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Synthesis and Solution Property of Water-Soluble Polyisocyanate as Rod-Like Materials

A Dissertation for the Degree of Doctor of Philosophy

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Chapter 1

General Introduction

1.1 Thermoresponsive Polymers

Thermoresponsive polymers that undergo a solubility transition in water have received major interest in recent decades based on their broad application potential in various interesting fields, such as controlled drug delivery,^{1,2} bioseparations,³ filtration,⁴ and regulating enzyme activity.⁵ The thermoresponsive polymers investigated for these applications generally have a flexible main chain and show a coil-to-globule phase transition property in aqueous solution,^{6,7} which can be influenced by changes in temperature (Figure 1-1). There are two types of the phase transition systems, such as lower critical solution temperature (LCST) and upper critical solution temperature (UCST), as shown in Figure 1-2.⁸

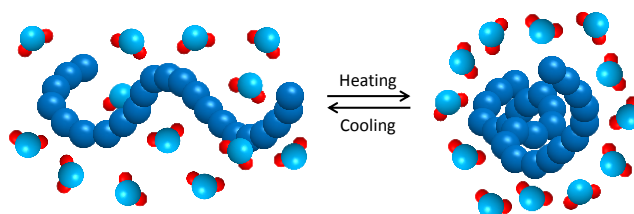


Figure 1-1. Coil-to-globule transition of a thermoresponsive polymer in aqueous solution

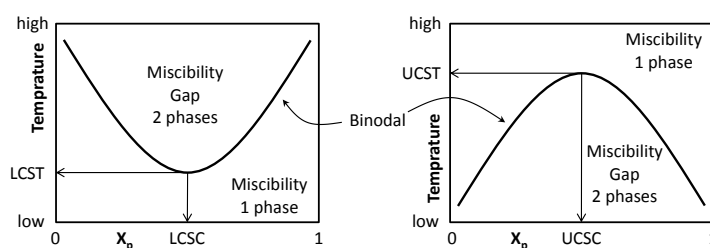
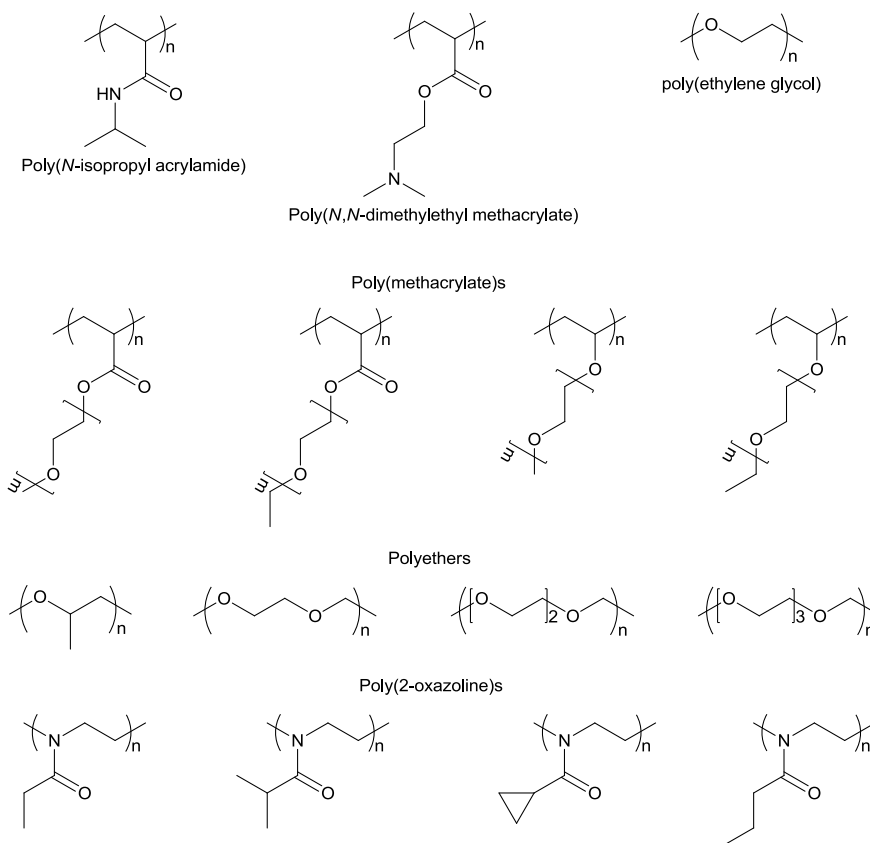


Figure 1-2. Phase diagram for a binary polymer-solvent mixture exhibiting (a) LCST behavior and (b) UCST behavior

Since the earliest report of the thermoresponsive property of poly(*N*-isopropylacrylamide) (PNIPAM) in 1967 by Scarpa *et al.*,^{9,10} many kinds of thermoresponsive polymers showing a difference in the phase transition temperature, such as poly(ethylene glycol),¹¹ poly(2-ethyl-2-oxazoline),¹² poly(methyl vinyl ether),¹³ poly(dimethylaminoethyl methacrylate),¹⁴ poly[bis((ethoxyethoxy)ethoxy)phosphazene],¹⁵ poly(*N*-vinylcaprolactam),¹⁶ and their derivatives,¹⁷ have been reported (Chart 1-1). Moreover, the influence of the end group and side-chain group of the polymer backbone on the thermoresponsive property also was investigated for various thermoresponsive polymers.

Chart 1-1. Chemical structures of the thermoresponsive polymers



1.2 Amphiphilic Diblock Polymers

Amphiphilic diblock copolymers consisting of hydrophobic and hydrophilic segments in a polymer chain are well-known as self-assembling materials in solution (Figure 1-3),^{18–21} which show nanoscaled suprastructures, such as spherical micelle, cylindrical micelle, spherical vesicle, hollow vesicle, and lamella, as shown in Figure 1-4. Micelle composed of core-shell structure can encapsulate the hydrophobic molecule due to the hydrophobic core.^{22–25} In addition, vesicle composed of a bilayered membrane can encapsulate the hydrophilic molecule due to the hydrophilic space in the self-assembled structure of the amphiphilic diblock copolymer.^{26–28}

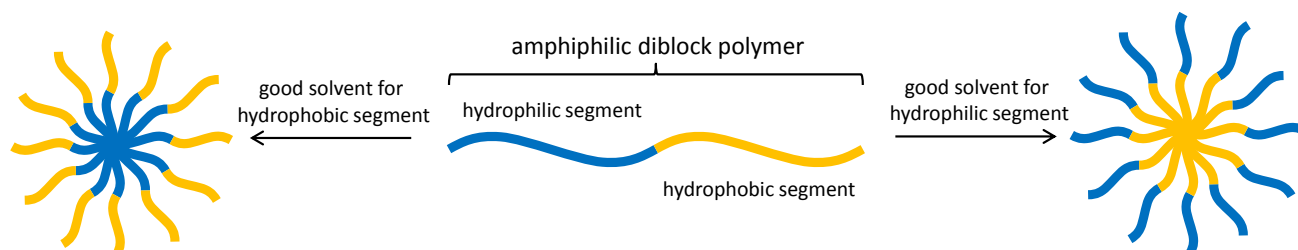


Figure 1-3. Self-assembling property of amphiphilic block polymer in a selective solvent

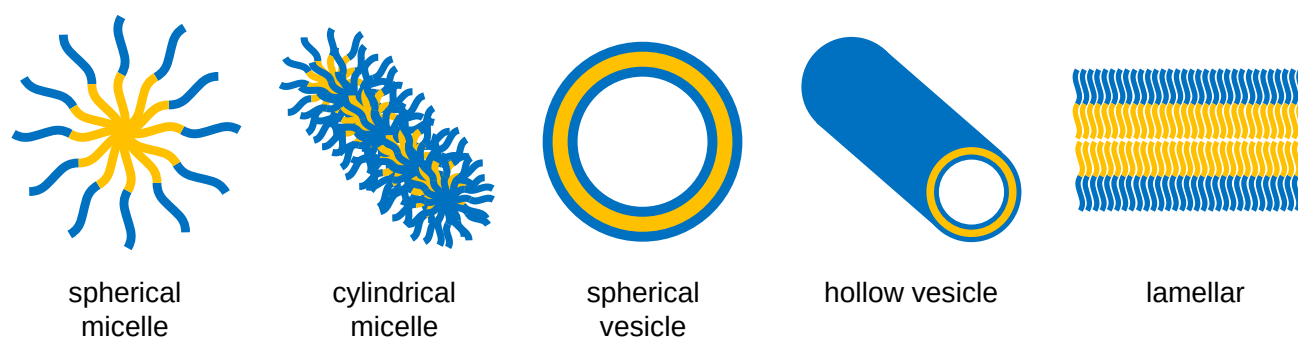
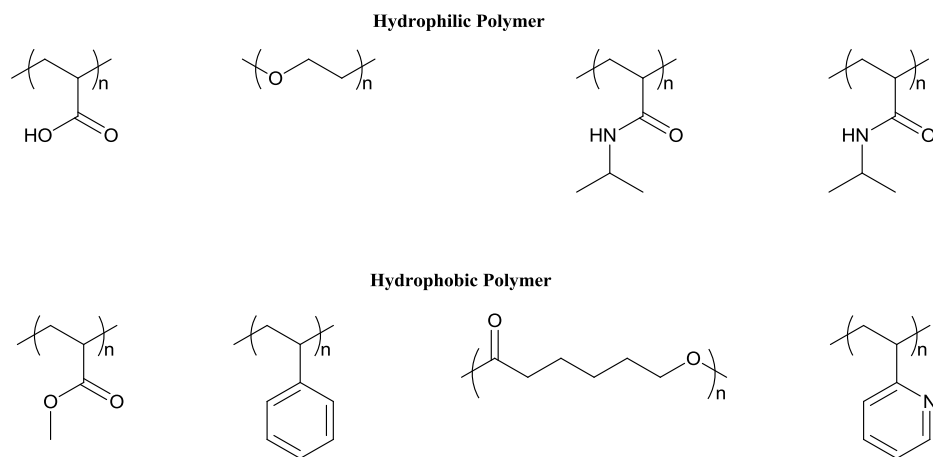


Figure 1-4. Self-assembled structures of amphiphilic diblock polymer

In general, these structures can transform by changing the solution conditions such as the concentration, pH, or temperature.^{29–35} The self-assembled structure is also dependent on the molecular weight distribution, solubility and hydrophobic/hydrophilic ratio.^{36–40} In addition, the stability of the self-assembled materials typically increased with the increasing molecular weight.⁴¹ Although there are many reports on the synthesis and characterization of coil-coil^{18,42} and rod-coil-types^{36,43–44} of amphiphilic diblock copolymer assemblies in aqueous solution, a few reports exist on the rod-rod-type^{45,46} of amphiphilic diblock copolymer due to the limitation of the water-soluble rod-type polymers. such as polythiophene,⁴⁷ polyfluorene,⁴⁸ polyisocyanide,^{49,50} and polypeptide.⁵¹ Therefore, the synthesis and characterization of the novel rod-rod-type of amphiphilic diblock copolymer is one of the challenging issues and the most remarkable research area because of their potential application for biological and medical chemistry.

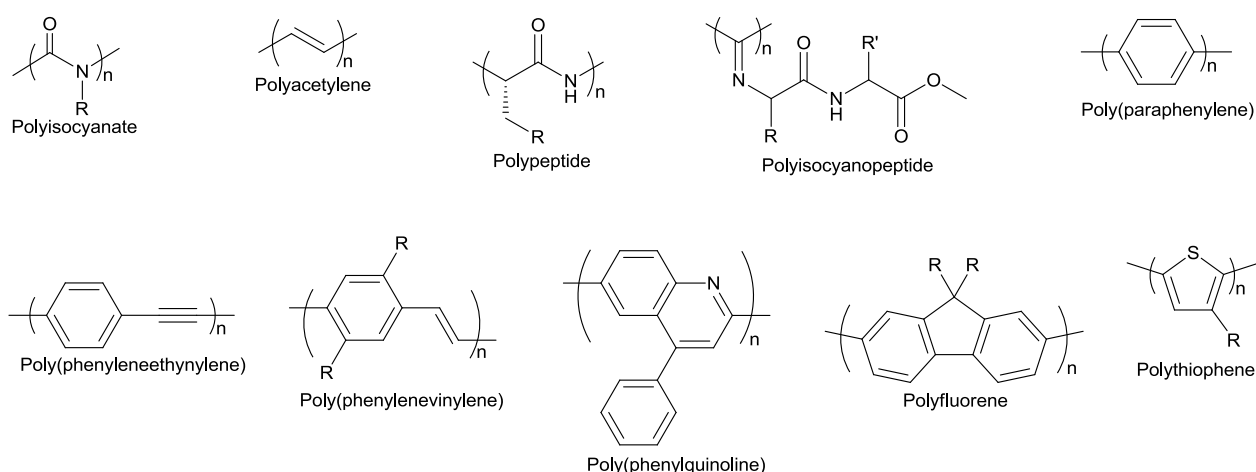
Chart 1-2. Common chemical structures of hydrophilic and hydrophobic segments for the amphiphilic diblock polymers



1.3 Rod-Like polymers

Physical properties of the rod-like polymers with rigid main chain are fundamentally different from those of the coil polymer with a flexible main chain due to the effect of chain topology on conformational entropy and molecular packing geometries and additional interactions that can occur between anisotropic rod-like polymers.⁵² Moreover, rod-like polymers show different scaling behaviors as a function of molecular weight compared to the coil polymers. These differences produced the unique properties of the rod-like polymer. There are many reports on the synthesis of rod-like polymers, such as polyisocyanate, polyacetylene, polypeptide, polyisocyanopeptide, poly(paraphenylene), poly(phenyleneethynylene), poly(phenylenevinylene), poly(phenylquinoline), polyfluorene, and polythiophene (Chart 1-3).^{36,53-54} Although the coil polymers with a flexible main chain have been widely studied, the rod-like polymer with a rigid main chain was limited.

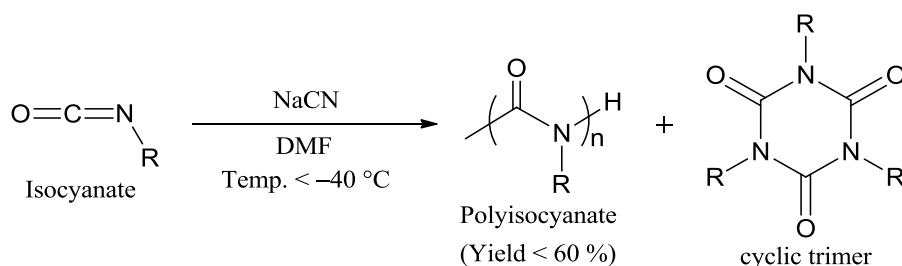
Chart 1-3. Chemical structures of the common rod-like polymers



1.4 Polyisocyanates

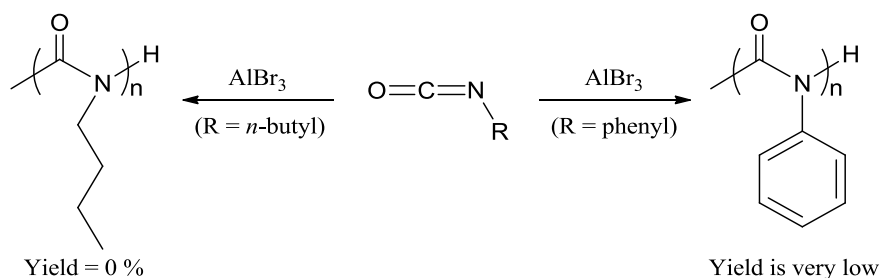
Polyisocyanate (PIC) has received a great deal of attention due to its unique characteristics, such as chain stiffness, dynamic helical conformation, chiral amplification, optical switch, and liquid crystal properties.^{55,56} Shashoua and co-workers reported, in 1959, the homopolymerization of various isocyanate monomers using sodium cyanide (NaCN) as an initiator, which was needed at low temperature from $-40\text{ }^{\circ}\text{C}$ to $-100\text{ }^{\circ}\text{C}$, as shown in Scheme 1-1.⁵⁷ However, there was a cyclic trimer due to a backbiting reaction as a by-product.

Scheme 1-1. Anionic polymerization of isocyanate initiated by sodium cyanide (NaCN)



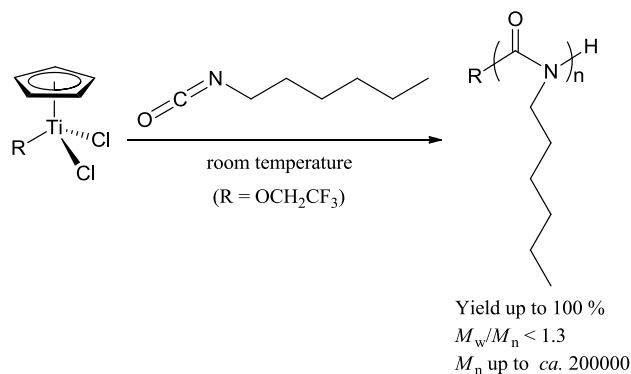
In 1962, Natta and co-workers reported the synthesis of polyisocyanates using tribromoaluminium (AlBr_3) as a catalyst.⁵⁸ Although a small amount of poly(phenyl isocyanate)s could be obtained, there was no polymerization for *n*-butyl isocyanate due to the small reactivity compared to the phenyl isocyanates, as shown in Scheme 1-2.

