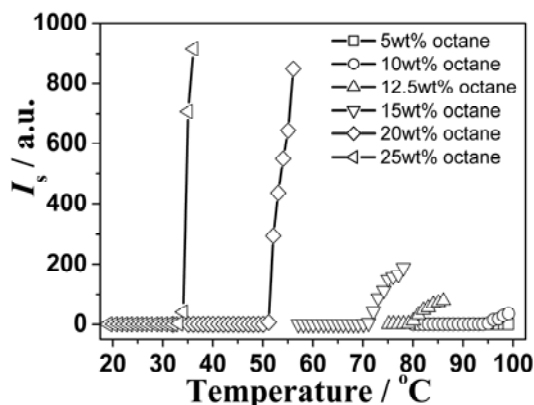


Fig. 4-2. Temperature dependence of scattered light intensity (I_s) of P(CVE-MA)-5 solutions with 1wt% polymer concentration in mixed solvent of BuAc and *n*-octane. The weight percentage of *n*-octane is indicated in the graph.

T_{cp} of polymer solution decreased with the increase of M_w of polymer. Higher molecular weight polymer (P(CVE-MA)-1, 2 and 3) can exhibit LCST-type phase behavior at a relative lower T_{cp} (< 90 °C) at lower polymer concentration range, and T_{cp} of lower molecular weight polymer P(CVE-MA)-4 was about 97 °C even at relative higher polymer concentration of 1wt%. The lowest molecular weight polymer P(CVE-MA)-5 could not exhibit thermoresponsive phase behavior until 99 °C (the upper limit of the apparatus) even at concentration of 10 wt%. In order to evaluate T_{cp} for P(CVE-MA)-5 in pure BuAc, *n*-octane as a nonsolvent was added into the polymer solution of BuAc. As shown in the latter part of this report, the addition of co-solvent can influence T_{cp} with depending on solvent quality of the co-solvent. Fig. 4-2 indicates that a small amount of *n*-octane (5 wt%) added into the polymer solution in BuAc could not induce the thermoresponsive behavior below 100 °C. As the weight percentage of *n*-octane in mixed solvent was over 10wt%, the LCST-type phase behavior can be recognized, and by further increase in *n*-octane content in mixed solvent, the increasing ratio of I_s became distinct and T_{cp} became small. In Fig. 4-3, T_{cp} values for 1 wt% polymer solutions in BuAc/*n*-octane are plotted against *n*-octane content in the mixed solution. T_{cp} decreased linearly with increase in *n*-octane content, and the intercept on the vertical axis by the extrapolated line was about 132 °C, which is higher than BP of BuAc. This value could be a clue about the T_{cp} of P(CVE-MA)-5 in pure BuAc with polymer concentration of 1 wt%.

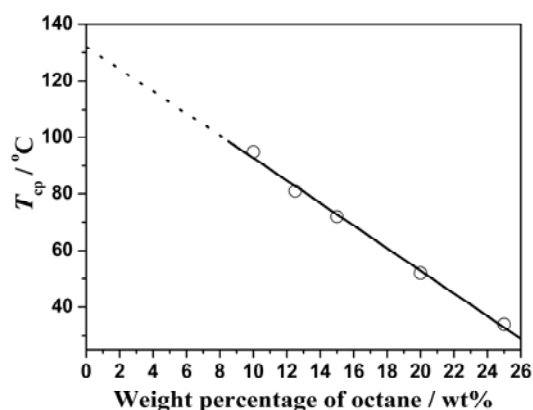


Fig. 4-3. Octane weight percentage dependence of T_{cp} of P(CVE-MA)-5 solution.

The plots of T_{cp} of polymer solution versus polymer concentration in BuAc are shown in Fig. 4-4. T_{cp} values increased with the decrease of M_w of P(CVE-MA), and this kind of molecular weight dependence of T_{cp} or LCST behavior has been often observed in aqueous polymer solutions.³³⁻³⁵ As mentioned above, the lowest molecular weight P(CVE-MA)-5 could not exhibit thermoresponsive phase behavior even in 10 wt% solution, and evaluated T_{cp} from the extrapolation method in Fig.4-3 is indicated in Fig.4-4. The T_{cp} of P(CVE-MA)-4/BuAc was much higher than that of other higher molecular weight polymers such as P(CVE-MA)-1, -2, and -3, and can be changed in a wide polymer concentration range from 1 wt% to 10 wt%. Molecular weight dependence on T_{cp} became small as the M_w of polymer approached higher values. For these polymers, T_{cp} initially decreased significantly with increase of polymer concentration and then converged to an almost constant value above a certain polymer concentration (> 1 wt%). Similar polymer concentration dependences of T_{cp} have been reported in other water soluble polymers.³⁶⁻³⁹

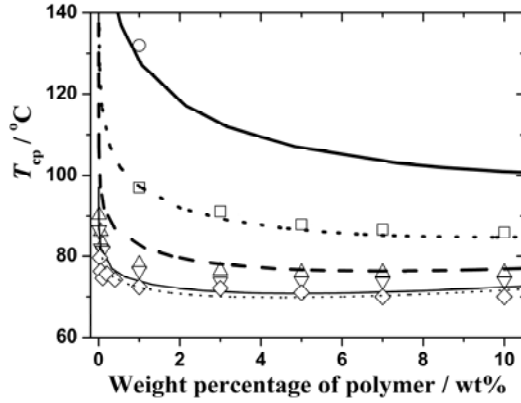


Fig. 4-4. T_{cp} of polymer solutions at different polymer concentrations in BuAc. M_w is (\circ) 7,700, (\square) 17,500, (\triangle) 36,400, (∇) 77,200 (\diamond) 92,200 g/mol. For these molecular weight polymers, binodal curves were calculated by using Equations (5) and (6), and presented by solid ($P = 38$), broken ($P = 86$), dashed ($P = 178$), thin solid ($P = 378$) and thin broken ($P = 451$) lines, respectively.

It should be noted that the T_{cp} for P(CVE-MA)/BuAc with higher M_w is enough below the BP of BuAc (126 °C), so this LCST phase behavior is not caused by the free-volume difference between the polymer and solvent, but probably originated from some specific interaction between polymer and solvent. This kind of phase behavior of polymer solution can be conventionally described by Flory-Huggins (F-H) lattice model based on mean-field theory, in which the chemical potential of the solvent (1) and polymer (2) is expressed by Equations (1) and (2), respectively, considering that used polymers are monodisperse in molecular weight.

$$\mu_1 - \mu_1^0 = \Delta\mu_1 = RT \left\{ \ln(1 - \phi) + \left(1 - \frac{1}{P}\right)\phi + \chi\phi^2 \right\} \quad (1)$$

$$\mu_2 - \mu_2^0 = \Delta\mu_2 = RT \left\{ \ln\phi - (P-1)(1-\phi) + \chi P(1-\phi)^2 \right\} \quad (2)$$

Here, R is the gas constant, T is the absolute temperature, P is the number of segments per polymer chain, and ϕ is the volume fraction of polymer in solution. χ is the thermodynamic segmental interaction parameter between polymer and solvent, and its temperature dependence is conventionally assumed by Shultz-Flory equation⁴⁰ defined by Equation (3).

$$\chi(T) = \frac{1}{2} - \psi \left(1 - \frac{\Theta}{T} \right) \quad (3)$$

In Equation (3), Θ is the theta temperature and ψ is the entropy parameter. The lower molecular weight polymer revealed the higher critical temperature, which means that the apparent χ value becomes larger with the increase of temperature, so the sign of parameter ψ must be negative. According to Equation (3), T_{cp} at the critical point, T_c , can be represented by Equation (4).⁴⁰

$$\frac{1}{T_c} = \frac{1}{\Theta} + \frac{1}{\Theta\psi} \left(\frac{1}{\sqrt{P}} + \frac{1}{2P} \right) \quad (4)$$

Because the minimum value of T_{cp} for each polymer in Fig. 4-4 can be regarded as the critical point, inverse of the minimum T_{cp} was plotted against $1/\sqrt{P} + 1/2P$ as shown in Fig. 4-5. Here, P was evaluated by M_w/M_0 , where $M_0=204.6$ is the molecular weight for repeating unit of P(CVE-MA). Derived values of intercept and slope for the straight line in Figure 4-5 give the parameters in Equations (3) and (4), and evaluated as $\Theta = 333$ K and $\psi = -1.62$. The value of $\Theta = 333$ K = 60 °C means that BuAc is a good solvent for P(CVE-MA) below 60 °C ($\chi < 1/2$), and above 60 °C ($\chi > 1/2$), BuAc becomes a poor solvent and the quality of solvent for polymer becomes poorer and poorer with increase in temperature, resulting in the phase separation at a certain temperature.

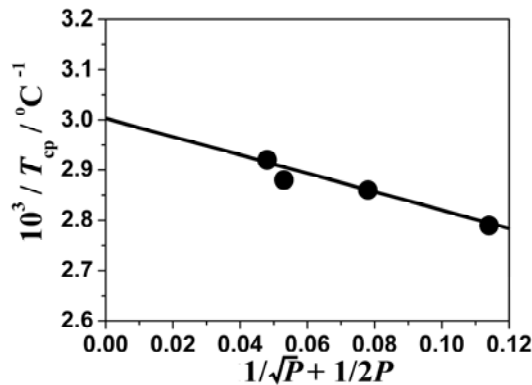


Fig.4-5. Plot of $\frac{1}{T_{cp}}$ versus $\left(\frac{1}{\sqrt{P}} + \frac{1}{2P} \right)$.

Because the χ parameter varies with temperature, the chemical potential in Equations

(1) and (2) can be represented as a function of P , T , and ϕ , i.e., $\Delta\mu_i(\phi, T, P)$. In liquid-liquid phase separated state, the chemical potential for solvent ($i = 1$) and polymer ($i = 2$) in each separated phase should satisfy Equations (5) and (6), respectively.

$$\Delta\mu_1(\phi', T, P) = \Delta\mu_1(\phi'', T, P) \quad (5)$$

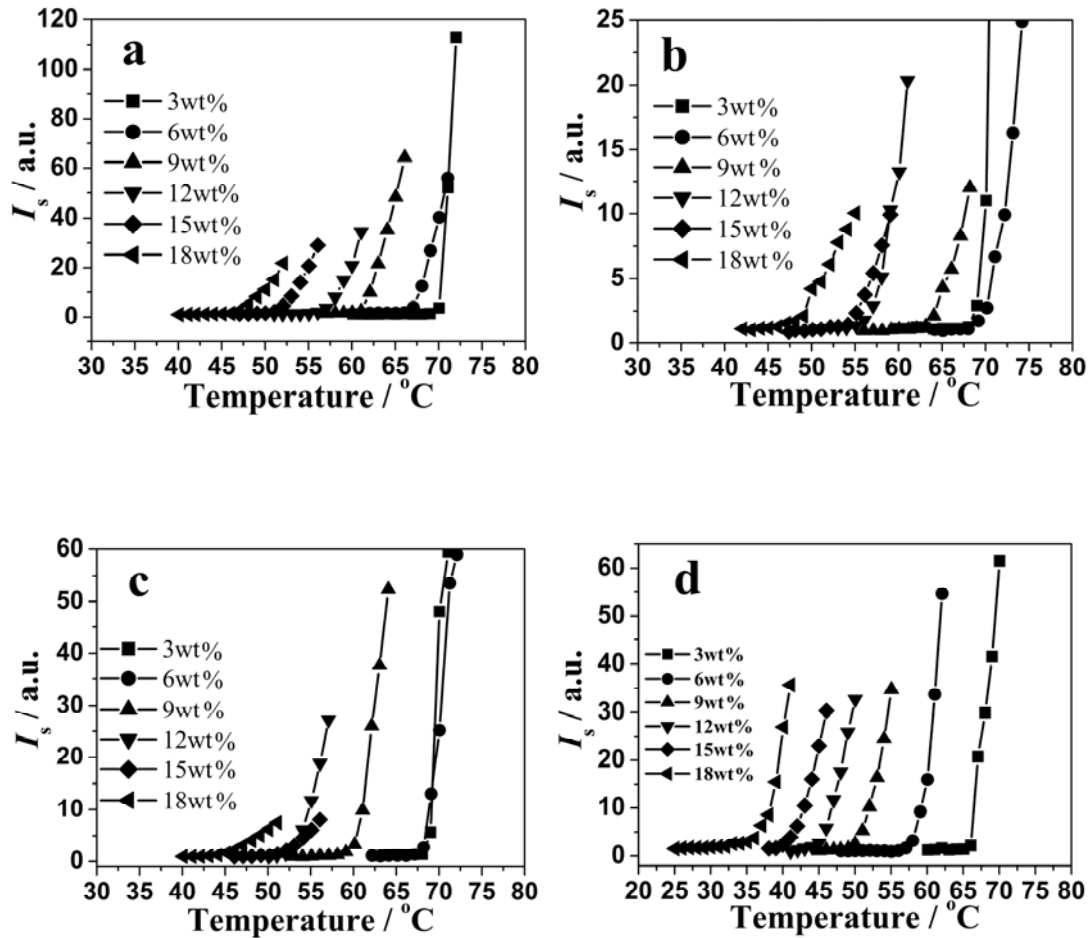
$$\Delta\mu_2(\phi', T, P) = \Delta\mu_2(\phi'', T, P) \quad (6)$$

Here, ϕ' and ϕ'' are the volume fractions of polymer in the phase-separated dilute and concentrated solutions, respectively. For solution of polymer with its degree of polymerization is P , χ can be calculated at a given temperature T from Equation (3), and by solving Equations (5) and (6), values of ϕ' and ϕ'' for each separated phase can be obtained at the given temperature. By this procedure, binodal curves for P(CVE-MA)/BuAc with different molecular weight can be calculated, and are shown by lines in Fig. 4-4. In these calculations, P values for P(CVE-MA)-1 ($M_w = 77,200$), -2 (92,200), -3 (36,400), -4 (17,500), and -5 (7,700) was assumed to be 378, 451, 178, 86, and 38, respectively. The calculated curves almost reproduced the experimental phase diagram reasonably, i.e., (i) the binodal lines exhibit lower-critical-type curve, (ii) the lines shift to lower temperature with increase in molecular weight of polymer, and (iii) when M_w is high, the lines shows sudden decrease in lower concentration region and level off in higher concentration region. The deduced value of $T_{cp} = 132$ °C for P(CVE-MA)-5 from BuAc/octane mixed solvent at 1 wt% is also located near the calculated line. Of course, the present calculation is based on the condition that the polymer is monodisperse, although the used polymers in experiments own a certain molecular weight distribution. This may be a reason why some quantitative discrepancies between the experimental and calculated T_{cp} was observed, for example, the concentration dependence of T_{cp} for P(CVE-MA)-3 was broader than the calculated binodal line, and in P(CVE-MA)-1, the calculated line locates at lower temperature region than the experimental results. In spite of these discrepancies, the trend of T_{cp} variation with polymer concentration and molecular weight can be reproduced by F-H calculation, which suggests that the LCST-type phase diagram of P(CVE-MA)/BuAc can be described within the framework of the basic F-H theory. However, the negative temperature dependence of χ parameter cannot be explained by the original concept for

χ based on van Laar type segmental interaction between polymer and solvent, so some other specific interactions should exist.

4-3-3 Effect of Addition of Co-solvent on the T_{cp} of P(CVE-MA)/BuAc

The effect of the addition of various co-solvents on T_{cp} of P(CVE-MA)/BuAc solution was investigated by using P(CVE-MA)-2. In these experiments, the polymer concentration was fixed at 0.1 wt%. The temperature dependences of I_s in different mixed solvents are shown in Fig.4-6. Similarly with the behavior in pure BuAc, I_s of polymer solution increased sharply at a certain T_{cp} . When the co-solvents were benzene, toluene, cyclohexane, and 1,2-dichloroethane, T_{cp} decreased with the increase of added amounts of co-solvent in BuAc as shown in Fig.4-6a, 6b, 6c, and 6d, respectively, as observed in P(CVE-MA)-5/BuAc/*n*-octane solutions in Fig.4-2. This phenomenon can be ascribed to that these solvents make the mixed solvent more poor than BuAc, in other words, these used solvents as well as *n*-octane should be non-solvent for P(CVE-MA).



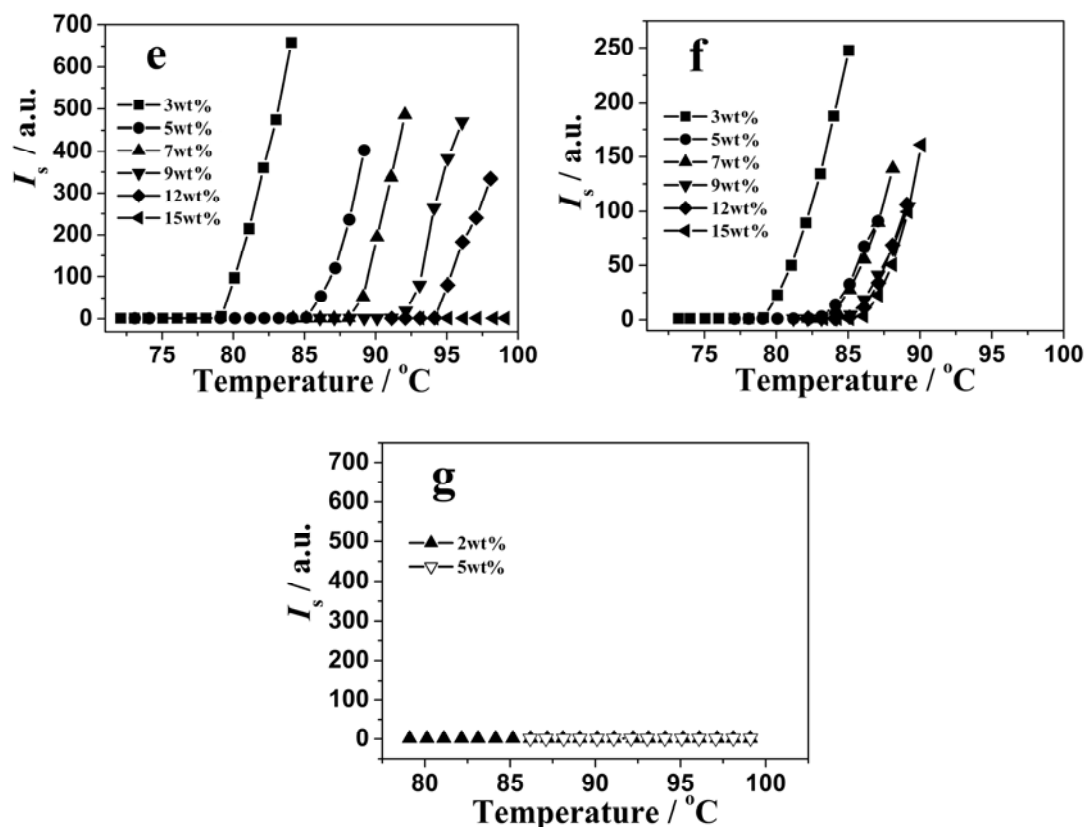


Fig. 4-6. Temperature dependence of I_s of polymer solution with different added amounts of various co-solvents. (a) benzene, (b) toluene, (c) 1,2-dichloroethane, (d) cyclohexane, (e) 2-hexanone, (f) propyl acetate, (g) DMSO.

Relationship between T_{cp} and added amounts of these solvents is shown in Fig.4-7. There exists an overall tendency that T_{cp} of polymer solution decreased with increasing added amounts of co-solvents. In case of addition of benzene, toluene and 1,2-dichloroethane, there was a little difference among the slope of lines although the effectiveness for lowering the T_{cp} was in the following order: 1,2-dichloroethane > benzene > toluene. As for cyclohexane, it owns a highest effectiveness for lowering the T_{cp} . This means that the aliphatic cyclohexane is the most non-solvent for P(CVE-MA) among the solvents in Fig.4-7.

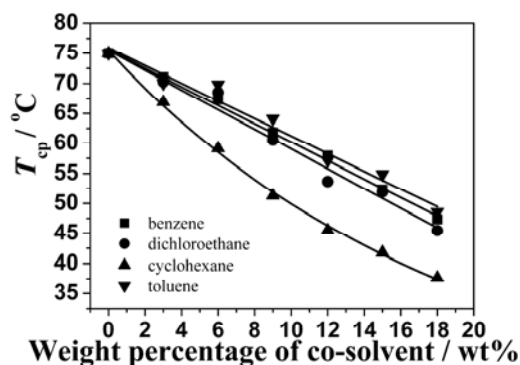


Fig. 4-7. T_{cp} of polymer solutions in BuAc with different added amounts of co-solvents as indicated.

On the other hand, in Fig. 4-6e – 6g, 2-hexanone, propyl acetate, and DMSO were used as co-solvents added to P(CVE-MA)/BuAc solutions. As 2-hexanone was added into the polymer solution in BuAc, T_{cp} shifted to higher temperature until the added weight percentage of 2-hexanone was up to 15 wt%, at which no thermoresponsive behavior was observed below 100 °C (Fig. 4-6e). T_{cp} shifted to higher temperature slowly with increasing added amount of propyl acetate into BuAc (Fig. 4-6f). In the experiments of addition of DMSO in Fig.4-6g, the solution maintained in transparent until 100 °C without any thermoresponsive behavior even when the added DMSO amounts was 2 wt%.

Fig. 4-8 shows T_{cp} of polymer solution as a function of added amounts of solvents such as 2-hexanone and propyl acetate. It is obvious that 2-hexanone was more effective for increasing the T_{cp} of polymer solution in BuAc than propyl acetate. The behavior that T_{cp} increases with increasing addition of good solvent was also observed in aqueous poly(vinyl methyl ether) solutions, and these phenomena may be attributed to that interaction between added good solvent and polymers are much more favored than the interaction between polymer and original solvent.⁴¹ The increase of T_{cp} in Fig. 4-8 may be attributed to that these co-solvents interact with polymer more strongly than with BuAc. These phenomena in Fig. 4-7 and 8 present a clue about the quality of solvent for polymer. In our experiments, P(CVE-MA) can be dissolved in 2-hexanone and propyl acetate, but can not be dissolved in solvents in Fig. 4-7. Fig. 4-6g shows that DMSO should be the most good solvent used in this work, and gave a pink solution by dissolution of polymer.

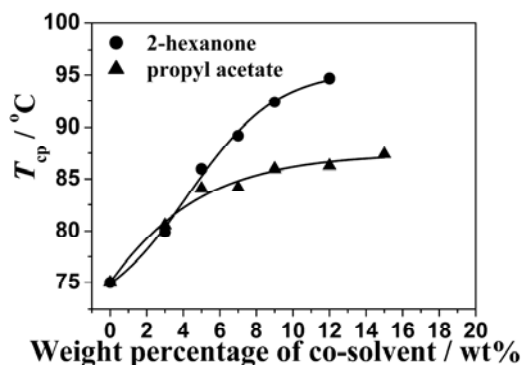


Fig. 4-8. T_{cp} of polymer solutions in BuAc with different added amounts of co-solvents as indicated.

Table 2 Various physical properties of used co-solvents

co-solvent	slope ^a ($^\circ\text{C}/\text{wt}\%$)	dielectric constant ϵ	solubility parameter δ	polar term in solubility parameter δ_p
cyclohexane	-2.1	2.02	16.8	0
1,2-dichloroethane	-1.8	10.4	20.9	7.4
benzene	-1.7	2.27	18.6	0
toluene	-1.6	2.38	18.2	1.4
propyl acetate	1.6	$\sim 5.5^b$	17.8^b	4.5^b
2-hexanone	2.0	$\sim 17^c$	17	6.1
DMSO	very large	46.5	26.6	16.4

^a Slope of the plot for T_{cp} against co-solvent's weight fraction in Fig. 3-7 and 8.