Scheme 1-2. Polymerization of isocyanate using cationic catalyst (AlBr_3)



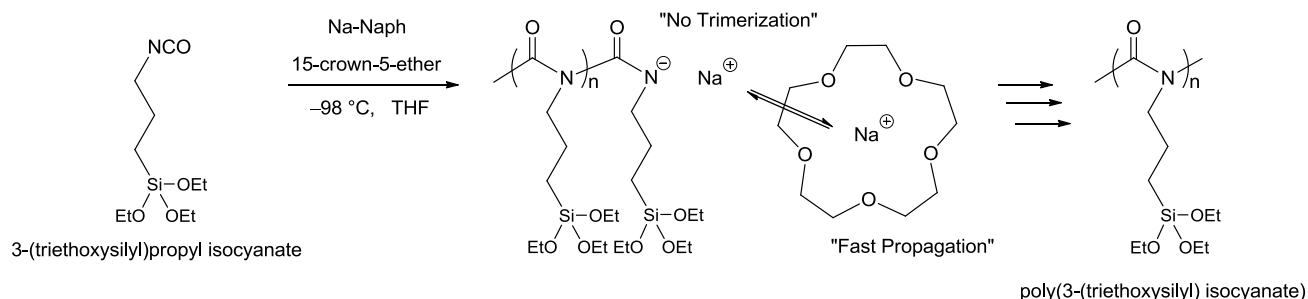
In 1992, Okamoto and co-workers reported the synthesis of poly(*n*-hexyl isocyanate) (PHIC) with a high yield at $-100\text{ }^{\circ}\text{C}$ by anionic polymerization using NaCN as initiator and *N,N*-dimethylformamide/toluene as solvent.⁵⁹ In 1996, Inoue and co-workers reported the preparation of the PHIC by anionic polymerization using lanthanoid isopropoxide as initiator, which has a 90–73% yield at $-78\text{--}30\text{ }^{\circ}\text{C}$.⁶⁰ In 1991, Novak et al. reported the living coordination polymerization system for the alkyl isocyanates using organo-titanium compounds as catalyst, as shown in Scheme 1-3.⁶¹ They can be obtained as polyisocyanates with high molecular weight and narrow polydispersity.

Scheme 1-3. Coordination polymerization of alkylisocyanate catalyzed by organo-titanium



In 1999, Jae-Suk Lee and co-workers developed the anionic living polymerization for 3-(triethoxysilyl)propyl isocyanate using sodium naphthalenide (Na-Naph) and 15-crown-5-ether complex as the initiation system in THF at $-98\text{ }^{\circ}\text{C}$, as shown in Scheme 1-4.⁶² The chain end could not attack the polymer backbone due to the highly steric hindrance of the bulky cation-ligand complexes. Moreover, they achieved the synthesis of a diblock copolymer, *i.e.*, poly(3-(triethoxysilyl) isocyanate)-*block*-poly(*n*-octyl isocyanate), with high molecular weight and yield. They improved the living polymerization condition for the alkyl isocyanate by utilizing sodium tetraphenylborate (NaBPh₄) as additive.

Scheme 1-4. Living anionic polymerization of alkylisocyanate using an additive

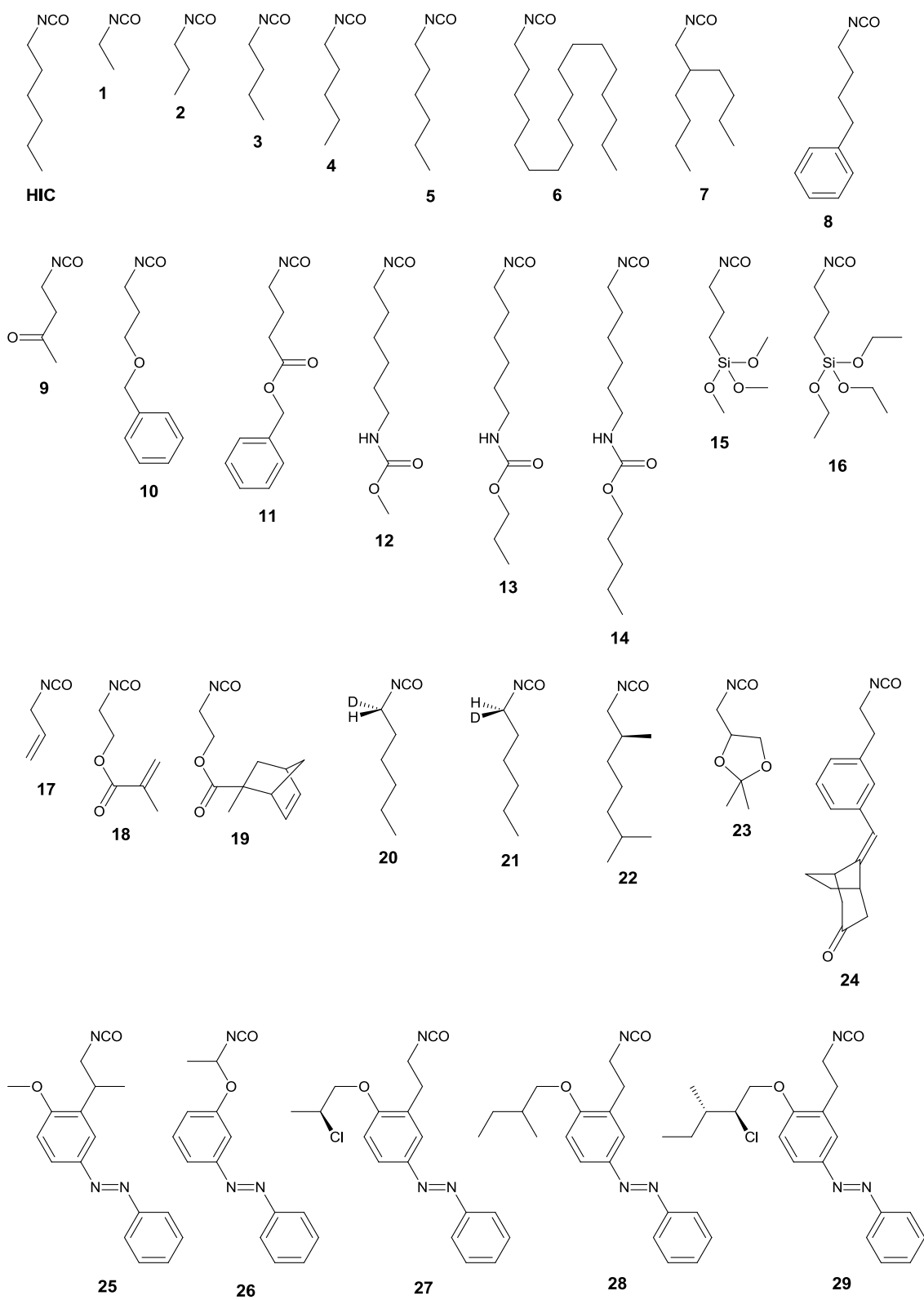


n-Hexyl isocyanate (HIC) is the most utilized monomer in the field of polyisocyanates due to its simple structure.⁶³ In addition, there are many kinds of alkyl isocyanates, such as ethyl isocyanate (1), *n*-propyl isocyanate (2), *n*-butyl isocyanate (3), *n*-amyl isocyanate (4), *n*-heptyl isocyanate (5), *n*-undecyl isocyanate (6), and *n*-octadecyl isocyanate (7), that can also be employed as the monomers.⁶⁴ The solution properties of poly(*n*-alkyl isocyanate)s dominate the physical

measurements of this class of polymers because their extended molecular conformation results in unique behavior. The rigid rod character of these polymer molecules is dramatically reflected in solution measurements of dielectric relaxation, intrinsic viscosity, light scattering, Kerr effect, and electric dichroism. Moreover, there are polyisocyanates with various side chain units characterizing of the physical properties for poly(4-phenylbutyl isocyanate) (8), poly(3-oxobutyl isocyanate) (9), poly(3-(benzyloxy)-*n*-propyl isocyanate) (10), poly(3-(benzyloxycarbonyl)-*n*-propyl isocyanate) (11), poly(6-(methoxycarbonylamino)hexyl isocyanate) (12), poly(6-(propoxycarbonylamino)hexyl isocyanate) (13), poly(6-(pentoxycarbonylamino)hexyl isocyanate) (14), poly(3-(trimethoxysilyl)propyl isocyanate) (15), and poly(3-(triethoxysilyl)propyl isocyanate) (16).^{65–67} Moreover, there are few reports of the synthesis of polyisocyanates with a reactive group such as allyl isocyanate (17), 2-isocyanatoethyl methacrylate (18), and 2-((2-isocyanatoethoxy)carbonyl)-2-methylbicyclo[2,2,1]-hept-5-ene (19).^{68,69} Furthermore, the chiral polyisocyanates have received much attention due to their fascinating properties in solution and the bulk state. Green et al. polymerized several chiral isocyanates, such as 1-deuterio-*n*-hexyl isocyanate (20 and 21), 2,6-dimethylheptyl isocyanate (22), and 4-(isocyanatomethyl)-2,2-dimethyl-1,3-dioxolane (23). Moreover, Selinger and co-workers also synthesized polyisocyanates with an axially chiral bicyclo[3,2,1]octan-3-one derivative as the side chain (24), which could be switched to the helical conformation using circularly polarized light.^{70–73} Zentel and co-workers reported the synthesis of polyisocyanate containing the optically active

azobenzene group as side chain, which could control the helical conformation of the polymer backbone by the *cis-trans* isomerization of the azobenzene groups (25–29).^{74,75} The effect of the end structure on the helical conformation of the polyisocyanate main chain was also investigated using the chiral terminal groups. Jae-Suk Lee and co-workers prepared the α - and α,ω -end functionalized PHIC and elucidated the chirality of the backbone by circular dichroism measurement.⁷⁶ Moreover, Feringa and co-workers reported the reversible induction and inversion of the helicity of a polymer backbone by a single light-driven molecular motor positioned at the terminus.⁷⁷ On the other hand, Satoh and co-workers reported the precise synthesis of end-functional polyisocyanates with clickable azido or alkyne groups, which are useful for the building blocks of the polymer architectures.⁷⁸

Chart 1-4. Chemical structures of isocyanate monomers



1.5 Objective and Outline of the Thesis

As described above, the thermoresponsive and amphiphilic polymers have attracted much attention because of their potential application in the field of biological chemistry and medical science. Although the rod-like polymers possessed the unique property in the solution state, the synthesis and characterization of rod-like polymers are still restricted due to the difficulty of the synthetic method compared to the general polymers with a flexible main chain. Polyisocyanates are a class of the rod-like polymer, which can be synthesized with controlled molecular weight, narrow polydispersity, and end-functionality, by coordination polymerization using a half-titanocene catalyst. Furthermore, there are a few reports on the synthesis and characterization of the rod-rod-type of amphiphilic diblock copolymer which is a challenging issue due to the difficulty of synthesis. Rod-rod-type amphiphilic diblock polymers show a unique self-assembling property in water due to the difference in the solubility in water of each segment, *i.e.*, hydrophilic and hydrophobic. Thus the objective of this thesis was the development of a preparation of rod-type water-soluble polyisocyanates, such as poly(2,5,8-trioxadecyl isocyanate) (PMeEO₃IC), poly(3,6,9-trioxaundecyl isocyanate) (PEtEO₃IC), and poly(2,5,8,11-tetraoxatridecyl isocyanate) (PMeEO₄IC), with a thermoresponsive property in aqueous solution. In addition, the thermoresponsive property of these polymers was characterized, which strongly depends on the structure of the polymer end and side chain unit. Furthermore, the author tried to synthesize well-defined rod-rod-type amphiphilic diblock polyisocyanates (PHIC-*b*-PMeEO₄IC) and characterize the self-assembling property in aqueous solution.

An outline of this thesis is as follows:

Chapter 2 describes the molecular design, synthesis, and polymerization of isocyanates possessing the oligo(ethylene glycol) (OEG) unit as a side-chain. Isocyanates with oligo(ethylene glycol) units have been designed and synthesized as 2,5-dioxaheptyl, 2,5,8-trioxadecyl, 3,6,9-trioxaundecyl, and 2,5,8,11-tetraoxatridecyl isocyanates (MeEO₂IC, MeEO₃IC, EtEO₃IC, and MeEO₄IC, respectively). The bulk polymerization of the isocyanates using *n*-butoxy(η 5-cyclopentadienyl)dichlorotitanium(IV) at 10 °C proceeded in a living manner to produce the well-defined water-soluble polyisocyanates of PMeEO₃IC, PEtEO₃IC, and PMeEO₄IC except for PMeEO₂IC. The phase transition property of the obtained polyisocyanates was estimated by their cloud point temperatures (T_{cp} s) in an aqueous solution (40 g L⁻¹). For PMeEO₃IC, the T_{cp} decreased from 90.0 to 74.9 °C with the increasing molecular weight ($M_{n,NMR}$) from 1960 to 9000 g mol⁻¹. The T_{cp} of 94.0 °C for PMeEO₄IC (4460 g mol⁻¹) was higher than that of 79.6 °C for PMeEO₃IC (4560 g mol⁻¹), and the T_{cp} decreased from 79.6 to 34.7 °C by changing from the methyl to an ethyl group in the oligo(ethylene glycol) units from PMeEO₃IC to PEtEO₃IC (4470 g mol⁻¹).

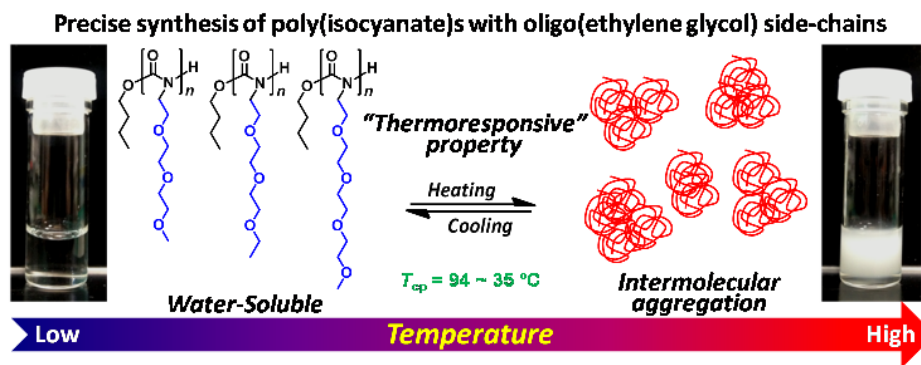


Figure 1-5. Schematic representation of the synthesis and thermoresponsive properties of the water-soluble polyisocyanates with oligo(ethylene glycol) as a side-chain.

Chapter 3 describes the thermoresponsive property of the rod-like polymer which has been studied using the α -end-substituted polyisocyanates with *n*-butyl, *n*-hexyl, *n*-octyl, and *n*-decyl chains (C_4 -PMeEO₃IC, C_6 -PMeEO₃IC, C_8 -PMeEO₃IC, and C_{10} -PMeEO₃IC, respectively). Their cloud point temperatures (T_{cp} s) in an aqueous solution (30 g L⁻¹) were 81.3 °C for C_4 -PMeEO₃IC₂₁, 74.7 °C for C_6 -PMeEO₃IC₂₁, 64.3 °C for C_8 -PMeEO₃IC₂₀, and 63.9 °C for C_{10} -PMeEO₃IC₂₀, whose values were independent of the molecular weight. From the micro-DSC measurement, the enthalpy change (ΔH) due to the phase transition was determined to be 0.394, 1.33, 2.97, and 2.66 kJ mol⁻¹ of the repeating unit for C_4 -PMeEO₃IC₂₁, C_6 -PMeEO₃IC₂₁, C_8 -PMeEO₃IC₂₀, and C_{10} -PMeEO₃IC₂₀, respectively. The C_6 -PMeEO₃IC₂₁ and C_8 -PMeEO₃IC₂₀ showed a second endothermic peak above the T_{cp} . These phenomena were clarified by the hydrodynamic diameter (D) in aqueous solutions of C_m -PMeEO₃ICs using the DLS measurement.

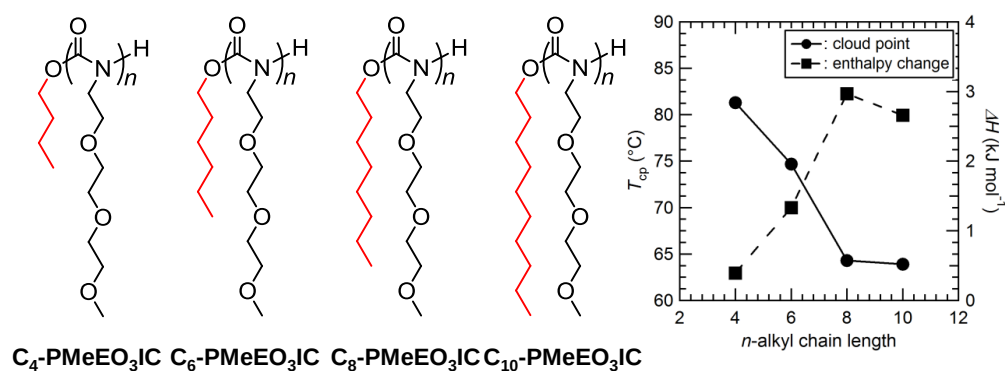


Figure 1-6. Schematic representation of the characterization of thermoresponsive properties for the end-functionalized water-soluble polyisocyanates.