^b Approximated value from ethyl acetate and *n*-butyl acetate.

^c Approximated value from 2-butanone and cyclohexanone.

The slope of the curve in Fig. 4-7 and 8 should represent the quality of solvent for P(CVE-MA). Evaluated values of the slope for the used co-solvents are listed in Table 2. For these solvents, dielectric constant (ϵ) and solubility parameter (δ) are also indicated; the former value relates to polarity of solvent, and the latter value is conventionally used to consider the solubility of polymer solution.⁴² These lists indicate that δ values do not have linear relationship with the solubility of P(CVE-MA), on the other hand, the value of slope seems to increase with ϵ except for 1,2-dichloroethane.

In Table 2, polar term in solubility parameter proposed by Hansene, δ_p , is also listed.⁴² Values of δ_p and the slope have similar relationship with the case of ϵ . In Fig. 4-9, values of slope are plotted against δ_p , which shows good linear relationship except for 1,2-dichloroethane. Therefore, except for the results of 1,2-dichloroethane, we can point out that the solvent quality of P(CVE-MA) is determined by the polarity of the solvent. As reported in chapter 2 and 3,^{21,43} THF is good solvent for P(CVE-MA), and *n*-hexane is non-solvent. Probably, some polar interactions between P(CVE-MA) and solvent might be an important factor for solubilization, and which seems reasonable that P(CVE-MA) contains polar ether and carboxylic anhydride groups and the good solvents also contain oxygen atoms in its chemical structure, but the non-solvents are oxygen-free non-polar solvents.

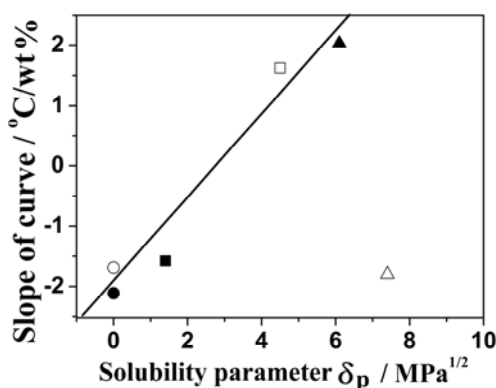


Fig. 4-9. Relationship between the slope of curve for T_{cp} versus added amounts of co-solvent evaluated from Figures 7 and 8, and polar term in solubility parameter (δ_p) of co-solvent. (●) cyclohexane, (○) benzene, (■) toluene, (□) propyl acetate, (▲) 2-hexanone, and (△) 1,2-dichloroethane. The straight line is guide for eye.

The LCST behavior of P(CVE-MA)/BuAc suggest that the polar interaction between polymer and solvent become weak with increase of temperature, which results in the segregation and precipitation of P(CVE-MA). Because of the similar chemical structure, 1,2-dichloroethane would prefer to make interaction between the 2-chloroethyl group in P(CVE-MA) and prevent the interaction between the polymer and BuAc, which might be the reason why 1,2-dichloroethane did not follow the linear relationship in Fig. 4-9.

4-4 Conclusion

Novel LCST-type phase behavior for polymer solutions in common organic media at mild conditions has been investigated. Alternating copolymers of 2-chloroethyl vinyl ether and maleic anhydride gave LCST-type solution when dissolved in BuAc, and T_{cp} values for higher molecular weight polymers were much lower than the boiling temperature of the solvent. With the increase of M_w of polymers, the T_{cp} of polymer solution decreased. Experimental LCST-type phase diagram of polymer solution can be reasonably described by Flory-Huggins theory. The T_{cp} of polymer solution in BuAc can be tuned by addition of co-solvent. Addition of non-solvent can decrease the T_{cp} , and addition of proper good solvent can increase the T_{cp} of polymer solution in BuAc, which can be ascribed into the polar interaction between P(CVE-MA) and solvent. Effects that can strengthen the polar interaction between polymers and solvents are inclined to increase T_{cp} of polymer solution.

In order to understand these LCST behavior of P(MA-CVE)/BuAc systems, dilute polymer solution properties such as second virial coefficient A_2 and its temperature dependency from precise light scattering or viscosity measurements around the evaluated Θ temperature (= 60 °C) will offer useful information. Further investigations for these novel polymer solution systems with LCST-type phase behavior will be reported in our future study.

Finally, we should point out that this copolymer can be chemically modified conveniently because it has functional alkyl chloride and carboxylic anhydride groups, so developments of some research and application are expected based on this novel polymer solution in organic solvent exhibiting the tunable LCST thermoresponsive behavior at mild condition.

REFERENCES

- 1 Dimitrov, I., Trzebicka, B., Müller, A. H. E., Dworak, A. & Tsvetanov, C. B. Thermosensitive water-soluble copolymers with doubly responsive reversibly interacting entities. *Prog. Polym. Sci.* **32**, 1275-1343 (2007).
- 2 Liu, R., Fraylich, M. & Saunders, B. R. Thermoresponsive copolymers: from fundamental studies to applications. *Colloid. Polym. Sci.* **287**, 627-643 (2009).
- 3 Hchild, H. G. Poly(*N*-isopropylacrylamide): experiment, theory and application. *Prog. Polym. Sci.* **17**, 163-249 (1992).
- 4 Ueki, T. & Watanabe, M. Lower critical solution temperature behavior of linear polymers in ionic liquids and the corresponding volume phase transition of polymer gels. *Langmuir* **23**, 988-990 (2007).
- 5 Ueki, T., Karino, T., Kobayashi, Y., Shibayama, M. & Watanabe, M. Difference in lower critical solution temperature behavior between random copolymers and a homopolymer having solvatophilic and solvatophobic structures in an ionic liquid. *J. Phys. Chem. B* **111**, 4750-4754 (2007).
- 6 Kodama, K., Nanashima, H., Ueki T., Kokubo, H. & Watanabe, M. Lower critical solution temperature phase behavior of linear polymers in imidazolium-based ionic liquids: effects of structural modifications. *Langmuir* **25**, 3820-3824 (2009).
- 7 Ueki, T. & Watanabe, M. Macromolecules in ionic liquids: progress, challenges, and opportunities. *Macromolecules* **41**, 3739-3749 (2008).
- 8 Siow, K. S., Delmas, G. & Patterson, D. Cloud-point curves in polymer solutions with adjacent upper and lower critical solution temperatures. *Macromolecules* **5**, 29-34 (1972).
- 9 Konno, S., Saeki, S., Kuwahara, N., Nakata, M. & Kaneko, M. Upper and lower critical solution temperatures in polystyrene solutions. IV. Role of configurational heat capacity. *Macromolecules* **8**, 799-804 (1975).
- 10 Bae, Y. C., Lambert, S. M., Soane, D. S. & Prausnitz, J. M. Cloud-point curves of polymer solutions from thermo-optical measurements. *Macromolecules* **24**, 4403-4407 (1991).
- 11 Patterson, D., Delmas, G. & Somcynsky, T. A comparison of lower critical solution temperatures of some polymer solutions. *Polymer* **8**, 503-516 (1967).
- 12 Burchard, W. Thermodynamic solution properties of three polymers exhibiting lower critical solution temperature. *Polymer* **10**, 467-475 (1969).
- 13 Cowie, J. M. G. & Swinyard, B. Location of three critical phase boundaries in poly(acrylic acid)-dioxane solutions. *Polymer* **31**, 1507-1513 (1990).

- 14 Cowie, J. M. G., Maconnachie, A. & Ranson, R. J. Phase equilibria in cellulose acetate-acetone solutions. The effect of the degree of substitution and molecular weight on upper and lower critical solution temperatures. *Macromolecules* **4**, 57-61 (1971).
- 15 Jang, J. G. & Bae, Y. C. Phase behaviors of binary polymer solutions: The extended lattice fluid model. *J. Appl. Polym. Sci.* **70**, 1143-1150 (1998).
- 16 Wang, F., Saeki, S. & Yamaguchi, T. Absolute prediction of upper and lower critical solution temperatures in polymer/solvent systems based on corresponding state theory. *Polymer* **40**, 2779-2785 (1999).
- 17 Patterson, D. Free volume and polymer solubility. A qualitative view. *Macromolecules* **2**, 672-677 (1969).
- 18 Migisawa, M., Ohnishi, K. & Sawada, H. Preparation of novel fluoroalkyl-end-capped 2-acrylamido-2-methylpropanesulfonic acid cooligomeric nanoparticles containing adamantane units possessing a lower critical solution temperature characteristic in organic media. *Langmuir* **23**, 5848-5851 (2007).
- 19 Kuroiwa, K., Shibata, T., Takada, A., Nemoto, N. & Kimizuka, N. Heat-set gel-like networks of lipophilic Co(II) triazole complexes in organic media and their thermochromic structural transitions. *J. Am. Chem. Soc.* **126**, 2016-2021 (2004).
- 20 Seno, K-I., Kanaoka, S. & Aoshima, S. Synthesis and LCST-type phase separation behavior in organic solvents of poly(vinyl ethers) with pendant imidazolium or pyridinium salts. *J. Polym. Sci. part A: Polym Chem.* **46**, 5724-5733 (2008).
- 21 Liu, Z., Guo, Y. & Inomata, K. Lower critical solution temperature behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in organic media. *Polym. J.* **42**, 901-904 (2010).
- 22 Inomata, K., Kasuya, M., Sugimoto, H. & Nakanishi, E. Effect of helix-coil transition on association behavior of both-ends hydrophobically-modified water-soluble polypeptide. *Polymer* **46**, 10035-10044 (2005).
- 23 Castelvetro, V., Pittaluga, G. B. & Ciardelli, F. Multifunctional poly(vinyl ethers) by controlled cationic polymerization in a fluorinated solvent. *Macromol. Chem. Phys.* **202**, 2093-2103 (2001).
- 24 Nukyen, O. & Ingrisich, S. Block copolymers from isobutyl vinyl ether and 2-chloroethyl vinyl ether. *Macromol. Chem. Phys.* **199**, 607-612 (1998).
- 25 Heischkel, Y. & Schmidt, H-W. Synthesis of ABC-triblock copolymers for light emitting diodes. *Macromol. Chem. Phys.* **199**, 869-880 (1998).

- 26 Bennevault, V., Peruch, F. & Deffieux, A. Influence of various proton traps on the bifunctional cationic polymerization of chloroethyl vinyl ether mediated by \square -iodo ether/zinc dichloride. *Macromol. Chem. Phys.* **197**, 2603-2613 (1996).
- 27 Schappacher, M. & Deffieux, A. New comblike copolymers of controlled structure and dimensions obtained by grafting by polystyryllithium onto poly(chloroethyl vinyl ether) chains. *Macromol. Chem. Phys.* **198**, 3953-3961 (1997).
- 28 Hall, Jr. H. K. Bond-forming initiation in spontaneous addition and polymerization reactions of alkenes. *Angew. Chem. Int. Ed. Engl.* **22**, 440-445 (1983).
- 29 Fujimori, K., Organ, P. P., Costigan, M. J. & Craven, I. E. Relative reactivity of free monomers and donor-acceptor complex in alternating copolymerization of isobutyl vinyl ether with maleic anhydride from the rate of polymerization. *J. Macromol. Sci. Chem.* **A23(5)**, 647-655 (1986).
- 30 Hallensleben, M. L. Elektron-donator-akzeptor-komplexe und polymerisation. III. Über die copolymerisation von maleins äureanhydrid mit isomeren butylvinyl äthern. *Makromol. Chem.* **144**, 267-281 (1971).
- 31 Braun, D., Schacht, M., Elsässer, H. & Tüdös, F. Alternating terpolymerization of three non-homopolymerizable monomers. *Macromol. Rapid Commun.* **18**, 335-342 (1997).
- 32 Ha, N. T. H., Fujimori, K., Henry, P. C. & Tucker, D. J. Assignment of ^{13}C NMR chemical shift and microstructure of copolymers of 2-chloroethyl vinyl ether-maleic anhydride and n-butyl vinyl ether-maleic anhydride. *Polym. Bull.* **43**, 81-85 (1999).
- 33 Den, J., Shi Y., Jiang, W., Peng Y., Lu L. & Cai, Y. Facile synthesis and thermoresponsive behaviors of a well-defined pyrrolidone based hydrophilic polymer. *Macromolecules* **41**, 3007-3014 (2008).
- 34 Xia, Y.; Yin, X., Burke, N. A. D. & Stölver H. D. H. Thermal response of narrow-disperse poly(*N*-isopropylacrylamide) prepared by atom transfer radical polymerization. *Macromolecules* **38**, 5937-5943 (2005).
- 35 Yamamoto, S-I., Pietrasik, J. & Matyjaszewski, K. The effect of structure on the thermoresponsive nature of well-defined poly(oligo(ethylene oxide) methacrylates) synthesized by ATRP. *J. Polym. Sci. part A: Polym. Chem.* **46**, 194-202 (2008).
- 36 Gao, J., Zhai, G., Song, Y. & Jiang, B. Multidimensionally stimuli-responsive phase transition of aqueous solutions of poly((*N,N*-dimethylamino) ethyl methacrylate) and poly(*N,N*-dimethyl-*N*-(methacryloyl) ethyl ammonium butane sulfonate). *J. Appl. Polym. Sci.* **107**, 3548–3556 (2008).

- 37 Yamamoto, K., Serizawa, T. & Akashi, M. Synthesis and thermosensitive properties of poly[(*N*-vinylamide)-*co*-(vinyl acetate)]s and their hydrogels. *Macromol. Chem. Phys.* **204**, 1027–1033 (2003).
- 38 Mori, T., Shiota, Y., Minagawa, K. & Tanaka, M. Alternative approach to the design of thermosensitive polymers: The addition of hydrophobic groups to the ends of hydrophilic polyether. *J. Polym. Sci. part A: Polym. Chem.* **43**, 1007–1013 (2005).
- 39 Hua, F., Jiang, X., Li, D. & Zhao, B. J. Well-defined thermosensitive, water-soluble polyacrylates and polystyrenics with short pendant oligo(ethylene glycol) groups synthesized by nitroxide-mediated radical polymerization. *J. Polym. Sci. part A: Polym. Chem.* **44**, 2454–2467 (2006).
- 40 Shultz, A. R. & Flory, P. J. Phase equilibria in polymer—solvent systems. *J. Am. Chem. Soc.* **74**, 4760–4767 (1952).
- 41 Schild, H. G., Muthukumar, M. & Tirrell, D. A. Cononsolvency in mixed aqueous solutions of poly(*N*-isopropylacrylamide). *Macromolecules* **24**, 948–952 (1991).
- 42 Grulke, E. A. “Solubility parameter values”, in *Polymer Handbook*, 4th Edition (eds Brandrup, J., Immergut, E. H., & Grulke, E. A.) Ch.VII, 675 (Wiley, New York, 1999).
- 43 Liu, Z., Guo, Y. & Inomata, K. Reversible thermoresponsive behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in mixed solvent of tetrahydrofuran/hexane *Colloid Polym. Sci.* **289**, 791–798 (2011).

Chapter 5

Thermoreversible UCST-type Phase Behavior of Comb-like Poly(phenyl maleimide-*co-n*-octadecyl vinyl ether) Copolymer in Organic Media

5-1 Introduction

Thermoresponsive polymers can respond to change of temperature in the environment, and as one class of stimuli responsive polymers many important applications such as sensors¹, controlled release²⁻³, intelligent gels⁴⁻⁵ and smart materials⁶ have been developed. Usually, there exist two kinds of solution phase behavior according to the phase diagram. One is that polymer solution is homogeneous at lower temperature and becomes heterogeneous at higher temperature and in this case the polymer solution owns lower critical solution temperature (LCST) and the this thermoresponsive behavior can be called LCST-type phase behavior. In contrast, the other behavior is that polymer solution is homogeneous at higher temperature and phase separation will occur at lower temperature, and this kind of polymer solution presents upper critical solution temperature (UCST) in the phase diagram and this phase behavior is called UCST-type. UCST-type as well as LCST-type polymer solution has been studied a lot in the past⁷⁻⁹ and the enthusiasm for research on thermoresponsive polymers is still full nowadays¹⁰⁻¹³.

Though LCST-type thermoresponsive water soluble polymer systems have been paid much attention and many theories and applications have been developed^{8, 9, 12, 14}, UCST-type thermoresponsive polymer systems also attract much research interest in the past and nowadays¹⁵⁻¹⁷. UCST-type water soluble polymer systems is useful for some applications such as drug delivery¹⁸⁻¹⁹, however it is also necessary and important for industry to investigate the UCST-type phase behavior of polymer in organic media¹⁶⁻¹⁷, which can help to understand the properties of polymer solution and can present some useful clues for some industrial applications^{16, 20-25}.

Recently besides those studies on the conventional UCST-type polymer systems¹⁶⁻¹⁷, some new UCST-type thermoresponsive polymer systems in which the phase separation and the cloud point (CP) of polymer in organic media can be well tuned attract much attention²⁶⁻³¹. Some studies on new UCST-type phase behavior in organic media are as follows. Stereocontrolled poly(*N*-isopropylacrylamide) can exhibit UCST-type thermoresponsive behavior and study on the UCST-type behavior of stereocontrolled

poly(*N*-isopropylacrylamide) in organic media can help to understand the rule of tacticity of polymer chain on thermoresponsive behavior²⁶. Poly(vinyl ethers) with proper pendants can exhibit UCST-type phase behavior in some certain organic media, and phase separation can be controlled by solvent species, polymer concentration and so on²⁸⁻²⁹. Recently well-tunable UCST-type phase behavior of poly[oligo(ethylene glycol) methyl ether methacrylate] in organic media was also studied, and the cloud point of polymer solution in organic depended on the solvent species, addition of co-solvent, molecular weight and chemical structure of polymer chain³⁰. As polymer chains were grafted onto the surface of some colloid particles, based on the UCST-type thermoresponsive behavior in organic media the aggregation of related colloidal particles can be controlled by temperature, e.g., temperature-induced aggregation of magnetic nanoparticles grafted by poly(2-methoxyethyl methacrylate) in methanol²⁷ or polystyrene in cyclohexane³¹. Based on UCST-type behavior in organic media some potential applications may be developed, for instance smart materials or self assembly of related macromolecules.

Herein a novel reversible thermoresponsive UCST-type behavior in organic media is reported. The copolymer of *N*-phenyl maleimide and *n*-octadecyl vinyl ether can exhibit UCST-type behavior in some proper organic media and the cloud point of polymer solution can be tuned by some aspects such as solvent and addition of co-solvent conveniently.

5-2 Experimental

5-2-1 Materials

Toluene (Nacalai tesque; 99.5%), dimethylsulfoxide (DMSO; Kishida Chemical Co. LTD; 99%), azobisisobutyronitrile (AIBN; Wako; > 98%), ethylene glycol (Nacalai tesque; 99%), 1-butanol(Nacalai tesque; 99%), 1-octanol (TCI; >98.0%), 1-hexanol (TCI; >98.0%), *n*-octadecyl vinyl ether (ODVE; TCI; >85.0%), *N*-phenylmaleimide (PMI; TCI; >97%), ethanol (Nacalai tesque; 99.5%), ethylene glycol (EG; Nacalai tesque; 99%), diethyl ether (Kishida Chemical Co. LTD; >99.0%), chloroform (Wako; >99.0%), 1,2-dichloroethane(Nacalai tesque; 99.5%), dichloromethane(Nacalai tesque; 99.5%), 1,4-dioxane (Kishida Chemical Co. LTD;>99.0%), methanol (Kanto Chemical Co. LTD; >99.8%), isopropanol (Nacalai tesque; 99.7%) acetone (Kishida Chemical Co. LTD;>99.0%), cyclohexane(Nacalai tesque; 99.5%), benzene(Nacalai tesque; 99.5%), *N,N*-dimethylformamide(DMF; Nacalai tesque; 99.5%),

N,N-dimethylacetamide (DMAc; Kishida Chemical Co. LTD; 99.0%), chloroform- d_1 ($CDCl_3$; SCETI Co. LTD; 99.9%), *N,N*-dimethylformamide- d_7 (DMF- d_7 ; Aldrich; 99.5 atom% D) were used as received.

5-2-2 Synthesis of polymers

N-Phenyl maleimide (2.165 g), *n*-octadecyl vinyl ether (3.707 g), AIBN (0.01 g), toluene (15 g) were added into a 50 mL three-neck flask. The reaction was carried out at an atmosphere of nitrogen at 70 °C for 4 hours. Resultant copolymer solution was poured into ethanol and precipitated polymers were filtered and dried in vacuum drying oven at 80 °C for 12 hours.

5-2-3 Gel Permeation Chromatograph (GPC)

Molecular weight of the prepared copolymer was determined by GPC using 2 columns of TSKgel -3000 and -5000 connected to SD-8022 system (Tosoh) at a 1.0 mL/min flow rate of THF. Polystyrene standards were used for molecular weight calibration.

5-2-4 FT-IR measurement

Infrared spectrum of copolymer was recorded in a Nicolet AVATAR 320S FT-IR spectrophotometer in KBr pellet.

5-2-5 1H NMR measurement

1H NMR in $CDCl_3$: Polymer solution with 1wt.% polymer concentration was added into a NMR tube with an outer diameter of 5 mm, and 1H NMR spectrum in $CDCl_3$ at 40 °C was measured using BRUKER AVANCE 600 (600 MHz) spectrometer.

1H NMR in DMF- d_7 : Polymer solution with 1wt.% polymer concentration was added into a NMR tube with an outer diameter of 5 mm, and 1H NMR spectra in DMF- d_7 at different temperature were measured using BRUKER AVANCE 600 (600 MHz) spectrometer. Scanning times was 128 and receiver gain was kept constant in all NMR measuring experiments.

5-2-6 ^{13}C NMR measurement

Polymer solution with 10wt.% polymer concentration was added into a NMR tube with an outer diameter of 5 mm, and ^{13}C NMR spectrum in CDCl_3 at room temperature was measured using BRUKER AVANCE 200 (200 MHz) spectrometer.

5-2-7 Preparation of polymer solution

Polymer solutions were prepared by dissolving certain amount of polymer in various organic solvents above temperature of cloud point (T_{cp}) above which polymer can dissolve in solvent resulting in a homogeneous transparent solution.

5-2-8 Static Light Scattering (SLS) Measurement

Thermoresponsive phase behavior of the polymer solution was characterized by the scattered light intensity (I_s) at different temperatures at a fixed angle of 90° . I_s was measured by a laboratory-made apparatus equipped with an ALV/SO-SIPD detector using He-Ne laser (the wavelength $\lambda_0 = 633 \text{ nm}$)³². The transparent polymer solution above T_{cp} was transferred into optical tube immediately and then the static light scattering (SLS) measurement was carried out directly. The heating and cooling rate of the system was about $0.2 \text{ }^\circ\text{C}/\text{min}$. I_s of the polymer solution was measured immediately as the temperature of the system reached the desired temperature. Unless pointing out, the I_s of polymer solution at different temperature was measured during cooling process.

5-3 Results and discussion

5-3-1 Synthesis of copolymer

It is well known that *N*-phenyl maleimide and electron-rich vinyl ether monomer form alternating copolymer in conventional free radical polymerization³³⁻³⁴ and the copolymer of maleimide owned some useful applications such as thermo stable materials, Langmuir-Blodgett (LB) films and functional surface³³⁻³⁶. Herein, copolymer of *N*-phenyl maleimide and *n*-octadecyl vinyl ether (PPMIODVE) was synthesized by conventional free radical polymerization in the solution of toluene with AIBN as initiator and 1:1 molar mixture of PMI and ODVE. After copolymerization, some

amounts of polymer were obtained with a conversion of 60% (conversion= W_p/W_m , where W_p is quantity of obtained polymer, and W_m is the total quantity of added monomer of PMI and ODVE). Due to long *n*-alkyl (*n*-octadecyl) group of ODVE, a copolymer with comb-like side chains would be obtained after copolymerization as shown in Fig 5-1a. The GPC graph of synthesized copolymer was shown in Fig 5-1b, and the weight-averaged molecular weight of copolymer was 79600 g/mol and the molecular weight distribution was 3.06.