Chapter 4 describes the the synthesis of an amphiphilic rod-rod-type BCP of poly(*n*-hexyl isocyanate)-*block*-poly(2,5,8,11-tetraoxatridecyl isocyanate)s (PHIC-*b*-PMeEO₄ICs) with similar molecular weights and different ratios of the hydrophobic and hydrophilic segments, *i.e.*, the PHIC/PMeEO₄IC segment, by coordination polymerization using the titanium catalyst. The self-assembling property of an amphiphilic rod-rod-type diblock copolymer has been demonstrated using poly(*n*-hexyl isocyanate)-*block*-poly(2,5,8,11-tetraoxatridecyl isocyanate) (PHIC-*b*-PMeEO₄IC) with different degrees of polymerization for the PHIC and PMeEO₄IC segments. The critical aggregation concentrations (CAC) of PHIC-*b*-PMeEO₄IC decreased with the increasing fraction of the hydrophobic PHIC segment. The relation between the hydrodynamic radius (R_h) and the PHIC/PMeEO₄IC ratio differed from that for the radius of gyration (R_g). The self-assembled PHIC-*b*-PMeEO₄IC was stable in various polymer concentrations. The ρ parameter (R_g/R_h) strongly suggested that the macromolecular architecture was a cylindrical micelle for

PHIC₁₃-*b*-PEOIC₄₁ ($\rho = 1.63$) and a spherical vesicle for PHIC₂₂-*b*-PMeEO₄IC₃₆ ($\rho = 1.09$) and PHIC₃₁-*b*-PMeEO₄IC₃₁ ($\rho = 1.09$). Transmission electron microscope (TEM) images closely agreed with the structures of the cylindrical micelle and spherical vesicle, which were expected based on the ρ parameter.

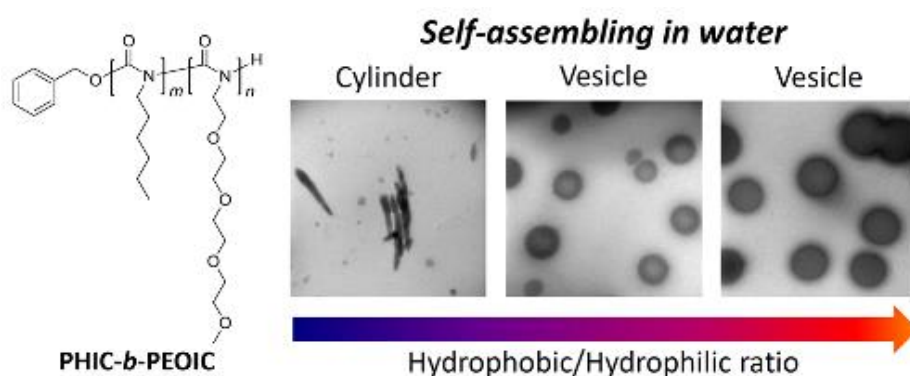


Figure 1-7. Schematic representation of the synthesis and self-assembling properties of an amphiphilic rod-rod type diblock copolymer of poly(*n*-hexyl isocyanate)-*block*-poly(2,5,8,11-tetraoxatridecyl isocyanate).

The concluding Chapter 5 summarized the synthesis of water-soluble rod-like polyisocyanates and amphiphilic rod-rod-type diblock polyisocyanates and characterization of thermoresponsive property and self-assembling property of these polymers.

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Chapter 2

***Synthesis of Water-Soluble Polyisocyanates
with the Oligo(ethylene glycol) Side-Chain as
New Thermoresponsive Polymers***

2.1 Introduction

Synthetic polymers capable of responding to external or internal stimuli, *i.e.* stimuli-responsive polymers, have been paid much attention in various fields. By expanding applicable stimuli, such as temperature, light, and pH, many types of stimuli-responsive polymers have been designed and synthesized as smart materials.^{1–5} For instance, there are many efforts for the design, synthesis, and application of thermoresponsive polymers^{5–7} since poly(*N*-isopropylacrylamide) was found to exhibit a coil-to-globule phase transition at 32 °C in an aqueous solution.^{8,9} The thermoresponsive property is usually controlled by tuning the side-chain groups^{10,11} in the polymers except for poly(ethylene glycol). Oligo(ethylene glycol) (OEG) is widely used as a common side-chain unit in various polymers, such as polymetacrylates,^{12,13} polyacrylates,¹⁴ poly(vinyl ether),¹⁵ polystyrenes,¹⁶ polyisocyanide,¹⁷ and polycarbonate.¹⁸ Thus, it is interesting to elucidate the applicable polymer main-chain structures from the viewpoint of the thermoresponsive control based on the OEG units.

Polyisocyanate (PIC) has received a great deal of attention due to its unique characteristics, such as chain stiffness, dynamic helical conformation, chiral amplification, optical switch, and liquid crystal properties.^{19,20} Thus, there has been many attempts to synthesize, characterize, and apply various kinds of PICs. For example, Novak *et al.* reported that alkoxy-substituted (η^5 -cyclopentadienyl)dichlorotitanium(IV), $\text{CpTiCl}_2(\text{OR})$, was an effective catalyst for the controlled/living polymerization of isocyanates leading to well-defined PICs.^{21,22} For optically active PICs, Green *et al.* reported the chiral amplification of helical PICs prepared using chiral monomers,²³

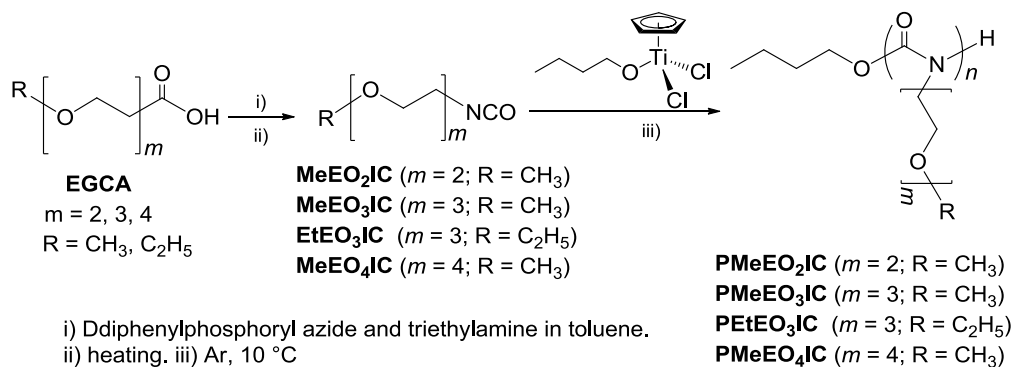
and Lee *et al.* synthesized one-handed helical PICs using the chiral chain-end group.²⁴ Feringa *et al.* reported the chiral liquid crystal property of PIC with a single photochemically bistable chiroptical molecular switch.²⁵ In addition, we reported the synthesis of clickable PICs possessing an azido or alkyne end group as rod-like building blocks.²⁶ However, there are no reports on the synthesis of a water-soluble PIC as a novel stimuli-responsive material. We now report the molecular design, synthesis, and polymerization of isocyanates possessing the OEG unit as a side-chain. In addition, the obtained PICs are characterized as novel types of water-soluble polymers and their thermoresponsive property are clarified in aqueous solutions.

2.2 Results and Discussion

2.2.1 Synthesis and Polymerization of Isocyanates with Oligo(ethylene glycol) Side-Chains

The synthesis and polymerization of the OEG isocyanates are illustrated in Scheme 2-1. The 2,5-dioxaheptyl, 2,5,8-trioxadecyl, 3,6,9-trioxaundecyl, and 2,5,8,11-tetraoxatridecyl isocyanates (MeEO₂IC, MeEO₃IC, EtEO₃IC, and MeEO₄IC, respectively) were synthesized by the reaction of the OEG carboxylic acid (EGCA) and diphenylphosphoryl azide in the presence of triethylamine in toluene, followed by heating. All monomers were purified by distillation under vacuum. A titanium catalyst of *n*-butoxy(η^5 -cyclopentadienyl)dichlorotitanium(IV), CpTiCl₂(O^{*n*}C₄H₉), was prepared from the equimolar mixture of (η^5 -cyclopentadienyl)trichlorotitanium(IV) and *n*-butanol prior to the polymerization. The PICs with the OEG unit, PMeEO₂IC, PMeEO₃IC, PEtEO₃IC, and PMeEO₄IC, were synthesized by the coordination polymerization of the OEG isocyanates using CpTiCl₂(O^{*n*}C₄H₉). Table 2-1 lists the polymerization results. For the bulk polymerization at 10 °C, the polymerization mixture was quenched by the addition of an excess amount of methanol and the crude polymer was purified by preparative size exclusion chromatography (SEC) to remove the catalyst residue and a slight amount of the monomer. The obtained polymer was solid after drying under vacuum, which was soluble in water, methanol, acetone, THF, diethyl ether, CHCl₃, and CH₂Cl₂ and insoluble in hexane.

Scheme 2-1. Synthesis and polymerization of isocyanates of MeEO₂IC, MeEO₃IC, EtEO₃IC, and MeEO₄IC leading to poly(isocyanate)s with oligo(ethylene glycol) units of PMeEO₂IC, PMeEO₃IC, PEtEO₃IC, and PMeEO₄IC, respectively.



For the polymerization of MeEO₃IC with the monomer-to-catalyst ratio ($[M]_0/[CpTiCl_2(O^iC_4H_9)]_0$) of 20/1 (run 2), the SEC of the obtained polymer displayed symmetrical monodispersed peaks, as shown in Figure 2-1, and the molecular weight distribution (M_w/M_n) of 1.10 was low. In the ¹H NMR spectrum (Figure 2-2), the signals at 4.50–3.40 ppm due to oxyethylene protons appeared with those at 3.37 ppm due to methyl protons in the side chain. In addition, the minor signals at 1.66 and 1.40 ppm and 0.954 ppm were assigned to the methylene and methyl protons of the butoxy group as an initiator, respectively. These results indicated that the obtained polymer possessed the *n*-butanol residue. The number average molecular weight ($M_{n,NMR}$) determined by the ¹H NMR spectrum was 3200 g mol⁻¹, which agreed with the calculated value ($M_{n,calcd.}$) of 3860 g mol⁻¹.

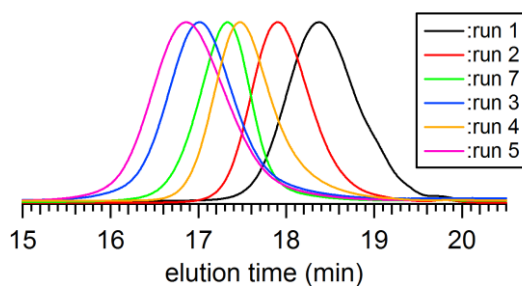


Figure 2-1. (a) SEC traces of obtained PMeEO₃ICs (runs 1–5, and 7) in THF.

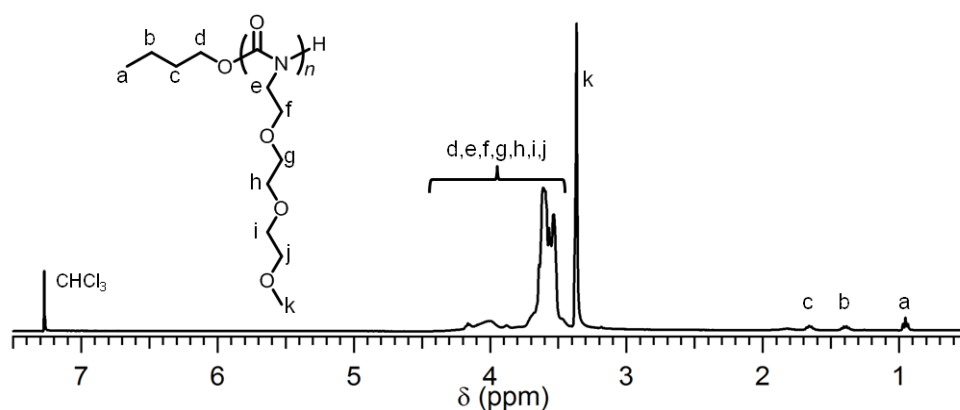


Figure 2-2. ¹H NMR spectrum of PMeEO₃IC (run2) in CDCl₃ at ambient temperature.

In the ¹³C NMR spectra of MeEO₃IC and its obtained polymer, the characteristic signal at 125.2 ppm due to the isocyanate carbons completely disappeared and that at 157.1 ppm due to the amide carbons in the main-chain appeared along with those at 72.04–68.91 and 59.12 ppm due the methylene and methyl carbons of the OEG unit, as shown in Figure 2-3. These results indicated that the polymerization of MeEO₃IC successfully proceeded to afford the PIC possessing the 2,5,8-trioxadecyl unit as the side chain.

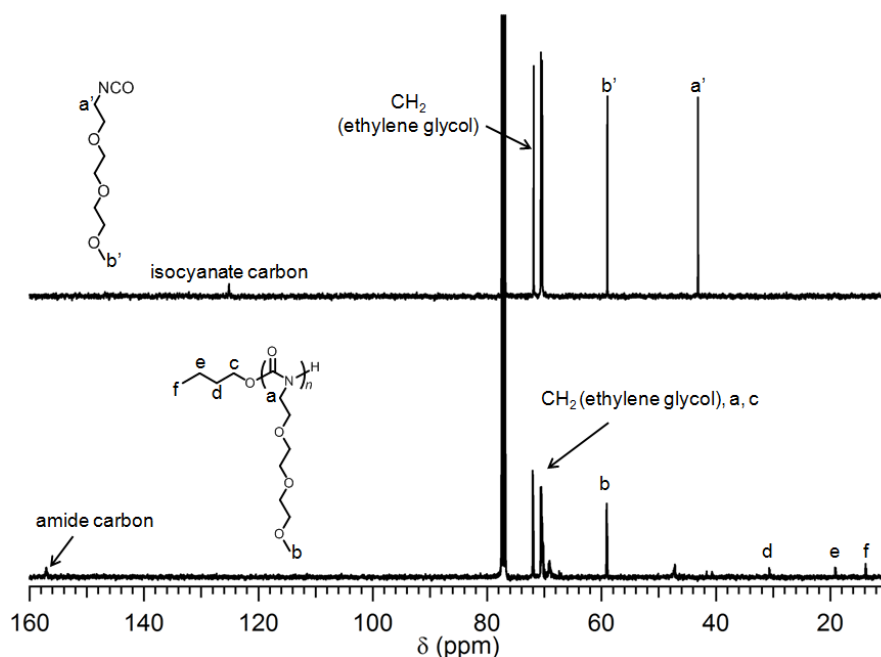


Figure 2-3. ^{13}C NMR spectra of **MeEO₃IC** (upper) and **PMeEO₃IC** (run 2, lower) in CDCl_3 .

To provide direct evidence for the obtained PIC structure, a MALDI-TOF MS measurement was carried out, as shown in Figure 2-4. The MALDI-TOF MS spectrum of the obtained polymer showed only one series of peaks, which had a molar mass regular interval of 189.07, which corresponds to the MeEO₃IC unit. In addition, the series of peaks for the obtained polymer is assignable to the expected PIC structure having the butoxy group at the α -chain end, PMeEO₃IC; as an example, for the 13-mer, the measured peak at the m/z of 2572.28 corresponds to the calculated value of 2572.34. In addition, the $M_{n,\text{NMRs}}$ increased from 1960 to 9000 g mol^{-1} with the increasing $[\text{MeEO}_3\text{IC}]_0/[\text{CpTiCl}_2(\text{O}^n\text{C}_4\text{H}_9)]_0$. These results meant that n -butoxy(η^5 -cyclopentadienyl)dichlorotitanium(IV) was efficient for the living coordination polymerization of the hydrophilic isocyanate due to the OGE unit leading to the water-soluble PIC.

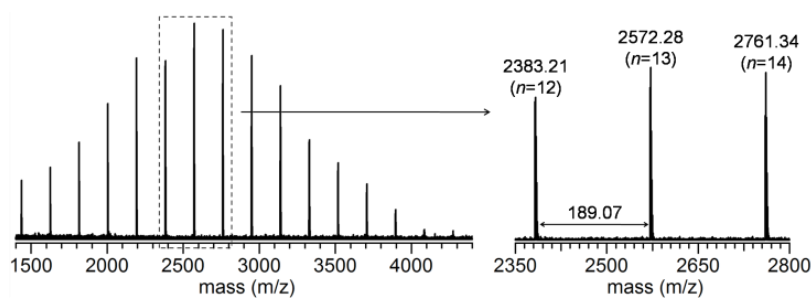


Figure 2-4. MALDI–TOF MS spectrum at reflector mode of **PMeEO₃IC** (run 2).

Table 2-1. Bulk Polymerization of MeEO₂IC, MeEO₃IC, EtEO₃IC, and MeEO₄IC Using CpTiCl₂(OⁿC₄H₉) at 10 °C ^a

run	monomer (M)	[M] ₀ /[CpTiCl ₂ (O ⁿ C ₄ H ₉)] ₀	Time (h)	Yield (%)	<i>M</i> _{n,calcd.} ^b (g mol ⁻¹)	<i>M</i> _{n,NMR} ^c (g mol ⁻¹)	<i>M</i> _w / <i>M</i> _n ^d
1	MeEO₃IC	10/1	19	95.0	1970	1960	1.13
2	MeEO₃IC	20/1	24	95.7	3860	3200	1.10
3	MeEO₃IC	30/1	41	84.0	5750	5560	1.06
4	MeEO₃IC	40/1	50	80.0	7640	7500	1.10
5	MeEO₃IC	50/1	72	82.8	9540	9000	1.11
6	MeEO₂IC	34/1	26	73.0	5010	4230	1.05
7	MeEO₃IC	26/1	36	86.4	5000	4560	1.10
8	EtEO₃IC	24/1	42	93.5	4950	4470	1.10
9	MeEO₄IC	21/1	42	80.2	4970	4460	1.10

^a Ar atmosphere. ^b Calculated from the equation of ([M]₀/[CpTiCl₂(OⁿC₄H₉)]₀) × (M.W. of a monomer) + (M.W. of *n*-butanol). ^c Determined by ¹H NMR in CDCl₃. ^d Determined by SEC in THF using polystyrene standards.

2.2.2 Thermoresponsive Property of the Water-Soluble Polyisocyanates with Oligo(ethylene glycol)

Side-Chains

To elucidate the thermoresponsive property of the water-soluble PICs in an aqueous solution, the phase transition behavior was characterized as the turbidity of the cloud point determined from the heating curve at 50% of the transmittance change. The data were recorded at 400 nm at the heating rate of 1.0 °C/min. All sample solutions were visually confirmed to be optically clear prior to the turbidity measurement. The polymer concentration was first optimized using the PMeEO₃IC with the $M_{n,NMR}$ of 5560 g mol⁻¹ (run 3). Although no phase transition was observed for the concentration of 20 g L⁻¹, the polymer solutions of 30 and 40 g L⁻¹ exhibited cloud point temperatures (T_{cp} s) of 76–82 °C and 74–79 °C, respectively (Figure 2-5). Thus, all the phase transition experiments were carried out with the polymer concentration of 40 g L⁻¹. The effect of the molecular weight on the thermoresponsive property was examined using PMeEO₃ICs of different molecular weights (runs 1–5 and 7). The T_{cp} decreased with the increasing molecular weight, as shown in Figure 2-6; the T_{cp} was 90.0, 83.9, 79.6, 77.3, 76.5, and 74.9 °C for the $M_{n,NMR}$ of 1960, 3200, 4560, 5560, 7500, and 9000 g mol⁻¹, respectively.

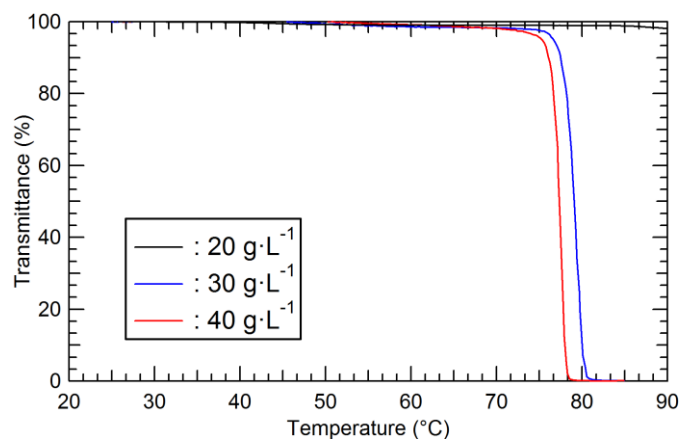


Figure 2-5. Transmittance versus temperature for the aqueous solutions of PMeEO₃IC (run 3, $M_{n,NMR} = 5560$) with polymer concentrations of 20, 30, and 40 g L⁻¹. The data were recorded at 400 nm at the heating rate of 1.0 °C/min.

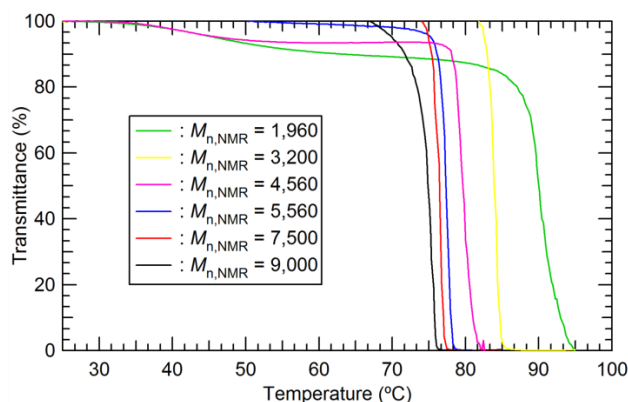


Figure 2-6. Effect of molecular weight of PMeEO₃IC on transmittance versus temperature for aqueous solutions with various molecular weights. The data were recorded at 400 nm at the heating rate of 1.0 °C/min.

The aggregation behavior in an aqueous solution was determined using PMeEO₃IC (run 4, $M_{n,NMR} = 7500$) based on the ¹H NMR measurement. In Figure 2-7, the proton signals at 3.60–3.75

ppm due to the oxyethylene group became broadened with the increasing temperature from 25 to 85 °C, indicating that the dehydration proceeded at the OEG side chain, resulting in the phase transition. Interestingly, the proton signal at 3.40 ppm due to the methyl group exhibited a behavior similar to the oxyethylene group, suggesting that the chain-end group of the OEG unit, *i.e.*, the methyl group, also affected the phase transition. After cooling from 85 to 25 °C, the shape and chemical shift of the ^1H NMR spectrum were the same as before heating, meaning that the phase transition behavior is reversible without any change in the chemical structure of PMeEO_3IC .

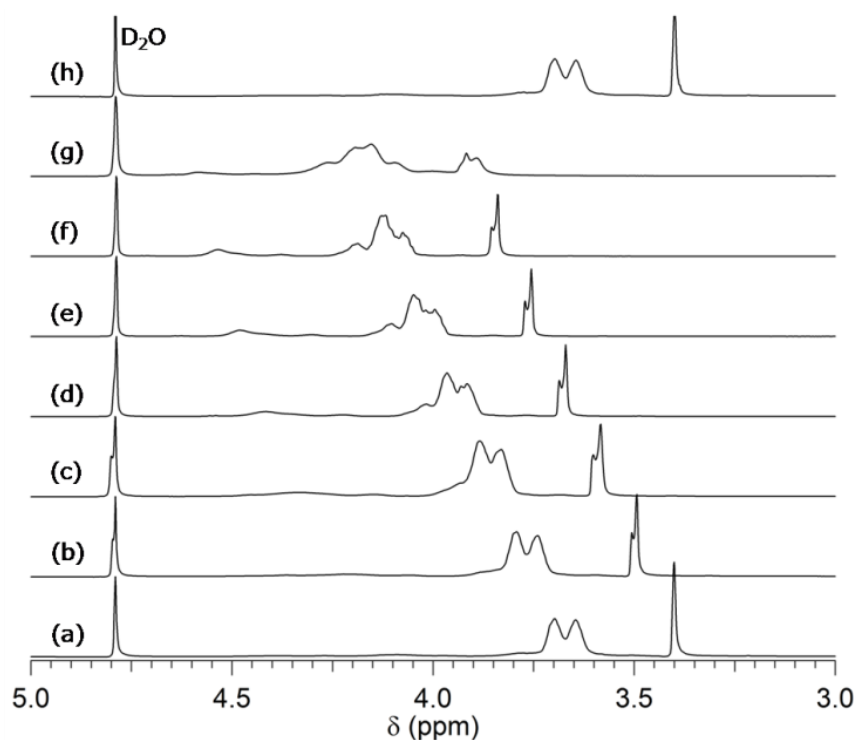


Figure 2-7. ^1H NMR spectra of PMeEO_3IC (40 g L^{-1} , run 4, $M_{n,\text{NMR}} = 7500$) in D_2O at (a) 25 °C, (b) 35 °C, (c) 45 °C, (d) 55 °C, (e) 65 °C, (f) 75 °C, (g) 85 °C, and (h) 25 °C (after cooling from 85 °C).

In addition, the aggregation property of PMeEO₃IC in an aqueous solution was investigated below and above the T_{cp} of 76.5 °C by the dynamic light scattering (DLS) technique, as shown in Figure 2-8. The hydrodynamic radius (R_h) of PMeEO₃IC significantly increased from *ca.* 3.1 nm at 25 °C to *ca.* 192 nm at 81 °C, indicating that the larger aggregate should be generated through the intermolecular aggregation triggered by the phase transition. These ¹H NMR and DLS measurement results meant that the phase transition behavior of the water-soluble PIC caused by the dehydration from the OEG side chain below the T_{cp} , followed by the intermolecular aggregation above the T_{cp} .

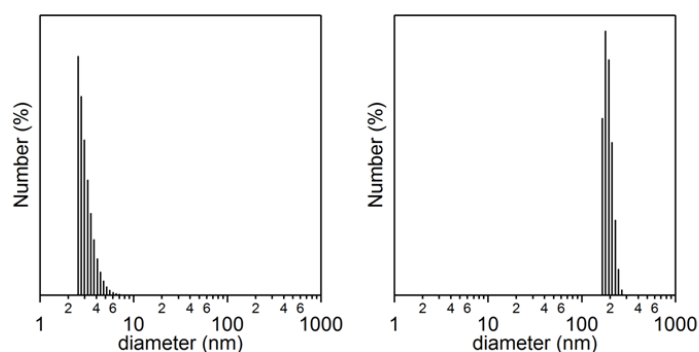


Figure 2-8. Particle size distribution and hydrodynamic radius (R_h) measured by dynamic light scattering (left) 25 °C (*i.e.*, below T_{cp}) and (right) 81 °C (*i.e.*, above T_{cp}) for an aqueous solution (40 g L⁻¹) of PMeEO₃IC (run 4, $M_{n,NMR}$ = 7500).

Finally, the effect of the side-chain structure in the water-soluble PICs on the thermoresponsive property was investigated using three PICs with similar molecular weights, such as PMeEO₂IC (run 6, $M_{n,NMR}$ = 4230 g mol⁻¹), PMeEO₃IC (run 7, 4560 g mol⁻¹), PEtEO₃IC (run 8, 4470 g mol⁻¹), and

PMeEO₄IC (run 9, 4460 g mol⁻¹) (the ¹H NMR, ¹³C NMR spectra and SEC traces of the PICs for runs 6, 8, and 9 are shown in Figure 2-9, 2-10, and 2-11, respectively). Although PMeEO₂IC was synthesized, its phase transition could not be determined due to being insoluble in water because of shorter OEG side chain and lower hydrophilicity. The T_{cp} was 79.6 °C for PMeEO₃IC and 94.0 °C for PMeEO₄IC, as shown in Figure 2-12. The increase in the T_{cp} from PMeEO₃IC to PMeEO₄IC was caused by the increase in the hydrophilicity due to the increasing number of oxyethylene units from PMeEO₃IC to PMeEO₄IC. Surprisingly, the T_{cp} significantly decreased from 79.6 to 34.7 °C by changing the methyl group in the OEG side-chain to an ethyl group, *i.e.*, from PMeEO₃IC to PEtEO₃IC. Although there is a slight difference in the terminal group of the side chain from the methyl to ethyl groups, the hydrophobicity of the polymer is significantly increased and the T_{cp} was dramatically changed.

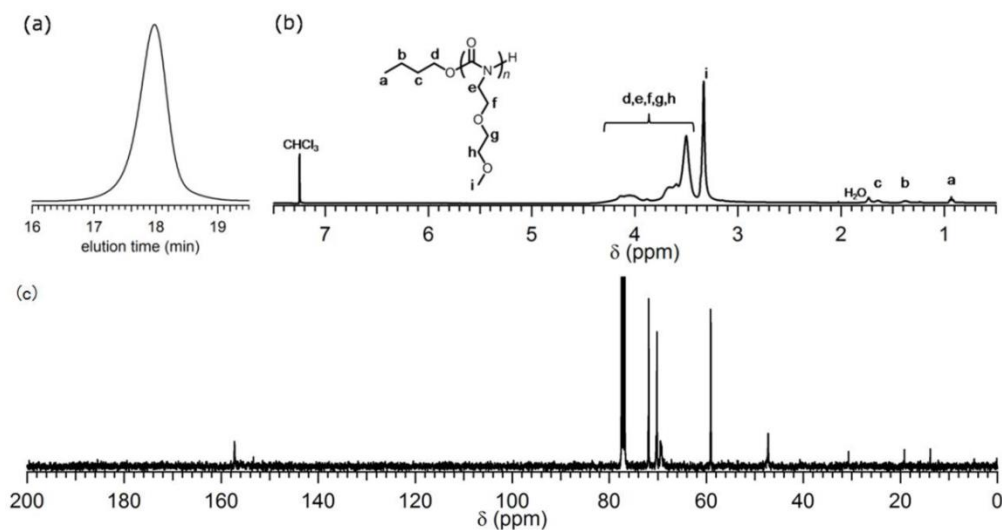


Figure 2-9. (a) SEC trace of PMeEO₂IC (run 6) in THF, (b) ^1H NMR spectrum of PMeEO₂IC (run 6) in CDCl_3 , and (c) ^{13}C NMR spectrum of PMeEO₂IC (run 6) in CDCl_3 .

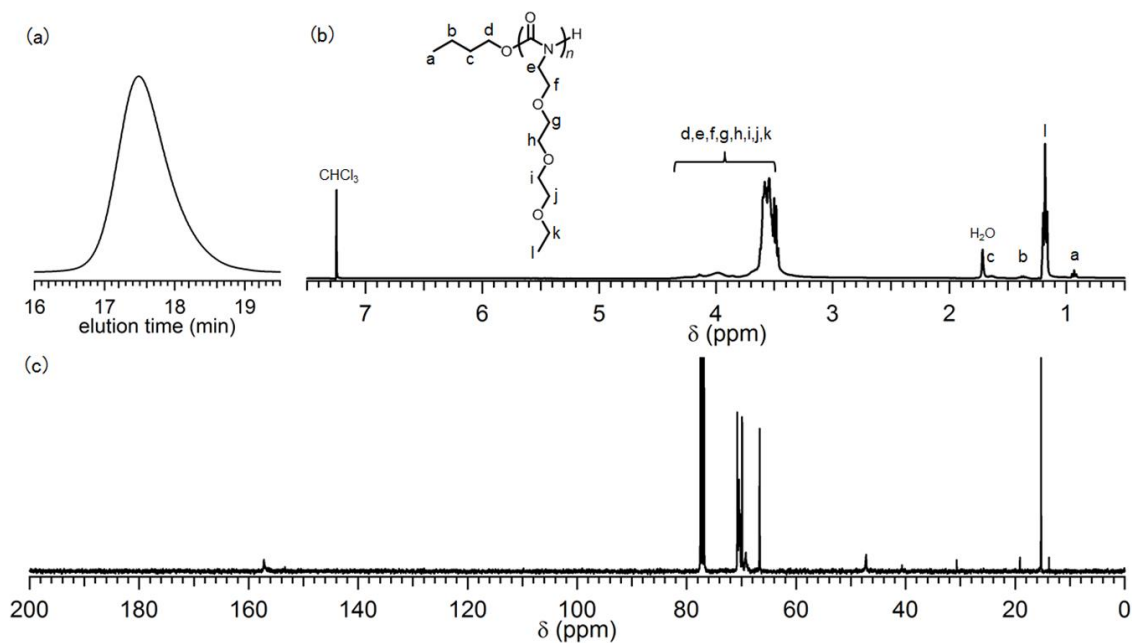


Figure 2-10. (a) SEC trace of PETEO₃IC (run 8) in THF and (b) ^1H NMR spectrum of PETEO₃IC (run 8) in CDCl_3 , and (c) ^{13}C NMR spectrum of PETEO₃IC (run 8) in CDCl_3 .

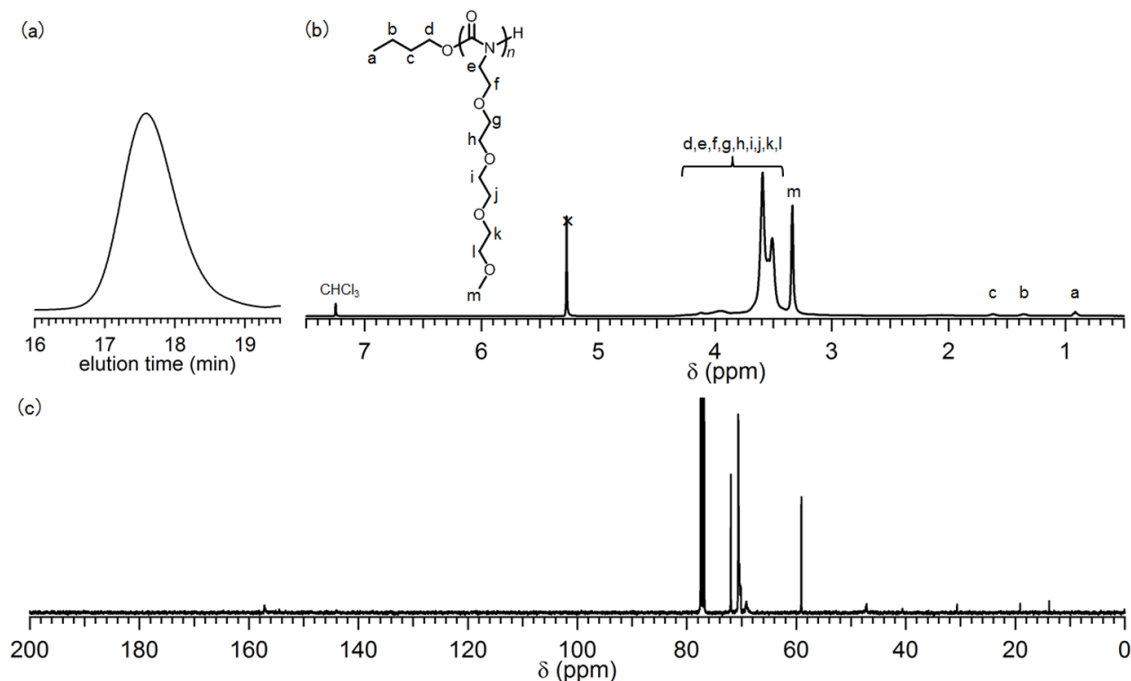


Figure 2-11. (a) SEC trace of PMeEO₄IC (run 9) in THF and (b) ^1H NMR spectrum of PMeEO₄IC (run 9) in CDCl_3 , and (c) ^{13}C NMR spectrum of PMeEO₂IC (run 9) in CDCl_3 .