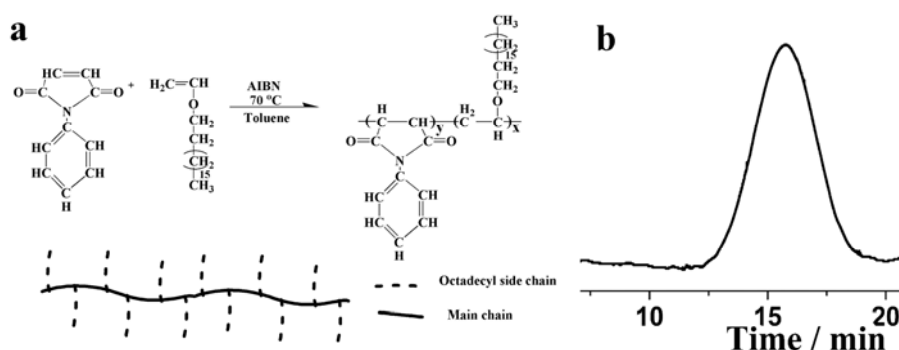


Fig. 5-1. (a) scheme for synthesis and chemical architecture of copolymer. (b) GPC graph of synthesized copolymer

In order to determine the chemical composition of copolymer, spectroscopy of FT-IR, ^1H and ^{13}C NMR was used and related spectra were shown in Fig 5-2. The peaks between 2932 and 2830 cm^{-1} associated with the C-H stretching vibrations. Peaks at 1467 and 1389 cm^{-1} associated with the $-\text{CH}_3$ asymmetric and symmetric vibrations. Peaks at 3070 , 1193 , 1082 and 750 cm^{-1} are characteristic adsorption of CH vibration of phenyl group. Peaks between 1600 and 1450 cm^{-1} associated with the C-C vibration of phenyl group. Strong peaks at 1722 cm^{-1} associated the C=O vibrations. It can be deduced from the FT-IR spectra shown in Fig 5-2a that the synthesized copolymer was a copolymer of PMI and ODVE. The ^1H NMR spectrum and the assignments of proton resonances of copolymer was shown in Fig 5-2b. The molar ratio of PMI to ODVE (y/x) in copolymer was calculated by the ratio of integral areas of the proton signals from the PMI units (phenyl group) and ODVE units (methyl group) in ^1H NMR spectrum. The

value of y/x was calculated by the following formula: $\frac{y}{x} = (A_{\text{phenyl}} / 5) / (A_{\text{methyl}} / 3)$,

where A_{phenyl} was the integral area of protons from phenyl group in PMI unit and A_{methyl} was integral area of proton from methyl group in ODVE unit in copolymer. The calculated y/x ratio of PMI to ODVE in copolymer was about 1.8, which indicated that the obtained copolymer was not a strictly alternating copolymer and there existed much more PMI unit in the structure of copolymer. Although there exists a big trend of forming alternating structure during copolymerization of maleimide monomer and vinyl ether monomer in theory, the obtained copolymer contained more PMI unit and this kind of results has been reported previously^{33, 37}. ^{13}C NMR spectrum of copolymer in CDCl_3 and the assignments of resonances for different protons in copolymer were shown in Fig 5-2c. It can be confirmed from the ^{13}C NMR spectrum that the synthesized polymer was a copolymer of PMI and ODVE.

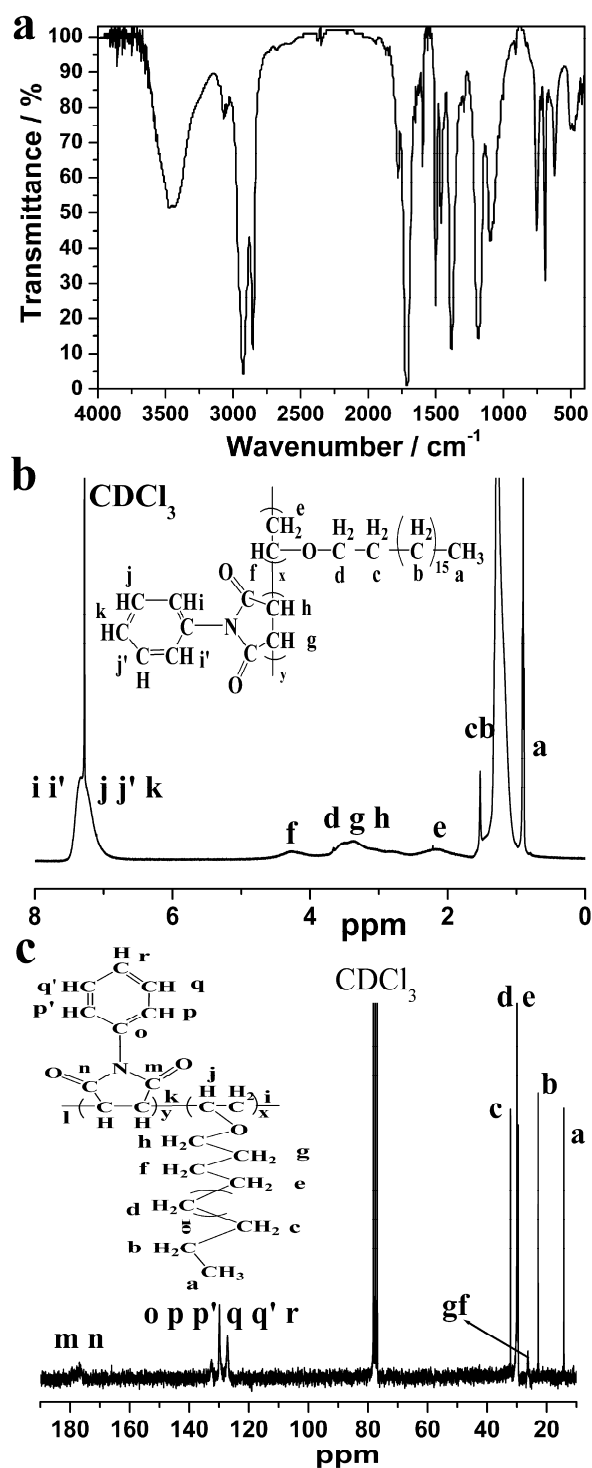


Fig. 5-2. (a) FT-IR spectrum (b) ¹H NMR spectrum (600 MHz) in CDCl₃ (13) ¹³C NMR spectrum (200 MHz) in CDCl₃

5-3-2 UCST-type thermoresponsive behavior of polymer solution

The thermoresponsive behavior of polymer solution was characterized by the scattered light intensity of polymer solution at different temperature at a fixed angle 90° in the measurement of SLS. The I_s of polymer solution in DMF decreased with increasing the temperature and the I_s remained constant with a small I_s value (Fig 5-3 a) as the polymer solution was heated, and after that the cooling process was carried out. As the temperature is below a critical solution temperature (51°C in Fig 5-3a), the I_s of polymer solution increased abruptly, and the critical temperature during the cooling process is defined as the temperature of cloud point (T_{cp}), e.g. point A in Fig 3a. At low temperature (20°C in Fig 5-3a) the polymer solution in DMF was turbid and above T_{cp} the polymer solution was transparent (60°C Fig 5-3a), which indicated that the polymer solution exhibited upper critical solution temperature (UCST) type behavior in DMF. Furthermore, the transition between the turbid and transparent state was reversible.

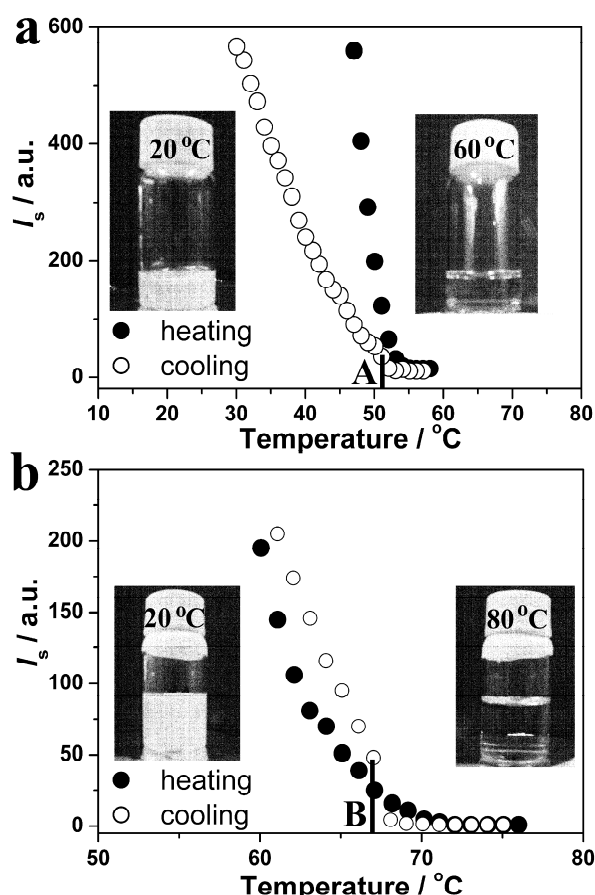


Fig. 5-3. Temperature dependence of I_s of copolymer in organic solvent. (a) 1wt.% polymer solution in DMF, (b) 0.1 wt.% polymer solution in 1-butanol. The temperature at which photograph was taken is indicated in the graph.

Similar to the solution in DMF, polymer solution in 1-butanol also exhibit reversible UCST-type behavior. The I_s of polymer solution in 1-butanol also exhibited temperature dependence and T_{cp} defined during cooling process was a little higher, e.g., point B (67 °C) in Fig 5-3b. The transition of polymer solution state between turbid (20 °C in Fig 5-3b) and transparent (80 °C in Fig 5-3b) was also reversible.

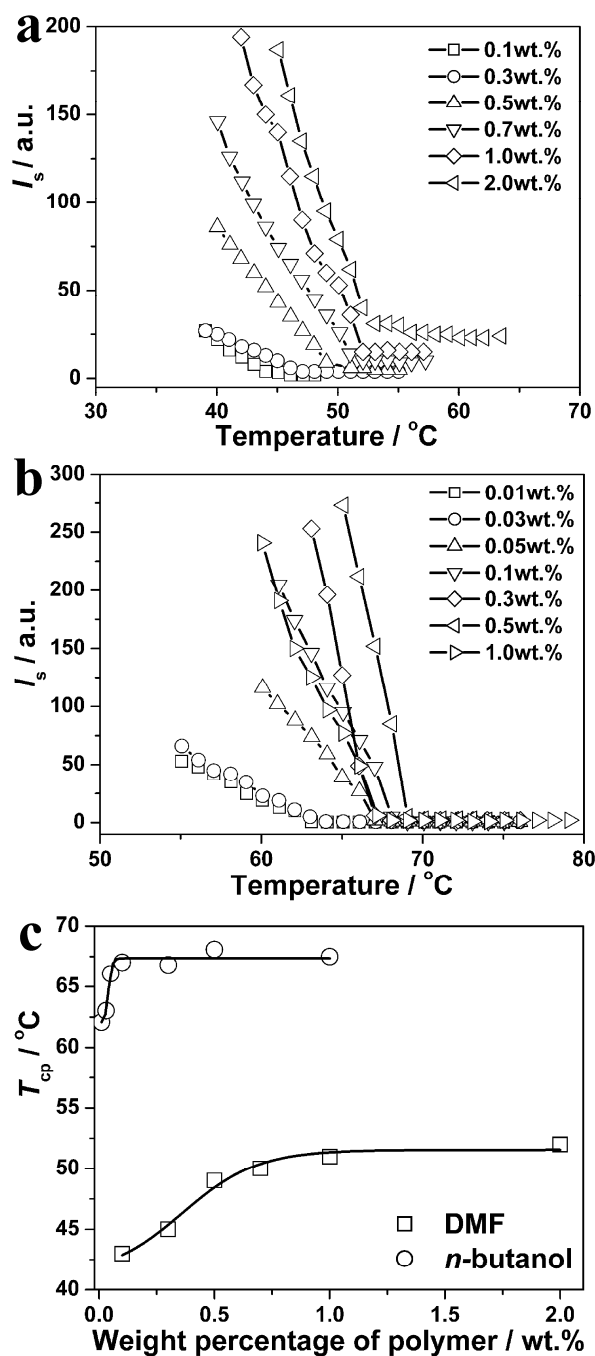


Fig. 5-4. (a) Temperature dependence of I_s of copolymer in DMF. (b) Temperature dependence of I_s of copolymer in 1-butanol. Polymer concentration is indicated in graph (a) and (b). (c) T_{cp} of polymer solution at different polymer concentration.