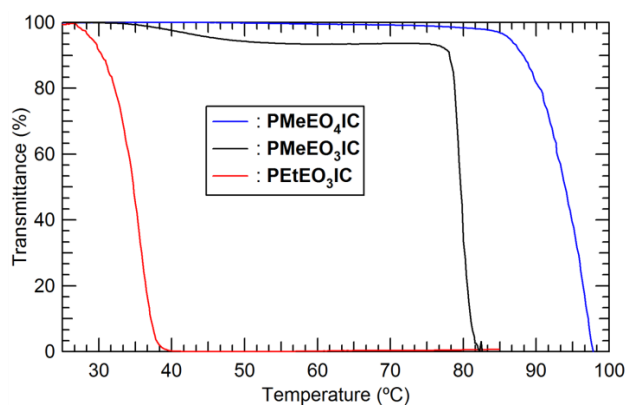


Figure 2-12. Transmittance versus temperature plots of 40 g L⁻¹ aqueous PMeEO₃IC (run 7, $M_{n,\text{NMR}} = 4560$), PEtEO₃IC (run 8, $M_{n,\text{NMR}} = 4470$), and PMeEO₄IC (run 9, $M_{n,\text{NMR}} = 4460$) solutions. The data were recorded at 400 nm at the heating rate of 1.0 °C/min.

2.3 Conclusions

In summary, we have successfully synthesized well-defined PICs conjugated with 2,5-dioxaoctyl, 2,5,8-trioxadecyl, 3,6,9-trioxaundecyl, and 2,5,8,11-tetraoxatridecyl groups as side chains by the living coordination polymerization using the half titanocene catalyst, *i.e.* *n*-butoxy(η^5 -cyclopentadienyl)di-chlorotitanium(IV). The aqueous solutions of PICs exhibited phase transition behaviors due to the intermolecular aggregation. The phase transition temperature decreased with the increasing molecular weight of the PICs, which is a typical property of thermoresponsive polymers. On the contrary, as an interesting feature of the obtained PIC, the side-chain group in the water-soluble PICs, particularly its chain-end group, significantly affected the thermoresponsive property. To the best of our knowledge, the present water-soluble PIC is a novel type of thermoresponsive polymers. Since PIC is generally expected to have a rod-like structure through the increasing polymerization degree, it may allow for the development of novel smart materials having stimuli-responsive properties, such as a sensory material, due to their unique properties like a main-chain stiffness.

2.4 Experimental Section

Material. Dry toluene (purity, >99.5%, water content, <0.001%), dry tetrahydrofuran (THF) (purity, >99.5%, water content, <0.001%), dry dichloromethane (DCM) (purity, >99.5%, water content, <0.001%), and 3-oxa-1-butanol were purchased from Kanto Chemicals Co., Inc., and used as received. The dichloromethane (DCM) for the polymerization was purchased from Kanto Chemicals Co., Inc., and distilled under an Ar atmosphere in the presence of CaH_2 . 3,6-Dioxa-1-heptanol, 3,6-dioxa-1-octanol, 3,6,9-trioxa-1-decanol, *tert*-butyl acrylate, and trifluoroacetic acid (TFA) were purchased from Tokyo Kasei Kogyo Co., Ltd. (TCI, Tokyo, Japan), and used as received. *n*-Butanol was purchased from Tokyo Kasei Kogyo Co., Ltd. (TCI, Tokyo, Japan), and distilled under an Ar atmosphere in the presence of CaH_2 . $(\eta^5\text{-Cyclopentadienyl})\text{trichlorotitanium(IV)}$ (CpTiCl_3) (ACROS), triethylamine (TEA) (Kanto Chemicals Co., Inc.), and diphenylphosphoryl azide (DPPA) (Kanto Chemicals Co., Inc.) were used as received. The monomer precursors were synthesized using previously reported techniques.^{27,28}

Instruments. The ^1H and ^{13}C NMR spectra were recorded using a JEOL ECS400 instrument. The polymerization was carried out in an MBRAUN stainless steel glovebox equipped with a gas purification system (molecular sieves and copper catalyst) and a dry argon atmosphere (H_2O , O_2 <1 ppm). The moisture and oxygen contents in the glovebox were monitored by an MB-MO-SE 1 and MB-OX-SE 1, respectively. The size exclusion chromatography (SEC) was performed at 40 °C in

THF (flow rate, 1.0 mL min⁻¹) using a Jasco GPC-900 system equipped with set two Shodex KF-804L columns (linear, 8 × 300 mm²). The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of the polymers were calculated on the basis of a polystyrene calibration. The preparative SEC was performed in CHCl₃ (3.5 mL min⁻¹) at room temperature using a JAI LC-9201 equipped with a JAI JAIGEL-2H column (20 × 600 mm²; exclusion limit, 5 × 10³) and JAI RI-50s refractive index detector. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) of the obtained polymers was performed using an Applied Biosystems Voyager-DE STR-H equipped with a 337 nm nitrogen laser (3 ns pulse width). Two hundred shots were accumulated for the spectra at a 25 kV acceleration voltage in the reflector mode and calibrated using insulin (TAKARA BIO, Inc.) as the internal standard. For the MALDI-TOF MS measurement, the polymer (5 g L⁻¹) in THF, a matrix (Dithranol, 50 g L⁻¹) in THF, and a cationizing agent (potassium trifluoroacetate, 25 g L⁻¹) in THF were mixed in the ratio of the polymer/matrix/cationizing agent of 100 μL/50 μL/100 μL, then 2 μL of the mixed solution was deposited on the sample holder. The dynamic light scattering (DLS) measurement was performed using an Otsuka Electronics FDLS-3000 light scattering spectrophotometer equipped with a solid state laser ($\lambda = 532$ nm, scattering angle = 90°). Before the measurement, the samples were filtered using 0.45 μm PTFE membrane filters to eliminate any dust. The data analysis was carried out using the histogram method including the Marquardt analysis. The turbidimetry analysis was performed using a Jasco V-550 spectrophotometer equipped with an EYELA NCB-1200 temperature controller.

The Fourier transform infrared spectroscopy (FT-IR) analysis was carried out using a Thermo Nicolet- Avatar 320 FT-IR spectrometer.

Synthesis of 2,5,8-Trioxadecyl Isocyanate (MeEO₃IC). Diphenylphosphoryl azide (17.5 mL, 81.2 mmol) was added to a solution of 3-(2-(2-methoxyethoxy)ethoxy)propanoic acid (15.6 g, 81.2 mmol) and triethylamine (11.3 mL, 81.2 mmol) in toluene (180 mL) at room temperature under an N₂ atmosphere. After stirring for 3h, the reaction mixture was heated at 70 °C and stirred for 2h. After cooling the reaction mixture to room temperature, the solution was washed with saturated aqueous ammonium chloride and water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure (86 °C/5 Pa) to give **MeEO₃IC** as a colorless liquid. Yield, 7.51 g (48.9 %); *d*, 1.05 g cm⁻³; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 3.72–3.61 (m, 8H, -OCH₂-), 3.56 (m, 2H, -OCH₂-), 3.41 (t, 2H, *J* = 5.00 Hz, -CH₂NCO), 3.39 (s, 3H, -OCH₃). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 125.2, 71.83, 70.57, 70.53, 70.47, 70.33, 58.96, 43.09. Anal. Calcd for C₈H₁₅NO₄: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.87; H, 8.17; N, 7.39. FT-IR: 2873 (m), 2258 (s), 2221 (s), 1455 (m), 1350 (m), 1287 (w), 1248 (m), 1199 (m), 1106 (s), 1029 (m), 985 (m), 931 (m), 850 (m), and 817 cm⁻¹ (m).

Synthesis of 2,5-Dioxaheptyl Isocyanate (MeEO₂IC). Yield, 45.8 %; b.p., 28 °C/5 Pa; *d*, 1.09 g cm⁻³; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 3.69–3.60 (m, 4H, -OCH₂-), 3.58 (m, 2H, -OCH₂-), 3.42

(t, 2H, $J = 5.38$ Hz, $-\text{CH}_2\text{NCO}$), 3.40 (s, 3H, $-\text{OCH}_3$). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 125.1, 71.86, 70.43, 70.39, 59.05, 43.07. Anal. Calcd for $\text{C}_6\text{H}_{11}\text{NO}_3$: C, 49.65; H, 7.64; N, 9.65. Found: C, 49.39; H, 7.43; N, 9.55. FT-IR: 2877 (m), 2257 (s), 2220 (s), 1455 (m), 1349 (m), 1247 (m), 1199 (m), 1105 (s), 1028 (m), 983 (m), 927 (m), 849 (m), and 816 cm^{-1} (m).

Synthesis of 3,6,9-Trioxaundecyl Isocyanate (EtEO_3IC). Yield, 71.7 %; b.p., $75\text{ }^\circ\text{C}/5\text{ Pa}$; d , 1.03 g cm^{-3} ; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.70–3.58 (m, 10H, $-\text{OCH}_2-$ and $-\text{CH}_2\text{CH}_2\text{NCO}$), 3.55 (q, 2H, $J=7.12\text{ Hz}$, $-\text{OCH}_2\text{CH}_3$), 3.41 (t, 2H, $J = 6.28$ Hz, $-\text{CH}_2\text{NCO}$), 1.21 (t, 3H, $J = 7.07$ Hz, $-\text{OCH}_2\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 125.2, 70.69, 70.57, 70.51, 70.35, 69.74, 66.57, 43.12, 15.11. Anal. Calcd for $\text{C}_9\text{H}_{17}\text{NO}_4$: C, 53.19; H, 8.43; N, 6.89. Found: C, 53.05; H, 8.46; N, 6.60. FT-IR: 2867 (m), 2258 (s), 2222 (m), 1454 (w), 1349 (m), 1295 (w), 1247 (m), 1108 (s), 986 (m), 937 (m), 849 (m), and 816 cm^{-1} (m).

Synthesis of 2,5,8,11-Tetraoxatridecyl Isocyanate (MeEO_4IC). Yield, 43.1 %; b.p., $123\text{ }^\circ\text{C}/5\text{ Pa}$; d , 1.09 g cm^{-3} ; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 3.68–3.59 (m, 12H, $-\text{OCH}_2-$ and $-\text{CH}_2\text{CH}_2\text{NCO}$), 3.53 (m, 2H, $-\text{OCH}_2-$), 3.39 (t, 2H, $J=5.41\text{ Hz}$, $-\text{CH}_2\text{NCO}$), 3.36 (s, 3H, $-\text{OCH}_3$). ^{13}C NMR (100MHz, CDCl_3): δ (ppm) 125.2, 71.88, 70.57, 70.52, 70.47, 70.37, 59.01, 43.14. Anal. Calcd for $\text{C}_{10}\text{H}_{19}\text{NO}_5$: C, 51.49; H, 8.21; N, 6.00. Found: C, 51.39; H, 8.11; N, 5.71. FT-IR: 2872 (m), 2259 (s), 2221 (m),

1454 (m), 1350 (m), 1296 (m), 1248 (m), 1198 (m), 1102 (s), 1029 (m), 985 (m), 938 (m), 851 (m), and 814 cm^{-1} (m).

Polymerization of 2,5,8-Trioxadecyl Isocyanate (MeEO₃IC). To a homogenous solution of (cyclopentadienyl)trichloro-titanium(IV) (CpTiCl₃) (69.5 mg, 317 μmol) in dry CH₂Cl₂ (1.59 mL) in a Schlenk flask was added *n*-butanol (23.5 mg, 29.0 μL , 317 μmol). The entire mixture was stirred at room temperature for several hours and the solvent was then removed under vacuum to give *n*-butoxy(η^5 -cyclopentadienyl)dichloro-titanium(IV) (CpTiCl₂(O^{*n*}C₄H₉)) as a yellow viscous liquid. MeEO₃IC (600 mg, 571 μL , 3.17 mmol) was added to the Schlenk flask, and the reaction was carried out for 19 h at 10 °C. The polymerization was quenched by the addition of methanol and purified by preparative size exclusion chromatography in chloroform to remove the catalyst residue and a slight amount of monomer to afford PMeEO₃IC as a soft solid material. Yield, 95.0 %; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.16 (t, 2H, *J* = 6.4 Hz, -CH₂OCO-), 4.50–3.25 (br, 150H, -OCH₂- and -OCH₃), 1.66 (m, 2H, -CH₂CH₂CH₃), 1.40 (m, 2H, -CH₂CH₂CH₃), 0.954 (t, 3H, *J* = 7.6 Hz, -CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 157.1, 71.93, 70.54, 70.41, 70.21, 69.11, 67.41, 59.02, 30.59, 19.05, 13.73. FT-IR: 2872 (m), 1698 (s), 1525 (w), 1450 (m), 1345 (s), 1278 (m), 1187 (s), 1100 (s), 933 (m), 849 (m), 751 (m), 713 (m), and 603 cm^{-1} (m).

Polymerization of 2,5-Dioxaheptyl Isocyanate (MeEO₂IC). Yield, 73.0 %; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.10 (br, 317H, -OCH₂-, -OCH₃ and -CH₂OCO-), 1.66 (m, 2H, -CH₂CH₂CH₃), 1.40 (m, 2H, -CH₂CH₂CH₃), 0.952 (t, 3H, J = 7.2 Hz, -CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 157.3, 71.88, 70.33, 70.19, 69.29, 59.10, 30.68, 19.17, 13.84. FT-IR: 2874 (m), 1695 (s), 1524 (w), 1447 (m), 1384 (m), 1345 (s), 1273 (m), 1183 (s), 1080 (s), 1036 (s), 964 (m), 850 (m), 747 (m), 722 (m), and 601 cm⁻¹ (m).

Polymerization of 3,6,9-Trioxaundecyl Isocyanate (EtEO₃IC). Yield, 93.5 %; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.16 (t, 2H, J = 6.4 Hz), 4.50–3.10 (br, 326H, -OCH₂-, -OCH₃ and -CH₂OCO-), 1.66 (m, 2H, -CH₂CH₂CH₃), 1.39 (m, 2H, -CH₂CH₂CH₃), 1.20 (t, 3H, J = 7.2 Hz, -OCH₂CH₃), 0.951 (t, 3H, J = 7.6 Hz, -CH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 157.2, 70.76, 70.64, 70.43, 70.22, 69.88, 69.21, 66.68, 30.67, 19.14, 15.27, 13.83. FT-IR: 2865 (m), 1699 (s), 1525 (w), 1446 (m), 1346 (s), 1275 (m), 1185 (s), 1104 (s), 943 (m), 844 (m), 749 (m), 719 (m), and 601 cm⁻¹ (m).

Polymerization of 2,5,8,11-Tetraoxatridecyl Isocyanate (MeEO₄IC). Yield, 80.2 %; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.00 (br, 359H, -OCH₂-, -OCH₃ and -CH₂OCO-), 1.66 (m, 2H, -CH₂CH₂CH₃), 1.40 (m, 2H, -CH₂CH₂CH₃), 0.952 (t, 3H, J = 6.8 Hz, -CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 157.2, 71.98, 70.61, 70.14, 69.14, 59.09, 30.65, 19.13, 13.82. FT-IR: 2870

(m), 1699 (s), 1525 (w), 1451 (m), 1346 (s), 1280 (m), 1186 (s), 1097 (s), 940 (m), 850 (m), 751 (m),

715 (m), and 600 cm^{-1} (m).

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Chapter 3

Phase Transition Property of Thermoresponsive Rod-Like Polyisocyanate with *n*-Alkyl Chain as α -End Group

3.1 Introduction

Thermoresponsive polymers are well-known as smart materials, which show a phase transition behavior from sol to gel in an aqueous solution at the lower critical solution temperature (LCST).¹⁻⁵ Thus, thermoresponsive polymers have been expected to be utilized for a range of biologically relevant applications, such as controlled drug delivery,⁶⁻⁸ bioseparation,⁹ filtration,¹⁰ and smart surface.¹¹ Since Scarpa et al. reported poly(*N*-isopropylacrylamide) as a thermoresponsive polymer with the LCST of *ca.* 32 °C,¹² there have been many studies of thermoresponsive polymers with different phase transition temperatures, such as poly(ethylene oxide),^{2,13} poly(2-ethyl-2-oxazoline),^{2,14} poly(methyl vinyl ether),¹⁵ poly(dimethylaminoethyl methacrylate),¹⁶ poly[bis((ethoxyethoxy)ethoxy)phosphazene],¹⁷ and poly(*N*-vinylcaprolactam).¹⁸ Their thermoresponsive phenomena based on the coil-to-globule transition have been studied in terms of polymer characteristics, such as molecular weights,¹⁹ molecular weight distributions,²⁰ stereoregularity,²¹ chain-end groups,²²⁻²⁴ and cyclic²⁵ and star shapes.²⁶

Contrary to the polymers possessing the coil-to-globule transition property, the thermoresponsive rod-like polymers in aqueous media are quite limited. Afang et al. reported the thermoresponsive polyisocyanide²⁷ and poly(phenylacetylene),²⁸ which were categorized as rod-like polymers due to the stiffness of the polymer backbones. Recently, we also reported that water-soluble rod-like polyisocyanates were synthesized as thermoresponsive polymers.²⁹ There are a very few reports for the thermoresponsive rod-like polymers, resulting in the fact that the details of the phase

transition behavior were still insufficient. Therefore, it is of significant importance to study the phase transition behavior of thermoresponsive rod-like polymers in terms of their molecular weights and chain-end groups.