The I_s of polymer solution at different polymer concentration at different temperature during cooling process was shown in Fig 5-4. I_s of polymer solution with different polymer concentration in DMF (Fig 5-4a) and 1-butanol (Fig 5-4b) depended on the temperature. The T_{cp} of polymer solution at different polymer concentration was shown in Fig 5-4c. It can be seen that the phase behavior of polymer solution in DMF and 1-butanol was UCST-type and T_{cp} of polymer solution in 1-butanol was higher than that of in DMF. In experiments, polymer solution became much more turbid visually after phase separation in 1-butanol than in DMF with same polymer concentration. It can be deduced that for this polymer DMF owns better solvent quality than 1-butanol.

5-3-3 Effect of solvent and co-solvent on UCST-type thermoresponsive behavior

In preliminary experiments, this copolymer can be dissolved in some nonpolar and weak polar solvents such as diethyl ether, toluene, chloroform, 1,2-dichloroethane, dichloromethane, 1,4-dioxane, cyclohexane, and benzene. This polymer can not dissolve in some strongly polar solvents such as methanol, ethanol, isopropanol, acetone, EG, and DMSO. Distinct from polymer solution in DMF, polymer can be dissolved in DMAc rather than exhibit UCST-type phase behavior. Although polymer solution in 1-butanol can exhibit reversible UCST-type behavior, polymer in methanol, ethanol, and propanol can not be dissolved even above the boiling point of used solvent. It seemed that some polar especially strongly polar solvents were non-solvent for this polymer and some nonpolar or weak polar solvents were solvent for this polymer, of course, depending on the situations. In some proper solvent such as DMF, 1-butanol, 1-hexanol, 1-octanol or in some mixed solvents, polymer can exhibit UCST-type behavior.

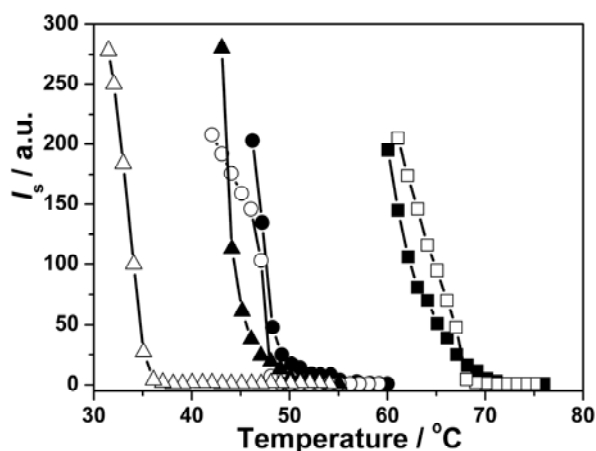


Fig. 5-5. Temperature dependence of I_s of copolymer in different alcohols. Triangle: 1-octanol, circle: 1-hexanol and square: 1-butanol. The solid and hollow symbols stand for heating and cooling process respectively.

Thermoresponsive behavior of polymer in some selected *n*-alkyl alcohols was also investigated, and the I_s of polymer solution at different alcohols during heating and cooling processes were shown in Fig 5-5. It can be seen polymer in all selected alcohols can exhibit UCST-type behavior. The value of T_{cp} of polymer solution during cooling processes in these selected alcohols was as follows: 1-butanol>1-hexanol>1-octanol, and the decreasing order of T_{cp} in alcohols was in accordance with the decreasing order of solvent polarity. So for this polymer some higher alcohols owned better solvent quality than some lower alcohols especially at higher temperatures. Compared with thermoresponsive behavior of polymer solution in 1-hexanol and 1-butanol, curve of I_s versus temperature in 1-octanol presented a distinct discrepancy between cooling and heating processes. This distinct discrepancy may be attributed to higher solvent viscosity which may restrict the diffusion of polymer in solvent resulting in the delay of precipitation of polymer during cooling process.

Effect of addition of co-solvent on thermoresponsive behavior of polymer solution in DMF was investigated, and results were shown in Fig 5-6. Polymer can dissolve in toluene, so toluene as a good solvent was added into the polymer solution in DMF. In the added toluene range shown in Fig 5-6a, polymer solution in mixed solvent of DMF and toluene can exhibit UCST-type behavior and T_{cp} of polymer solution decreased with increase in toluene as shown in Fig 5-6c. The decreasing in T_{cp} may be attributed to stronger interaction between polymer and good solvent. Because polymer can not dissolve in EG, EG was considered as a nonsolvent and added the polymer solution in DMF. In experimental added EG range shown in Fig 5-6b, polymer solution can also exhibit UCST-type behavior in mixed solvent of DMF and EG as shown in Fig 5-6b, and T_{cp} of polymer solution increased with increasing EG as shown in Fig 5-6c. With increasing EG, the solvent quality of the mixed solvent became poor and the polymer would soluble only at higher temperature resulting in increasing in T_{cp} .

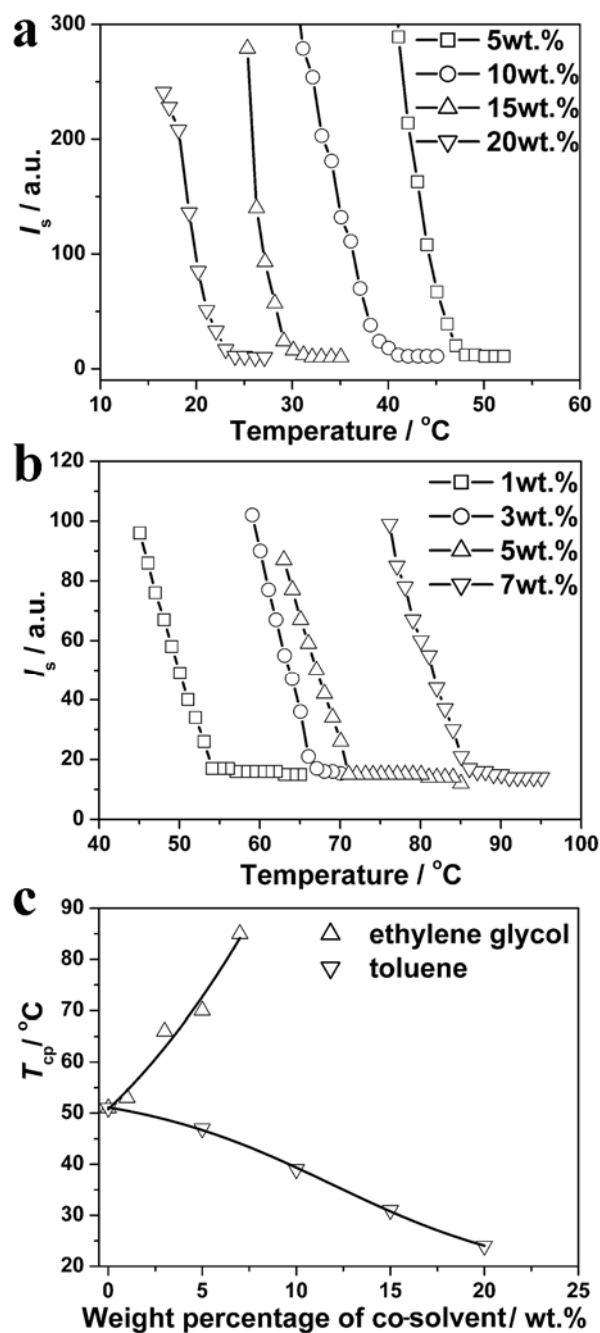


Fig. 5-6. Temperature dependence of I_s of copolymer in with different (a)toluene, (b) EG weight percentage in mixed solvent of DMF and co-solvent. (c) T_{cp} of polymer solution with different weight percentage of co-solvent in mixed solvent. The weight percentage of polymer in mixed solvent is 1.0 wt.%. The weight percentage of co-solvent in mixed solvent in graph (a) and (b) are indicated in the graph.

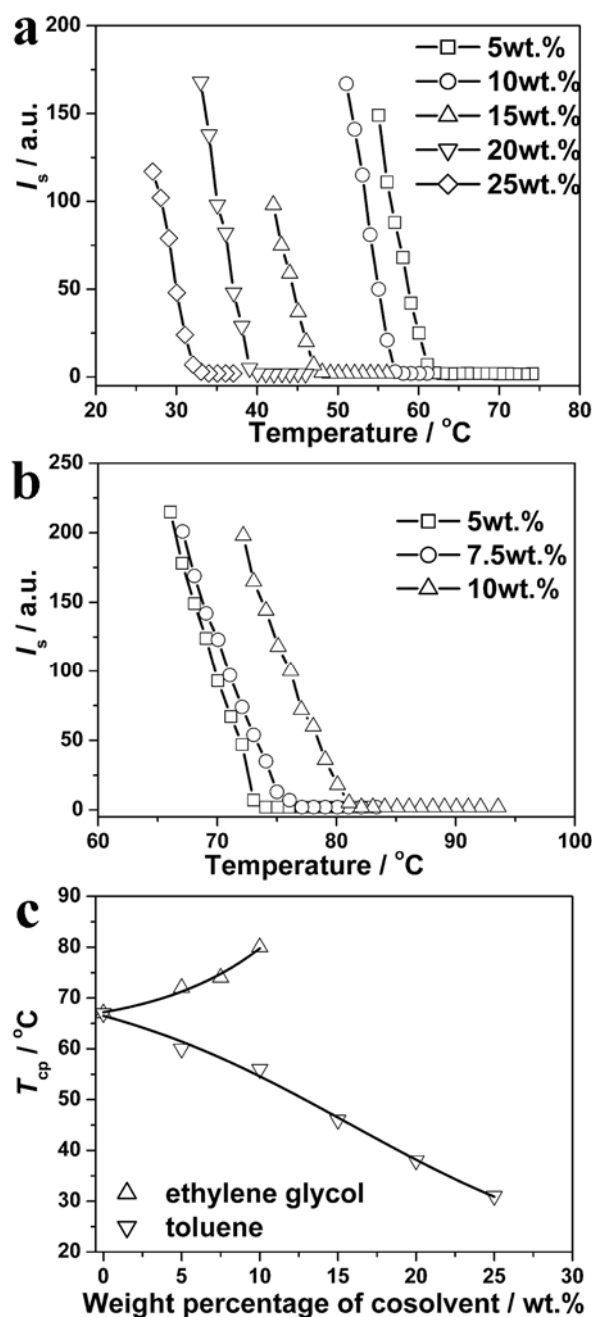


Fig. 5-7. Temperature dependence of I_s of copolymer in with different (a)toluene, (b) EG weight percentage in mixed solvent of 1-butanol and co-solvent. (c) T_{cp} of polymer solution with different weight percentage of co-solvent in mixed solvent. The weight percentage of polymer in mixed solvent is 0.1 wt.%. The weight percentage of co-solvent in mixed solvent in graph (a) and (b) are indicated in the graph.