We now report the thermoresponsive property of α -end-substituted polyisocyanates with *n*-alkyl chains (C_m -PMeEO₃IC) as the rod-like polymer, which were synthesized by the coordination polymerization of 2,5,8-trioxadecyl isocyanate using alkoxy half-titanocene(IV). The phase transition temperature of C_m -PMeEO₃IC was clarified by turbidity measurements in an aqueous solution. In addition, the details of their enthalpy change and aggregation behavior through the phase transition are discussed on the basis of the micro-differential scanning calorimetry and dynamic light scattering measurements.

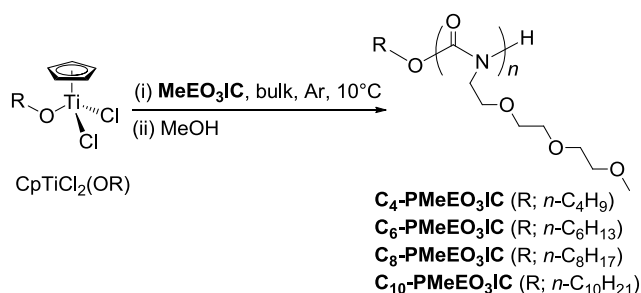


Table 3-1. Bulk polymerization of 2,5,8-trioxadecyl isocyanate (MeEO₃IC) using CpTiCl₂(OR) as catalyst ^a

Run	R	[MeEO ₃ IC]/ [CpTiCl ₂ (OR)]	Yield (%)	$M_{n,calcd}$ (g mol ⁻¹) ^b	$M_{n,NMR}$ (g mol ⁻¹) ^c	M_w/M_n ^d	samples ^c
1	C ₄	20	62.4	3860	4030	1.11	C ₄ -PMeEO ₃ IC ₂₁
2		30	84.0	5750	5560	1.10	C ₄ -PMeEO ₃ IC ₂₉
3		40	80.0	7640	7500	1.10	C ₄ -PMeEO ₃ IC ₃₉
4		50	82.8	9530	9000	1.11	C ₄ -PMeEO ₃ IC ₄₇
5	C ₆	20	75.6	3890	4090	1.10	C ₆ -PMeEO ₃ IC ₂₁
6		30	80.0	5780	5400	1.07	C ₆ -PMeEO ₃ IC ₂₈
7		40	75.3	7670	7380	1.09	C ₆ -PMeEO ₃ IC ₃₈
8		50	77.5	9560	9150	1.11	C ₆ -PMeEO ₃ IC ₄₇
9	C ₈	20	71.3	3910	3850	1.15	C ₈ -PMeEO ₃ IC ₂₀
10		30	71.3	5810	6040	1.16	C ₈ -PMeEO ₃ IC ₃₁
11		40	73.2	7700	7510	1.08	C ₈ -PMeEO ₃ IC ₃₉
12		50	83.3	9590	10400	1.16	C ₈ -PMeEO ₃ IC ₅₄
13	C ₁₀	20	61.8	3940	3890	1.12	C ₁₀ -PMeEO ₃ IC ₂₀
14		30	79.8	5830	5240	1.07	C ₁₀ -PMeEO ₃ IC ₂₇
15		40	81.8	7730	7530	1.09	C ₁₀ -PMeEO ₃ IC ₃₉
16		50	75.1	9620	10400	1.10	C ₁₀ -PMeEO ₃ IC ₅₄

^a Ar atmosphere, temp; 10 °C. ^b Calculated from [MeEO₃IC]/[CpTiCl₂(OR)] × (M.W. of MeEO₃IC) + (M.W. of ROH). ^c Determined from ¹H NMR spectra in CDCl₃. ^d Determined by SEC in THF using polystyrene standards.

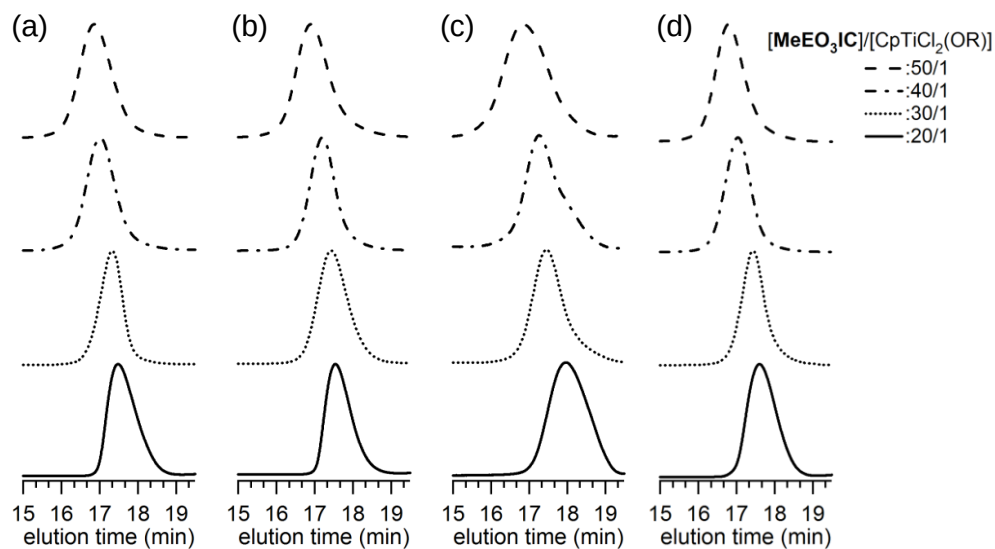


Figure 3-1. SEC traces of (a) C_4 -PMEO₃IC, (b) C_6 -PMEO₃IC, (c) C_8 -PMEO₃IC, and (d) C_{10} -PMEO₃IC with various molecular weights in THF.

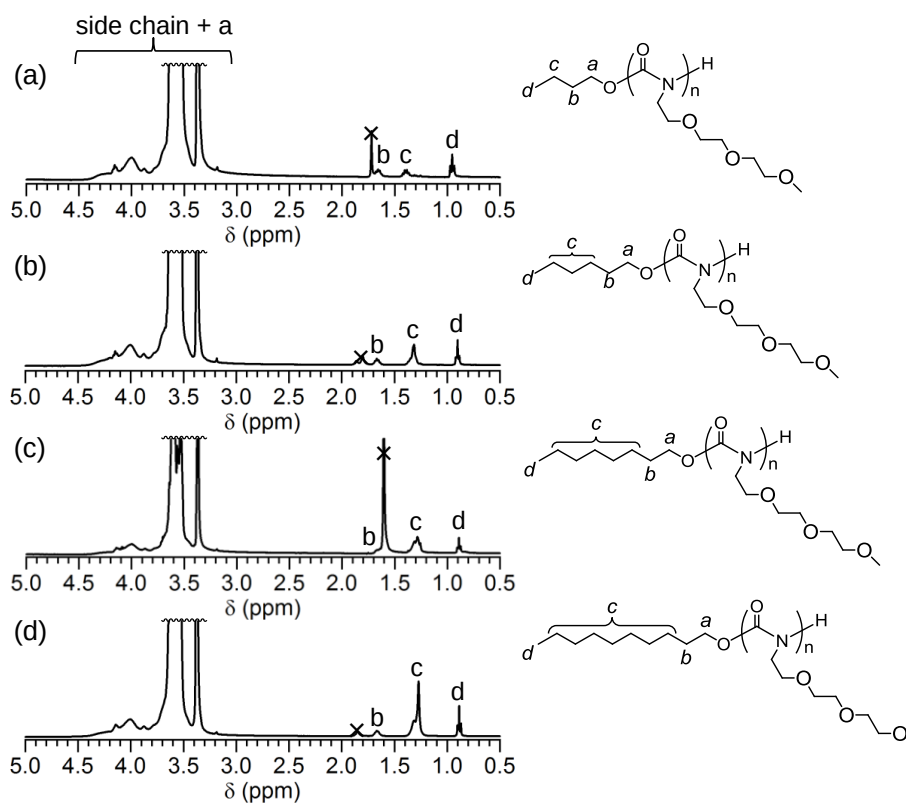


Figure 3-2. ¹H NMR spectra of (a) C_4 -PMEO₃IC₂₁, (b) C_6 -PMEO₃IC₂₁, (c) C_8 -PMEO₃IC₂₀, and (d) C_{10} -PMEO₃IC₂₀ in CDCl₃ at ambient temperature.

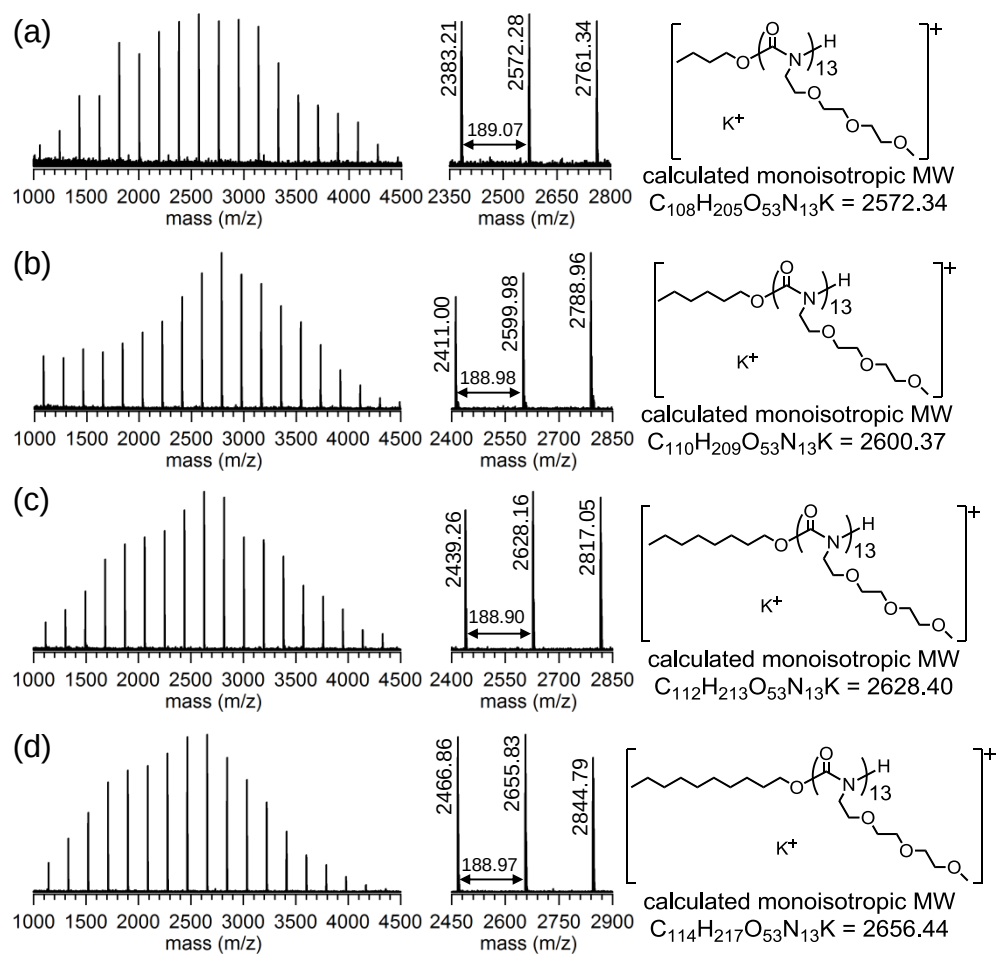


Figure 3-3. MALDI-TOF MS spectra at reflector mode of (a) $C_4\text{-PMEO}_3\text{IC}_{21}$, (b) $C_6\text{-PMEO}_3\text{IC}_{21}$, (c) $C_8\text{-PMEO}_3\text{IC}_{20}$, and (d) $C_{10}\text{-PMEO}_3\text{IC}_{20}$.

3.2.2 Thermoresponsive property for α -end-substituted polyisocyanate with n -alkyl chain

To investigate the thermoresponsive property of the water-soluble α -end-substituted polyisocyanates with n -alkyl chains in an aqueous solution, the phase transition behavior was characterized as the turbidity of the cloud point (T_{cp}) determined from the heating curve at 50 % of the transmittance change. All sample solutions were completely dissolved in deionized water at the concentration of 30 g L⁻¹. For the C_m-PMeEO₃IC with the DP of *ca.* 20, the T_{cp} during the heating process decreased with the increasing n -alkyl chain length of the α -end group, *i.e.*, C₄-PMeEO₃IC₂₁ > C₆-PMeEO₃IC₂₁ > C₈-PMeEO₃IC₂₀ $\approx$ C₁₀-PMeEO₃IC₂₀, and the T_{cp} was observed at 81.3 °C for C₄-PMeEO₃IC₂₁, 74.7 °C for C₆-PMeEO₃IC₂₁, 64.3 °C for C₈-PMeEO₃IC₂₀, and 63.9 °C for C₁₀-PMeEO₃IC₂₀, as shown in Figure 3-4. These results clearly suggested that the small difference in the n -alkyl chain-end significantly affected the phase transition temperature.

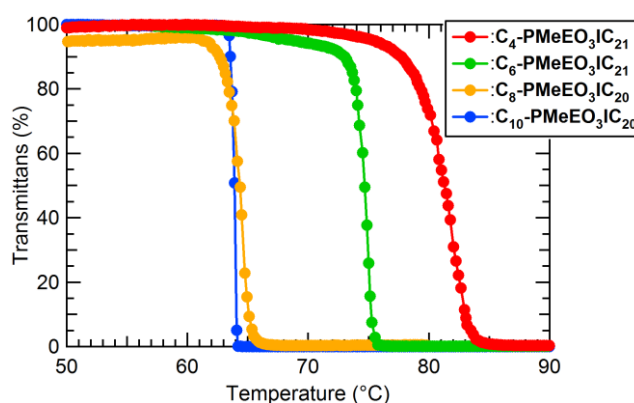


Figure 3-4. Temperature dependences of optical transmittance at 400 nm obtained for aqueous solutions of C₄-PMeEO₃IC₂₁, C₆-PMeEO₃IC₂₁, C₈-PMeEO₃IC₂₀, and C₁₀-PMeEO₃IC₂₀ at the heating rate of 1.0 °C min⁻¹.

In addition, a turbidity measurement was carried out for the C_m -PMeEO₃IC with the DPs of *ca.* 30, *ca.* 40, and *ca.* 50 to elucidate the effect of the molecular weights on the phase transition behavior, as shown in Figure 3-5. The T_{cp} slightly varied with the molecular weight for every C_m -PMeEO₃IC, such as from 81.3 to 78.4 °C for C_4 -PMeEO₃IC, from 74.7 to 74.4 °C for C_6 -PMeEO₃IC, 64.3 to 64.7 °C for C_8 -PMeEO₃IC, and 63.9 to 64.7 °C for C_{10} -PMeEO₃IC. The relation between the T_{cp} and molecular weights for C_m -PMeEO₃IC is summarized in Figure 3-6. Although the T_{cp} of C_4 -PMeEO₃IC gradually decreased with the increasing molecular weight, the other three samples exhibits an almost constant T_{cp} , such as *ca.* 75 °C for C_6 -PMeEO₃IC, *ca.* 65 °C for C_8 -PMeEO₃IC, and *ca.* 64 °C for C_{10} -PMeEO₃IC. The *n*-alkyl group in the α -polymer-chain end of C_m -PMeEO₃IC affected the T_{cp} though only a small difference in the methylene number, such as from *ca.* 80 °C for C_4 -PMeEO₃IC to *ca.* 65 °C for C_8 -PMeEO₃IC and C_{10} -PMeEO₃IC, suggesting that the hydrophobicity of the α -end of C_m -PMeEO₃IC preliminary controlled the thermal phase transition. The result is typical for the thermoresponsive polymers due to the coil-to-globule transition. However, the T_{cp} was almost independent of the molecular weight for C_m -PMeEO₃IC, which apparently differed from the usual thermoresponsive polymers, *i.e.*, the T_{cp} decreased with the increasing molecular weight, and the high molecular weight polymers showed constant T_{cp} s, such as 32 °C for poly(*N*-isopropylacrylamide) and 85 °C for poly(ethylene oxide). Thus, the thermoresponsive feature of C_m -PMeEO₃IC should be caused by its rod-like characteristics.

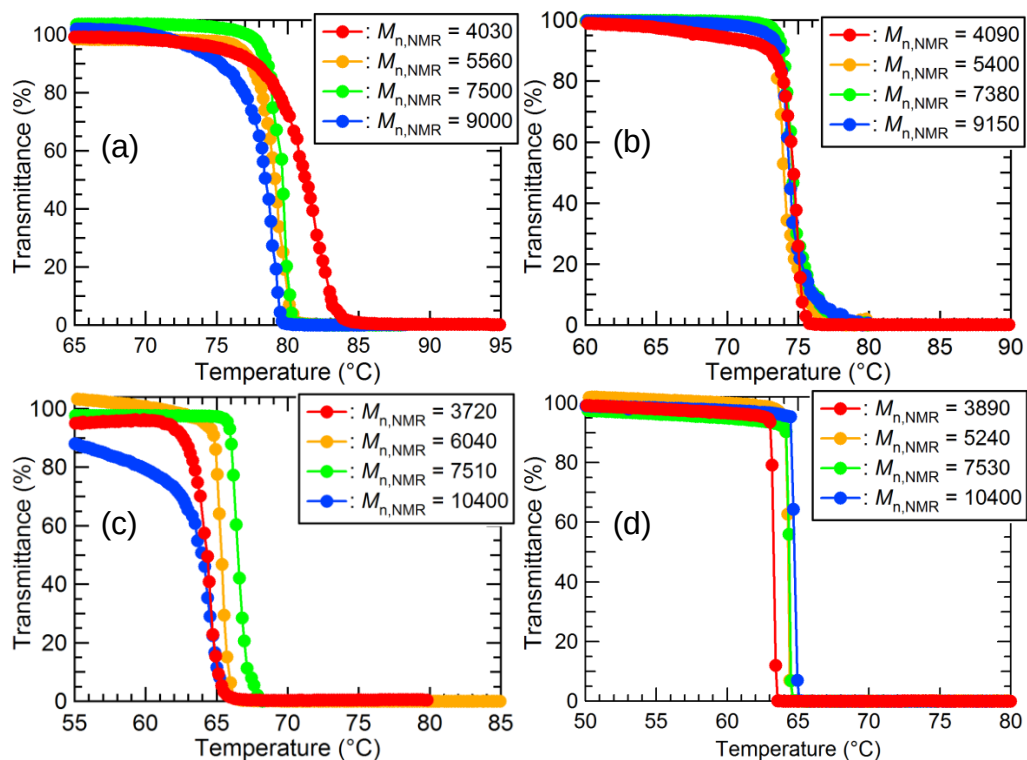


Figure 3-5. Temperature dependence of optical transmittance at 400 nm obtained for aqueous solutions of (a) C_4 -PMEO₃IC, (b) C_6 -PMEO₃IC, (c) C_8 -PMEO₃IC, and (d) C_{10} -PMEO₃IC, at varying molecular weights at the heating rate of $1.0\text{ }^{\circ}\text{C min}^{-1}$.

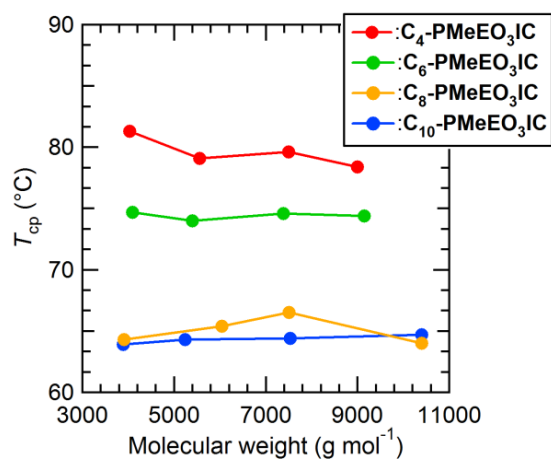


Figure 3-6. Molecular weight ($M_{n,NMR}$) dependences of cloud point temperature (T_{cp}) for C_m -PMEO₃ICs.

The detailed insight into the thermal phase transition behavior of C_m -PMeEO₃IC in an aqueous solution was investigated by micro-differential scanning calorimetry (micro-DSC) measurements. Figure 3-7 shows the micro-DSC thermograms measured at the concentration of 30 g L⁻¹, as same as the turbidity measurement. Although one endothermic peak is observed for C_4 -PMeEO₃IC₂₁ and C_{10} -PMeEO₃IC₂₀, C_6 -PMeEO₃IC₂₁ and C_8 -PMeEO₃IC₂₀ unexpectedly exhibited two endothermic peaks. The first peak tops (1st- $T_{\max}$ s) are 84.3 °C for C_4 -PMeEO₃IC₂₁, 74.6 °C for C_6 -PMeEO₃IC₂₁, 66.5 °C for C_8 -PMeEO₃IC₂₀, and 63.2 °C for C_{10} -PMeEO₃IC₂₀, which well agreed with the T_{cp} determined by the turbidity measurement, as listed in Table 3-2.

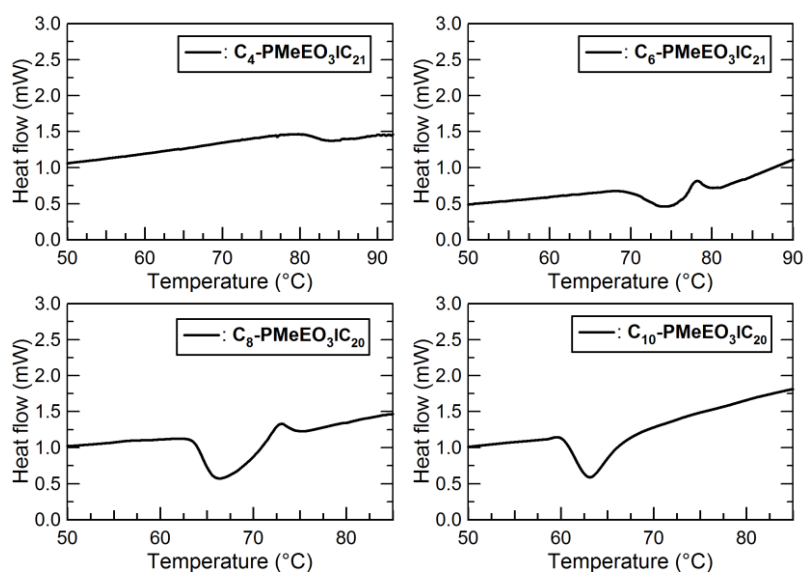


Figure 3-7. Micro-DSC thermograms for aqueous solutions of C_m -PMeEO₃ICs at the heating rate of 1.0 °C min⁻¹.

Table 3-2. Thermoresponsive property of α -end-substituted poly(2,5,8-trioxadecyl isocyanate) with n -alkyl chains (C_m -PMeEO₃IC) ^a

sample	T_{cp} (°C) ^b	1st- T_{max}	2nd- T_{max}	1st- ΔH	2nd- ΔH
		(°C) ^c		(kJ/mol) ^c	
C ₄ -PMeEO ₃ IC ₂₁	81.3	84.3	-	0.394	-
C ₆ -PMeEO ₃ IC ₂₁	74.7	74.6	81.0	1.33	0.454
C ₈ -PMeEO ₃ IC ₂₀	64.3	66.5	75.6	2.97	0.671
C ₁₀ -PMeEO ₃ IC ₂₀	63.9	63.2	-	2.66	-

^a Concentration; [C_m -PMeEO₃IC] = 30 g L⁻¹. ^b The cloud point (T_{cp}) determined from the heating curve at 50 % of the transmittance change. ^c Determined by micro-DSC measurement at the heating rate of 1.0 °C min⁻¹.

The phase transition enthalpy change (1st- ΔH) at the T_{cp} increased in the order of C₄-PMeEO₃IC₂₁ < C₆-PMeEO₃IC₂₁ < C₈-PMeEO₃IC₂₀ $\approx$ C₁₀-PMeEO₃IC₂₀. In addition, the 1st- ΔH was determined to be 0.394 kJ mol⁻¹ of the repeating unit for C₄-PMeEO₃IC₂₁, 1.33 kJ mol⁻¹ for C₆-PMeEO₃IC₂₁, 2.97 kJ mol⁻¹ for C₈-PMeEO₃IC₂₀, and 2.66 kJ mol⁻¹ for C₁₀-PMeEO₃IC₂₀, which should be caused by the dehydration from the thermoresponsive 2-(2-methoxyethoxy)ethoxy side-chain and the aggregation of C_m -PMeEO₃ICs due to the intermolecular hydrophobic interaction. Figure 3-8 shows the T_{cp} and 1st- ΔH plots as a function of the n -alkyl chain length as the α -end group. For C₄-PMeEO₃IC₂₁, C₆-PMeEO₃IC₂₁, and C₈-PMeEO₃IC₂₀, the relation between the T_{cp} and the n -alkyl chain length was opposite to that between the ΔH and the n -alkyl chain length. The 1st- ΔH increased with the increasing n -alkyl chain length from C₄-PMeEO₃IC₂₁ to C₈-PMeEO₃IC₂₀,

and C₁₀-PMeEO₃IC₂₀ showed a similar ΔH of C₈-PMeEO₃IC₂₀. The C_m-PMeEO₃IC with the higher ΔH should form the larger aggregate because the endothermic ΔH generally depends on the amount of dehydration from the thermoresponsive polymer.

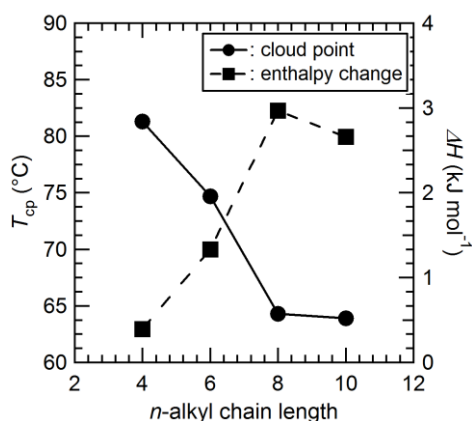


Figure 3-8. *n*-Alkyl chain length dependences of cloud point temperature (T_{cp}) (circle and solid line) and phase transition enthalpy change (1st- ΔH) (square and dashed line) for C_m-PMeEO₃ICs.

Furthermore, the 2nd- T_{max} s are observed above the T_{cp} s for C₆-PMeEO₃IC₂₁ and C₈-PMeEO₃IC₂₀, as shown in Figure 3-7, though no transmittance change was observed at the 2nd- T_{max} . In addition, the percentage of the 2nd- ΔH in the total ΔH for C₈-PMeEO₃IC₂₀ was lower than that for C₆-PMeEO₃IC₂₁. The 2nd- T_{max} s are 81.0 °C for C₆-PMeEO₃IC₂₁ and 75.6 °C for C₈-PMeEO₃IC₂₀, and the 2nd- ΔH s of C₆-PMeEO₃IC₂₁ and C₈-PMeEO₃IC₂₀ are 0.454 and 0.671 kJ mol⁻¹, respectively, whose values were smaller than those for their 1st- ΔH s. These results indicated that a small conformational change should occur above the T_{cp} , such as an intermolecular aggregation or reorientation for C₆-PMeEO₃IC₂₁ and C₈-PMeEO₃IC₂₀.

A dynamic light scattering (DLS) measurement was performed in order to clarify the phase transition behavior based on the hydrodynamic diameter (D) for C_m -PMeEO₃IC in an aqueous solution. To estimate the D value for the C_m -PMeEO₃IC aggregate before the phase transition, the DLS measurement was carried out at the concentration of 30 g L⁻¹ with the scattering angle of 90° at 25 °C, as shown in Figure 3-9, and the results are summarized in Table 3-3. A single peak is observed for every C_m -PMeEO₃IC and the D values were determined to be 1.6 nm for C₄-PMeEO₃IC₂₁, 1.5 nm for C₆-PMeEO₃IC₂₁, 1.9 nm for C₈-PMeEO₃IC₂₀, and 5.5 nm for C₁₀-PMeEO₃IC₂₀. For C₄-PMeEO₃IC₂₁, C₆-PMeEO₃IC₂₁, and C₈-PMeEO₃IC₂₀, the peaks were attributed to a unimolecular particle. In addition, C₁₀-PMeEO₃IC₂₀ shows a large D value compared to the D values for the C₄-, C₆-, and C₈-PMeEO₃ICs, clearly indicating that the aggregation property of C_m -PMeEO₃IC increased with the increasing n -alkyl chain length of the α -end group. The difference in the self-assembling structure between the unimolecule and the small aggregate caused the difference in the phase transition temperature.

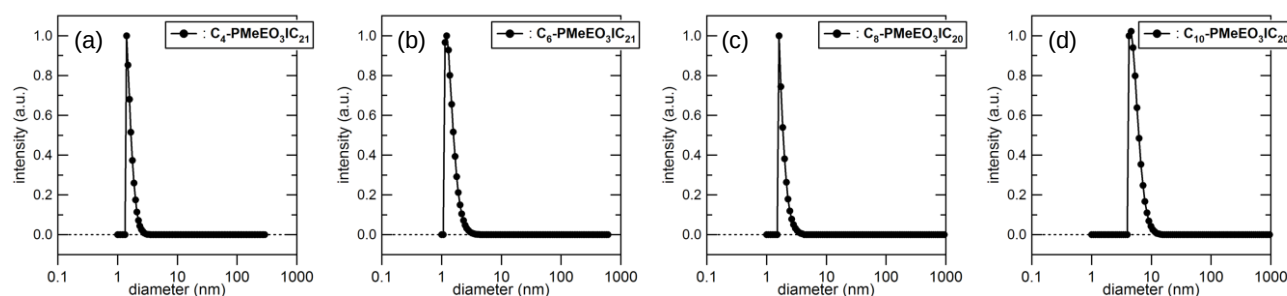


Figure 3-9. Hydrodynamic diameter distributions measured by DLS for (a) C₄-PMeEO₃IC₂₁, (b) C₆-PMeEO₃IC₂₁, (c) C₈-PMeEO₃IC₂₀, and (d) C₁₀-PMeEO₃IC₂₀, at 25 °C.

Table 3-3. Hydrodynamic diameter (D) of α -end-substituted poly(2,5,8-trioxadecyl isocyanate) with n -alkyl chains (C_m -P MeEO₃IC) before and after phase transition ^a

C_m -PMeEO ₃ IC	D (nm) at 25 °C	D (nm) at 1st- $T_{\max}$	D (nm) at 2nd- $T_{\max}$
C ₄ -PMeEO ₃ IC ₂₁	1.6	295	—
C ₆ -PMeEO ₃ IC ₂₁	1.5	415	518
C ₈ -PMeEO ₃ IC ₂₀	1.9	466	626
C ₁₀ -PMeEO ₃ IC ₂₀	5.5	630	—

^a Determined by DLS measurement at 25 °C, 1st- $T_{\max}$ (82 °C for C₄-PMeEO₃IC₂₁, 75 °C for C₆-PMeEO₃IC₂₁, 65 °C for C₈-PMeEO₃IC₂₀, and 65 °C for C₁₀-PMeEO₃IC₂₀), and 2nd- $T_{\max}$ (82 °C for C₆-PMeEO₃IC₂₁ and 75 °C for C₈-PMeEO₃IC₂₀).

To investigate the aggregation behavior at the phase transition temperature (T_{cp}), a DLS measurement was carried out for C_m -PMeEO₃IC at the T_{cp} . The monomodal peaks with the significantly high D values were observed for C₄-PMeEO₃IC₂₁, C₆-PMeEO₃IC₂₁, C₈-PMeEO₃IC₂₀, and C₁₀-PMeEO₃IC₂₀, and the determined D values are 304, 426, 482, and 653 nm, respectively, as shown in Figure 3-10. These large aggregates should be generated through the intermolecular aggregation triggered by the dehydration from the 2-(2-methoxyethoxy)ethoxy side-chain. Moreover, the D values were determined at the 2nd- $T_{\max}$ s for C₆-PMeEO₃IC₂₀ and C₈-PMeEO₃IC₂₀ to investigate the endothermic phenomenon above the phase transition temperature. Monomodal peaks are observed as the D values of 518 nm for C₆-PMeEO₃IC₂₀ and 626 nm for C₈-PMeEO₃IC₂₀, as shown in Figure 3-11, which are higher than those of the 1st- $T_{\max}$ s. This result suggested that

C_6 -PMeEO₃IC₂₀ and C_8 -PMeEO₃IC₂₀ had an additional aggregation behavior above the T_{cp} . This aggregation phenomenon is one of the characteristics for C_m -PMeEO₃IC, which needs to be clarified in detail in the near future.

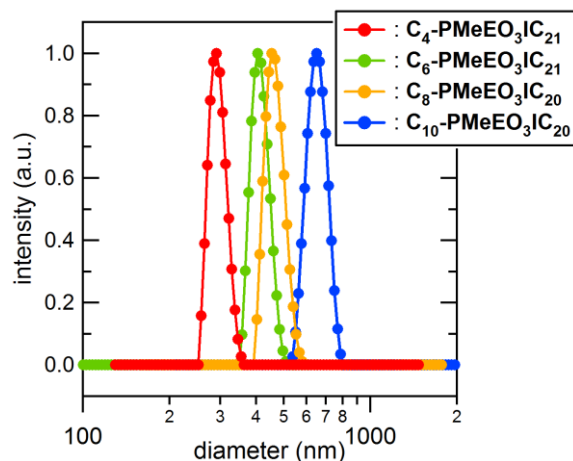


Figure 3-10. Hydrodynamic diameter distributions measured by DLS for C_4 -PMeEO₃IC₂₁, C_6 -PMeEO₃IC₂₁, C_8 -PMeEO₃IC₂₀, and C_{10} -PMeEO₃IC₂₀ in water at the T_{cp} s of 82, 75, 65, and 64 °C, respectively.