Effect of co-solvent on thermoresponsive behavior of polymer solution in 1-butanol was also studied, and results were shown in Fig 5-7. At the experimental added

co-solvent range, polymer solution can exhibit UCST-type behavior in mixed solvent of co-solvent and 1-butanol as shown in Fig 5-7a and 5-7b. Similar to situation of addition of co-solvent in DMF, the addition of toluene as good solvent decreased the T_{cp} of polymer solution and addition of EG as nonsolvent increased the T_{cp} of polymer solution, as shown in Fig 5-7c.

As mentioned above, T_{cp} of the polymer solution can be changed by addition of proper co-solvent conveniently, which present an easy way to tune the T_{cp} of polymer solution. Addition of co-solvent usually can tune the solvent quality and based on the changes in solvent quality some very useful applications can be obtained in the field of polymer solution, coordination and supramolecular chemistry. So well tunable thermoresponsive polymer systems in organic media may own some perspectives in the interdisciplinary of polymer science, coordination or supramolecular systems.

5-3-4 High resolution ^1H NMR spectra of copolymer in DMF- d_7 at different temperatures

Although many measurements can be used for studying the thermoresponsive behavior of polymer solutions, NMR is good choice for investigating mechanism of the thermoresponsive behavior of polymer in molecular level³⁸. High resolution ^1H NMR (600 MHz) measurement was made, and ^1H NMR spectra of polymer at different temperatures and assignments of resonances to various protons in the copolymer were shown in Fig 5-8a. At low temperatures, e.g., 20 °C, 25 °C and 30 °C the signals of protons from phenyl group and most of protons from *n*-octadecyl group can be recognized and the shape line of related protons seemed broaden, while the signals of protons from the backbone of the copolymer did not appear. These phenomena of ^1H NMR signals at low temperatures indicated that the mobility of polymer segments in DMF- d_7 was restricted at low temperatures resulting in broadened and poorly resolved proton lines in ^1H NMR spectra. With increasing the temperature the peaks of protons from methyl and methylene groups became sharp and intensity of these peaks became large, and similar tendency for peaks of protons from phenyl group was also observed. Further more, at higher temperature (e.g. above 55 °C) the signals of protons from the backbone of copolymer chain can be recognized and the shape line of all protons seemed resolved better than that at lower temperatures, which indicated that the mobility of polymer segments increased. However, compared to ^1H NMR (600 MHz) spectrum in CDCl_3 (Fig. 2), the ^1H NMR (600 MHz) spectrum of copolymer in DMF- d_7

seemed a little poorly resolved, which may indicate that chloroform was a better solvent than DMF for polymer even at high temperatures.

The half-height width (HW) of protons from methyl group (peak at 0.92 ppm) at different temperature in DMF-d₇ was shown in Fig 5-8b. The behavior of HW with increasing the temperature can be divided into two stages by a critical temperature (CT). It can be seen that the HW decreased sharply at the first stage (from 20 to 50 °C) and then remained almost constant (from 55 to 70 °C) at the second stage. The tangent intersection of those two stages can be defined as CT and the value of CT was about 52.5 °C which was close to the T_{cp} (51 °C) of polymer solution in DMF in Fig 4c. It is well-known that the HW can reveal the mobility of related polymer segments and narrower HW indicates better mobility of related polymer segments. So it can be deduced that the mobility of methyl group increased with increasing temperature and the mobility of polymer chain also did. In view of phase separation at lower temperatures visually, the decreasing mobility of methyl group can be attributed to the aggregation of polymer chains.

So according to the high resolution ¹H NMR spectra at different temperatures in DMF-d₇, the mechanism of thermoresponsive behavior could be described as follows. At high temperatures the polymer chain can be dissolved well in DMF resulting in a homogeneous transparent polymer solution and as the temperature decreases to a critical temperature the solvent quality of DMF becomes poor for polymer and the poor solvent condition leads to the aggregation of polymer resulting in phase separation. After phase separation the mobility of polymer segments decreases resulting in broadening of the proton line in ¹H NMR spectrum.

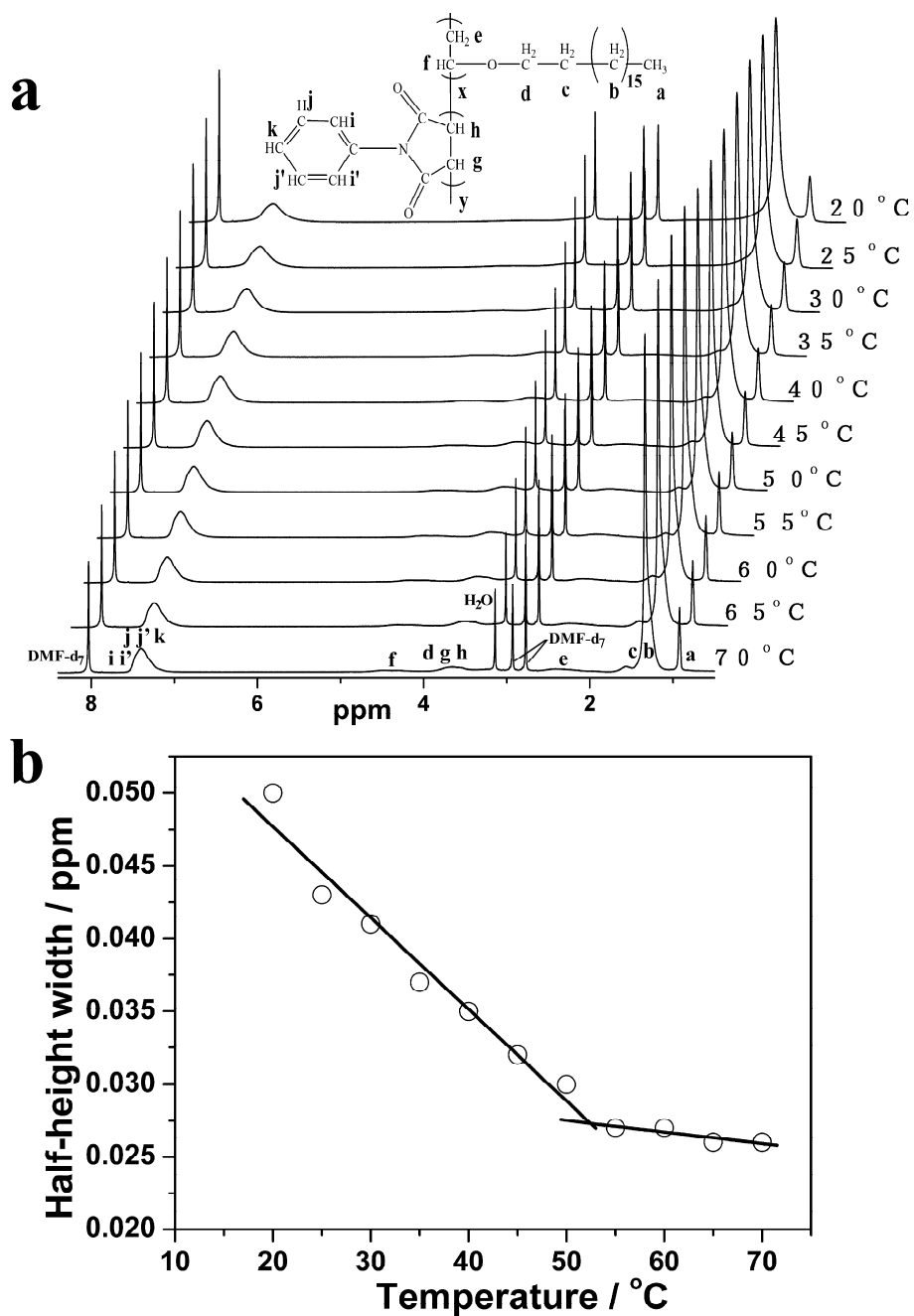


Fig. 5-8. (a) ^1H NMR of polymer in DMF-d_7 at different temperatures. (b) half-height width of peak of protons from methyl group at different temperatures.

5-4 Conclusion

Comb-like copolymer of *N*-phenyl maleimide and *n*-octadecyl vinyl ether was synthesized by conventional free radical solution polymerization. The synthesized copolymer was not a strictly alternating copolymer, while there were more units of

N-phenyl maleimide in the copolymer. The copolymer can exhibit UCST-type behavior in DMF, 1-butanol and other proper organic media reversibly. The cloud point of polymer solution in organic media can be tuned conveniently by adding proper certain co-solvent, and the good solvent decreased the cloud point while the nonsolvent increased the cloud point. The high resolution ¹H NMR spectrum in DMF-d₇ indicated that with decreasing the temperature solvent quality became poor and poor leading to phase separation at a critical temperature in the end and the mobility of polymer segments decreased after phase separation.

REFERENCES

- 1 Hu, J. & Liu, S. Responsive polymers for detection and sensing applications: current status and future developments. *Macromolecules* **43**, 8315-8330 (2010).
- 2 York, A. W., Kirkland, S. E. & McCormick, C. L. Advances in the synthesis of amphiphilic block copolymers via RAFT polymerization: Stimuli-responsive drug and gene delivery. *Adv. Drug. Delivery Rev.* **60**, 1018-1036 (2008).
- 3 Onaca, O., Enea, R., Hughes, D. W. & Meier, W. Stimuli-Responsive Polymersomes as Nanocarriers for Drug and Gene Delivery. *Macromol. Biosci.* **9**, 129-139 (2009).
- 4 Imran, A. B., Seki, T. & Takeoka, Y. Recent advances in hydrogels in terms of fast stimuli responsiveness and superior mechanical performance. *Polym. J.* **42**, 839-851 (2010).
- 5 Joseph, J-G. Polymeric gels and hydrogels for biomedical and pharmaceutical applications. *Polym. Adv. Technol.* **21**, 27-47 (2010).
- 6 Kirsebom, H., Galaev, I. Y. & Mattiasson, B. Stimuli-responsive polymers in the 21st century: elaborated architecture to achieve high sensitivity, fast response, and robust behavior. *J. Polym. Sci. Part B: Polym. Phys.* **49**, 173-178 (2011).
- 7 Gil, E. K., Hudson, S. M. Stimuli-responsive polymers and their bioconjugates. *Prog. Polym. Sci.* **29**, 1173-1222 (2004).
- 8 Jeong, B. & Gutowska, A. Lessons from nature: stimuli-responsive polymers and their biomedical applications. *Trends Biotechnol.* **20**, 305-311 (2002).
- 9 Schild, H. G. Poly(N-isopropylacrylamide): experiment, theory and application. *Prog. Polym. Sci.* **17**, 163-249 (1992).
- 10 Ahn, S-k., Kasi, R. M., Kim, S-C., Sharma, N. & Zhou, Y. Stimuli-responsive polymer gels. *Soft Matter* **4**, 1151-1157 (2008).
- 11 Liu, R., Fraylich, M. & Saunders, B. R. Thermoresponsive copolymers: from fundamental studies to applications. *Colloid Polym. Sci.* **287**, 627-643 (2009).
- 12 Liu, F. & Urban, M. W. Recent advances and challenges in designing

- stimuli-responsive polymers. *Prog. Polym. Sci.* **35**, 3-23 (2010).
- 13 Roy, D., Cambre, J. N. & Sumerlin, B. S. Future perspectives and recent advances in stimuli-responsive materials. *Prog. Polym. Sci.* **35**, 278-301 (2010).
 - 14 Maresov, E. A., Semenov, A. N. Mesoglobule morphologies of amphiphilic polymers. *Macromolecules* **41**, 9439-9457 (2008).
 - 15 Dimitrov, I., Trzebicka, B., Müller, A. H. E., Dworak, A. & Tsvetanov, C. B. Thermosensitive water-soluble copolymers with doubly responsive reversibly interacting entities. *Prog. Polym. Sci.* **32**, 1275-1343 (2007).
 - 16 Gharagheizi, F. & Sattari, M. Prediction of the θ (UCST) of polymer solutions: A quantitative structure–property relationship study. *Ind. Eng. Chem. Res.* **48**, 9054-9060 (2009).
 - 17 Jung, J. G. & Bae, Y. C. Liquid–liquid equilibria of polymer solutions: Flory-huggins with specific interaction. *J. Polym. Sci. Part B: Polym. Phys.* **48**, 162-167 (2010).
 - 18 Schmaljohann, D. Thermo- and pH-responsive polymers in drug delivery. *Adv. Drug. Delivery Rev.* **58**, 1655-1670 (2006).
 - 19 Wang, Q., Li, S., Wang, Z., Liu, H. & Li, C. Preparation and characterization of a positive thermoresponsive hydrogel for drug loading and release. *J. Appl. Polym. Sci.* **111**, 1417-1425 (2009).
 - 20 Nies, E., Li, T., Berghmans, H., Heenan, R. K. & King, S. M. Upper critical solution temperature phase behavior, composition fluctuations, and complex formation in poly (vinyl methyl ether)/D2O solutions: small-angle neutron-scattering experiments and wertheim lattice thermodynamic perturbation theory predictions. *J. Phys. Chem. B* **110**, 5321–5329 (2006).
 - 21 Li, D., McHugh, M. A., Zanten, J. H. V. Density-induced phase separation in poly(ethylene-co-1-butene)–dimethyl ether solutions. *Macromolecules* **38**, 2837–2843 (2005).
 - 22 Saeki, S., Kuwahara, N., Hamano, K., Kenmochi, Y. & Yamaguchi, T. Pressure dependence of upper critical solution temperatures in polymer solutions. *Macromolecules* **19**, 2353–2356 (1986).
 - 23 Bungert, B., Sadowski, G. & Arlt, W. Separations and material processing in solutions with dense gases. *Ind. Eng. Chem. Res.* **37**, 3208-3220 (1998).
 - 24 Pappa, G. D., Voutsas, E. C. & Tassios, D. P. Liquid–liquid phase equilibrium in polymer–solvent systems: correlation and prediction of the polymer molecular weight and the pressure effect. *Ind. Eng. Chem. Res.* **40**, 4654-4663 (2001).
 - 25 Le, L. Y., Liu, Q. L., Cheng, Z.F. & Zhang, X.B. Simplified nonrandom model for

- predicting solvent activity in polymer solutions. *Ind. Eng. Chem. Res.* **46**, 2191–2197 (2007).
- 26 Koyama, M., Hirano, T., Ohno, K. & Katsumoto, Y. Molecular understanding of the UCST-Type phase separation behavior of a stereocontrolled poly(*N*-isopropylacrylamide) in bis(2-methoxyethyl) ether. *J. Phys. Chem. B* **112**, 10854–10860 (2008).
- 27 Gelbrich, T., Feyen, M. & Schmidt, A. M. Magnetic Thermoresponsive Core–Shell Nanoparticles. *Macromolecules* **39**, 3469–3472 (2006).
- 28 Yoshida, T., Seno, K-I., Kanaoka, S. & Aoshima, S. Stimuli-responsive reversible physical networks. I. Synthesis and physical network properties of amphiphilic block and random copolymers with long alkyl chains by living cationic polymerization. *J. Polym. Sci. Part A: Polym. Chem.* **43**, 1155-1165 (2005).
- 29 Seno, K-I., Date, A., Kanaoka, S. & Aoshima, S. Synthesis and solution properties of poly(vinyl ether)s with long alkyl chain, biphenyl, and cholesteryl pendants. *J. Polym. Sci. Part A: Polym. Chem.* **46**, 4392-4406 (2008).
- 30 Roth, P. J., Jochum, F. D. & Theato, P. UCST-type behavior of poly[oligo(ethylene glycol) methyl ether methacrylate] (POEGMA) in aliphatic alcohols: solvent, co-solvent, molecular weight, and end group dependences. *Soft matter* **7**, 2484-2492 (2011).
- 31 Kaiser, A. & Schmidt, A. M. Phase behavior of polystyrene-brush-coated nanoparticles in cyclohexane. *J. Phys. Chem. B* **112**, 1894-1898 (2008).
- 32 Inomata, K., Kasuya, M., Sugimoto, H. & Nakanishi, E. Effect of helix-coil transition on association behavior of both-ends hydrophobically-modified water-soluble polypeptide. *Polymer* **46**, 10035-10044 (2005).
- 33 Tebbe, H., Ackern, F. V. & Tieke, B. New amphiphilic copolymers of *N*-phenylmaleimides and vinyl ethers: thermal properties, Langmuir and Langmuir-Blodgett films, gas permeation. *Macromol. Chem. Phys.* **196**, 1475-1486 (1995).
- 34 El-Guweri, M., Hendlinger, P. & Laschewsky, A. Partially fluorinated maleimide copolymers for Langmuir films of improved stability, 1. Synthesis, copolymerisation behaviour and bulk properties. *Macromol. Chem. Phys.* **198**, 401-418 (1997).
- 35 Hendlinger, P., Laschewsky, A., Bertrand, P., Delcorte, A., Legras, R., Nysten, B. & Möbius, D. Partially fluorinated maleimide copolymers for langmuir films of improved stability. 2. Spreading behavior and multilayer formation. *Langmuir* **13**, 310-319 (1997).
- 36 Kohli, P. & Blanchard, G. J. Design and growth of robust layered polymer

- assemblies with molecular thickness control. *Langmuir* **15**, 1418-1422(1999).
- 37 Beaune, O. , Bessiere, J-M. , Boutevin, B. & Robin, J-J. Synthesis of new maleimide monomers having a perfluoroaliphatic side chain and study of their copolymerization with vinelethers. *Polym. Bull.* **29**, 605-612 (1992).
- 38 Spěváček, J. NMR investigations of phase transition in aqueous polymer solutions and gels. *Curr. Opin. Colloid Interface Sci.* **14**, 184-191 (2009).

Chapter 6

Conclusion

Copolymer of 2-chloroethyl vinyl ether and maleic anhydride can exhibit LCST-type thermoresponsive behavior reversibly in some organic media under relatively mild conditions. The thermoresponsive behavior of copolymer solution depended on the organic media. The copolymer solution exhibited higher critical temperature in organic media with better solvent quality. There existed discrepancy between heating and cooling processes and this phenomenon became remarkable as the solvent quality became poorer.

Copolymer of 2-chloroethyl vinyl ether and maleic anhydride can exhibit LCST-type thermoresponsive behavior in mixed solvent of THF and hexane with proper solvent composition. The temperature of cloud point of polymer solution was lower than boiling point of THF and hexane. With increase in THF the temperature of cloud point of copolymer solution increased. The phase behavior of copolymer solution was LCST-type in the phase diagram of cloud temperature versus polymer concentration, and with increasing polymer concentration the temperature of cloud point decreased firstly at lower polymer concentration and then the curve in phase diagram leveled off in a wide range of polymer concentration. Higher molecular weight polymer owned lower temperature of cloud point than that of lower molecular weight polymer. ^1H NMR spectra suggested that addition of hexane into polymer solution in THF may create proper medium condition in which temperature change can induce variation of polymer chain's environment or mobility largely.

Copolymer of 2-chloroethyl vinyl ether and maleic anhydride can presented LCST-type behavior in pure *n*-butyl acetate. In most cases, the temperature of cloud point of copolymer solution was lower than the boiling point of *n*-butyl acetate. The higher molecular weight copolymer owned lower temperature of cloud point than that of lower molecular weight copolymer. The phase behavior of copolymer in *n*-butyl acetate was LCST-type and the temperature of cloud point of polymer solution decreased initially and then the curve in phase diagram of cloud point versus polymer concentration became flat in a wide polymer concentration range. The LCST-type phase behavior of copolymer in *n*-butyl acetate can be described by Flory-Huggins mean field theory in some degree although there existed some discrepancies between experimental results and theory values. The addition of good solvent increased the temperature of cloud point of copolymer solution, while the addition of nonsolvent decreased the

temperature of cloud point of copolymer solution. The effect of cosolvent on thermoresponsive behavior can be attributed to the interaction between polymer and solvent, especially the polar interaction between polar groups in polymer chain with solvent.

A comb-like copolymer of *N*-phenyl maleimide and *n*-octadecyl vinyl ether can be synthesized by conventional free radical solution polymerization. The synthesized copolymer contained more unit of *N*-phenyl maleimide. The copolymer can exhibit UCST-type thermoresponsive behavior reversibly in DMF and 1-butanol. The temperature of cloud point of copolymer solution with same polymer concentration was higher in 1-butanol than in DMF. The temperature of cloud point of polymer solution both in DMF and 1-butanol was lower than boiling point of solvent. The addition of nonsolvent increased the temperature of cloud point of polymer solution, while addition of good solvent decreased the temperature of cloud point. It can be deduced from ¹H NMR spectrum that at higher temperature the copolymer can dissolve in DMF well with good mobility of polymer chain segments but aggregation occurred at lower temperature resulting in phase separation and the mobility of polymer segments decreased with decreasing temperature.

As mentioned above the reversible thermoresponsive behavior of polymer in organic media can be obtained under mild conditions. Further more, the critical temperature of polymer solution can be tuned conveniently, which is advantageous for designing some supramolecular systems based on thermoresponsive polymer systems in organic media.

Publications

- 1 Zhenjie Liu, Yongliang Guo, Katsuhiko Inomata. Lower critical solution temperature behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in organic media. *Polym. J.* 2010, 42: 901-904 .DOI:10.1038/pj.2010.84
- 2 Zhenjie Liu, Yongliang Guo and Katsuhiko Inomata. Reversible thermoresponsive behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in mixed solvent of tetrahydrofuran/hexane. *Colloid Polym. Sci.* 2011, 289: 791–798 DOI: 10.1007/s00396-011-2395-y.
- 3 Zhenjie Liu, Yongliang Guo and Katsuhiko Inomata. LCST-type Phase Behavior of Poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in *n*-Butyl Acetate. *Polym. J.* *in press*. DOI:10.1038/pj.2011.41
- 4 Zhenjie Liu, Yongliang Guo and Katsuhiko Inomata. Thermoreversible UCST-type behavior of comb-like poly(phenyl maleimide-co-*n*-octadecyl vinyl ether) copolymer in organic media, *to be submitted*.

Academic conferences

- 1 Zhenjie Liu, Katsuhiko Inomata, Hideki Sugimoto, Eiji Nakanishi. Reversible thermoresponsive behavior of poly(chloroethyl vinyl ether-*alt*-maleic anhydride) in THF/hexane mixed solvent. **Oral**. 59th SPSJ Symposium on Macromolecules, May 26-28, 2010, Yakohama, Japan.
- 2 Zhenjie Liu, Yongliang Guo, Katsuhiko Inomata, Hideki Sugimoto, Eiji Nakanishi. Cloud point of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) with LCST-type phase behavior in alkyl acetate and effect of co-solvent. **Poster**. 59th SPSJ Symposium on Macromolecules, September 15-17, 2010, Sapporo, Japan.
- 3 Liu Zheijie, Guo Yongliang, 猪股克弘. 2-クロロエチルビニルエーテル-マレイン酸無水物共重合体溶液の相挙動. 高分子基礎研究会, January 28-30, 2011, 群馬.
- 4 Zhenjie Liu, Yongliang Guo, Katsuhiko Inomata. Lower critical solution temperature phase behavior of poly(2-chloroethyl vinyl ether-*alt*-maleic anhydride) in organic media. **Poster** 高分子基礎研究会 January 28-30, 2011, 群馬.
- 5 Zhenjie Liu, Yongliang Guo, Katsuhiko Inomata. LCST-type thermoresponsive behavior of alternating copolymer organic solution under mild conditions. **Poster**. The 2nd FAPS (The Federation of Asian Polymer Societies) Polymer Congress, May, 8-11, 2011, Beijing CHINA.