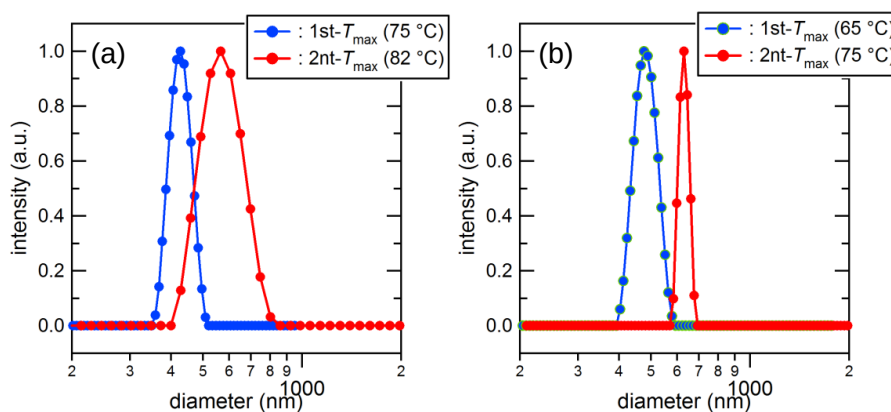


Figure 3-11. Hydrodynamic diameter distributions measured by DLS at the 1st- T_{max} and the 2nd- T_{max} for (a) C_6 -PMeEO₃IC₂₁ and (b) C_8 -PMeEO₃IC₂₀.

3.3 Conclusions

In conclusion, the phase transition behaviour was elucidated for the well-defined α -end-substituted polyisocyanates with an n -alkyl chain (C_m -PMeEO₃IC). The phase transition temperature was significantly changed, which decreased with the increasing n -alkyl chain length. An intermolecular aggregation was observed as the endothermic enthalpy change due to the phase transition, which was caused by the dehydration from the thermoresponsive 2-(2-methoxyethoxy)ethoxy side-chain unit. The aggregation behaviour of C_m -PMeEO₃IC below and above the phase transition temperature was significantly changed depending on the n -alkyl chain length. The effect of the polymer chain-end groups on the thermoresponsive property was typical, whereas the phase transition temperature was independent of the molecular weight of C_m -PMeEO₃IC, which apparently differed from the typical thermoresponsive polymers. The interesting thermoresponsive characteristics of C_m -PMeEO₃IC should be caused by the stiffness of the polymer backbone, *i.e.*, the rod-like polyisocyanate. Based on this demonstration, we should try to design, synthesize, and characterize other rod-like polymers as smart-materials.

3.4 Experimental Section

Materials. Tetrahydrofuran (THF) (purity >99.5%, water content <0.001%) was purchased from Kanto Chemicals Co., Inc., and distilled in the presence of sodium benzophenone ketyl under an Ar atmosphere. *n*-Butanol (TCI, Tokyo, Japan), *n*-hexanol (TCI, Tokyo, Japan), *n*-octanol (Kanto Chemicals Co., Inc.), and *n*-decanol (Wako Pure Chemical Industries, Ltd.) were distilled under an Ar atmosphere in the presence of CaH₂. (η⁵-Cyclopentadienyl)trichlorotitanium(IV) (CpTiCl₃, 99%) was purchased from Acros Organics Co., and used as received. 2,5,8-Trioxadecyl isocyanate (MeEO₃IC) was synthesized by the previously reported technique²⁹ and distilled in the presence of CaH₂ under an Ar atmosphere.

Instruments. The ¹H NMR spectrum was recorded using a JEOL ECS400 instrument. The polymerization was carried out in an MBRAUN stainless steel glovebox equipped with a gas purification system (molecular sieves and copper catalyst) and a dry argon atmosphere (H₂O, O₂ <1 ppm). The moisture and oxygen contents in the glovebox were monitored by an MB-MO-SE 1 and MB-OX-SE 1, respectively. The size exclusion chromatography (SEC) was performed at 40 °C in THF (flow rate, 1.0 mL min⁻¹) using a Jasco GPC-900 system equipped with set two Shodex KF-804L columns (linear, 8 × 300 mm²). The molecular weight distribution (M_w/M_n) of the polymer was calculated on the basis of a polystyrene calibration. The preparative SEC was performed in CHCl₃ (3.5 mL min⁻¹) at room temperature using a JAI LC-9201 equipped with a JAI JAIGEL-2H

column ($20 \times 600 \text{ mm}^2$; exclusion limit, 5×10^3) and JAI RI-50s refractive index detector. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) of the obtained polymers was performed using an Applied Biosystems Voyager-DE STR-H equipped with a 337 nm nitrogen laser (3 ns pulse width). Two hundred shots were accumulated for the spectra at a 25 kV acceleration voltage in the reflector mode and calibrated using insulin (TAKARA BIO, Inc.) as the internal standard. For the MALDI-TOF MS measurement, the polymer (5 g L^{-1}) in THF, a matrix (Dithranol, 50 g L^{-1}) in THF, and a cationizing agent (potassium trifluoroacetate, 25 g L^{-1}) in THF were mixed in the ratio of the polymer/matrix/cationizing agent of 100 μL /50 μL /100 μL , then 2 μL of the mixed solution was deposited on the sample holder. The turbidimetry analysis was performed using a Jasco V-550 spectrophotometer equipped with an EYELA NCB-1200 temperature controller. For the turbidity measurement, the sample was dissolved in deionized water and then the solution degassed at room temperature for 10 min. The differential scanning calorimetry (DSC) measurement was carried out on a Micro-DSCVII from SETRAM. The volume of the sample solution was 500 μL . The reference cell was added 500 μL with deionized water. The sample solution with a concentration of 30 g L^{-1} was degassed at room temperature for 10 min. Thermogram was measured with $1.0 \text{ }^\circ\text{C min}^{-1}$ heating rate. The dynamic light scattering (DLS) measurement was performed using an Otsuka Electronics FDLS-3000 light scattering spectrophotometer equipped with a solid state laser ($\lambda = 532 \text{ nm}$, $\theta = 90^\circ$). Samples were filtered using 0.20 μm PTFE membrane filter to remove any dust. The obtained data were analysed using the CONTIN program.

General procedure for the synthesis of α -end-substituted water-soluble polyisocyanates with *n*-alkyl chains. CpTiCl₃ was added to a Schlenk flask, followed by addition of dry THF, and the mixture was stirred to achieve homogeneity. After an alcohol was introduced to the flask, the whole mixture was stirred at room temperature for several hours, and the solvent was then removed under vacuum. MeEO₃IC was added to the Schlenk flask, and the polymerization was carried out for 24–72 h according to the monomer-to-catalyst ratio at 10 °C. The polymerization was quenched by the addition of methanol, and a crude product was purified by preparative size exclusion chromatography in chloroform to remove catalyst residues, a slight amount of the monomer, and by-products to afford a C_m-PMeEO₃IC as a soft solid material.

Synthesis of poly(2,5,8-trioxadecyl isocyanate) with butyl end group (C₄-PMeEO₃IC₂₁). Yield. 62.4 %. $M_{n,NMR} = 4030 \text{ g mol}^{-1}$. $M_w/M_n = 1.11$. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.16 (br, 316H, –COOCH₂–, –NCH₂–, –OCH₂– and –OCH₃), 1.66 (m, 2H, –CH₂CH₂CH₃), 1.39 (m, 2H, –CH₂CH₃), 0.935 (t, 3H, –CH₂CH₃).

Synthesis of poly(2,5,8-trioxadecyl isocyanate) with hexyl end group (C₆-PMeEO₃IC₂₁). Yield. 75.6 %. $M_{n,NMR} = 4090 \text{ g mol}^{-1}$. $M_w/M_n = 1.10$. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.16 (br, 318H, –CH₂(CH₂)₄–, –NCH₂–, –OCH₂– and –OCH₃), 1.67 (m, 2H, –CH₂(CH₂)₃–), 1.32 (br, 6H, –(CH₂)₃CH₃), 0.902 (t, 3H, –CH₂CH₃).

Synthesis of poly(2,5,8-trioxadecyl isocyanate) with octyl end group (C₈-PMeEO₃IC₂₀). Yield.

71.3 %. $M_{n,NMR} = 3850 \text{ g mol}^{-1}$. $M_w/M_n = 1.10$. ^1H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.16 (br, 297H, $-\text{CH}_2(\text{CH}_2)_6-$, $-\text{NCH}_2-$, $-\text{OCH}_2-$ and $-\text{OCH}_3$), 1.67 (m, 2H, $-\text{CH}_2(\text{CH}_2)_5-$), 1.28 (br, 10H, $-(\text{CH}_2)_5\text{CH}_3$), 0.889 (t, 3H, $-\text{CH}_2\text{CH}_3$).

Synthesis of poly(2,5,8-trioxadecyl isocyanate) with decyl end group (C₁₀-PMeEO₃IC₂₀). Yield.

61.8 %. $M_{n,NMR} = 3890 \text{ g mol}^{-1}$. $M_w/M_n = 1.12$. ^1H NMR (400 MHz, CDCl₃): δ (ppm) 4.50–3.16 (br, 298H, $-\text{CH}_2(\text{CH}_2)_8-$, $-\text{NCH}_2-$, $-\text{OCH}_2-$ and $-\text{OCH}_3$), 1.67 (m, 2H, $-\text{CH}_2(\text{CH}_2)_8-$), 1.41–1.19 (t, 16H, $-\text{CH}_2(\text{CH}_2)_8-$), 0.885 (t, 3H, $-\text{CH}_2\text{CH}_3$).

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Chapter 4

***Rod-Like Amphiphile of Diblock
Polyisocyanate Leading to Cylindrical
Micelle and Spherical Vesicle in Water***

4.1 Introduction

Diblock copolymers (BCPs), which contain two chemically different chains covalently connected to each other, are interesting macromolecular architectures because of their self-assembling property in the solution and bulk states.¹⁻⁴ Coil-coil, coil-rod, and rod-rod conformations of the BCP structures, which depend on the backbone stiffness of the block segments,⁵ can be varied by tuning the combination of two block segments. In addition, the hydrophobic and hydrophilic properties of the diblock segments significantly affect their self-assembling property. For instance, amphiphilic BCPs consisting of hydrophobic and hydrophilic segments are well-known as self-assembling materials in water, and self-assembled structures varied with the increasing hydrophobic segment in the order of spheres, cylinders, and vesicles.⁶⁻¹⁰ These structures are crucially affected by the hydrophobic/hydrophilic balance and the type of polymer backbones. Although there are many efforts regarding the synthesis and self-assembling characterization of coil-coil¹ and rod-coil^{2,5,11} types of amphiphilic BCPs, the amphiphilic rod-rod BCP is still restricted^{12,13} due to the limitation for the water-soluble rod polymers, such as polythiophene,¹⁴ polyfluorene,¹⁵ polyisocyanide,^{16,17} and polypeptide.¹⁸

Polyisocyanate, which is one of the rod-like polymers, is used for a wide range of application due to its unique properties, such as chain stiffness, dynamic helical conformation, chiral amplification, and liquid crystal properties.¹⁹⁻²² For instance, Mao et al.²³ and Hwang et al.²⁴ reported the unique phase separation morphology of poly(*n*-hexyl isocyanate)-*block*-polystyrene. In addition,

Balsara et al.²⁵ and Lee et al.²⁶ respectively reported the self-assembling properties of poly(*n*-hexyl isocyanate)-*block*-poly(ethylene glycol) and poly(*n*-hexyl isocyanate)-*block*-poly(2-vinylpyridine) in solution. Recently, we reported the synthesis of well-defined water-soluble polyisocyanates with an oligo(ethylene glycol) side chain as a new class of the thermoresponsive rod-like polymers.²⁷

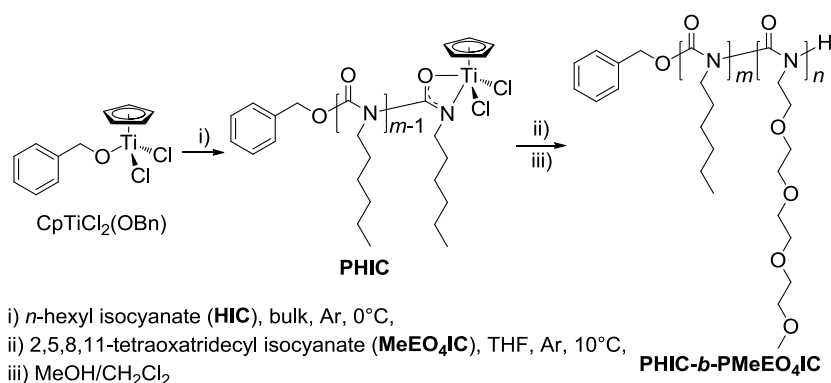
We now report the synthesis of an amphiphilic rod-rod type BCP of poly(*n*-hexyl isocyanate)-*block*-poly(2,5,8,11-tetraoxatridecyl isocyanate)s (PHIC-*b*-PMeEO₄ICs) with similar molecular weights and different ratios of the hydrophobic and hydrophilic segments, i.e., the PHIC/PMeEO₄IC segment, by coordination polymerization using the titanium catalyst, as shown in Scheme 1. The critical aggregation concentration (CAC) of PHIC-*b*-PMeEO₄IC was determined by a fluorescent method, and the hydrodynamic radius (R_h) and the radius of gyration (R_g) were estimated by the dynamic light scattering (DLS) and the static light scattering (SLS) measurements, respectively. In addition, a self-assembled structure of PHIC-*b*-PMeEO₄IC in water was discussed using the ρ parameter (R_g/R_h), and cylindrical micelle and spherical vesicle futures were confirmed by the transmission electron microscopy (TEM) images.

4.2 Results and Discussion

4.2.1 Synthesis of Amphiphilic Diblock Polyisocyanate

A diblock polyisocyanate, poly(*n*-hexyl isocyanate)-*block*-poly(2,5,8,11-tetraoxatridecyl isocyanate) (PHIC-*b*-PMeEO₄IC), was synthesized by the coordination polymerization of *n*-hexyl isocyanate (HIC) and 2,5,8,11-tetraoxatridecyl isocyanate (MeEO₄IC) using benzyloxy(η⁵-cyclopentadienyl)dichlorotitanium (IV) (CpTiCl₂(OBn)), as shown in Scheme 4-1.

Scheme 4-1. Synthesis of PHIC-*b*-PMeEO₄IC by the polymerization of HIC and MeEO₄IC using CpTiCl₂(OBn).



After the first polymerization of HIC at 0 °C was completed, which was confirmed by a size exclusion chromatography (SEC) measurement, MeEO₄IC as the second monomer and a slight amount of THF were added for the continuous polymerization at 10 °C. The polymerization was quenched by the addition of an excess amount of methanol/CH₂Cl₂, and the crude product was purified using preparative SEC to remove the catalyst residues, a small amount of residual MeEO₄IC,

and unknown byproducts to afford a polyisocyanate as a solid. For the product obtained from run 1, the proton signals due to the methyl and methylene groups of the PHIC segment were observed at 0.877, 1.29, and 1.61 ppm, and those due to the methoxy and oxyethylene groups of the PMeEO₄IC segment at 4.45–3.40 and 3.37 ppm, as shown in Figure 4-1. In addition, the minor signals at 5.19 and 7.37 ppm are assigned to the methylene and phenyl protons of the benzyloxy group as the initiating group, which was used as the internal standard to determine the number average degrees of polymerization (DPs) of 13 and 41 for the PHIC and PMeEO₄IC segments, respectively, *i.e.*, PHIC₁₃-*b*-PMeEO₄IC₄₁. The number average molecular weight ($M_{n,NMR}$) was 11300 g mol⁻¹, and the molecular weight distribution (M_w/M_n) estimated by the SEC measurement was 1.12 (Figure 4-2). In addition, two samples with different DPs of the PHIC and PMeEO₄IC segments, PHIC₂₂-*b*-PMeEO₄IC₃₆ (the $M_{n,NMR}$ of 11200 g mol⁻¹, the M_w/M_n of 1.14) and PHIC₃₁-*b*-PMeEO₄IC₃₁ (11300 g mol⁻¹, 1.13) were prepared (Figure 4-3 and 4-4, respectively), as listed in Table 4-1. These PHIC-*b*-PMeEO₄ICs were soluble in various solvents, such as *n*-hexane, chloroform, diethyl ether, tetrahydrofuran, acetone, dimethylformamide, methanol, and water.

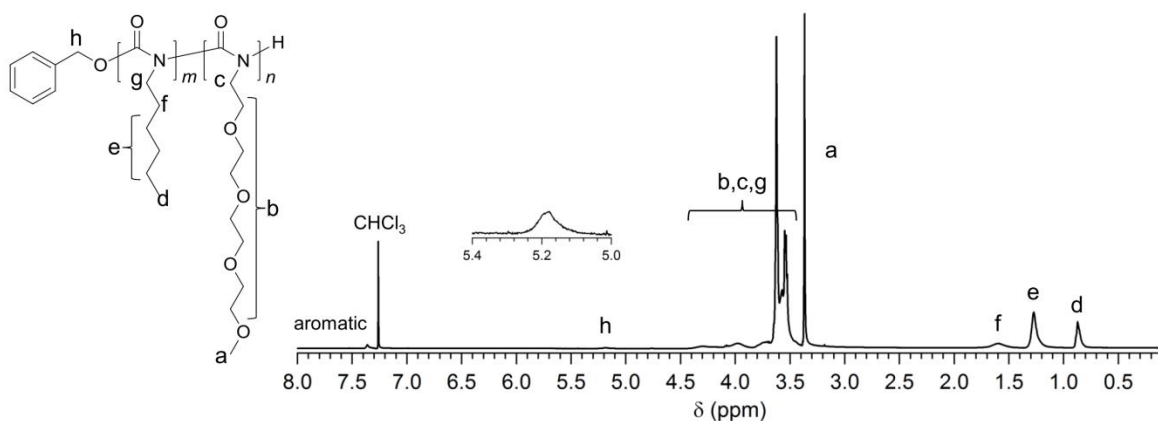


Figure 4-1. ^1H NMR spectrum of $\text{PHIC}_{13}\text{-}b\text{-PMeEO}_4\text{IC}_{41}$ in CDCl_3 , at ambient temperature.

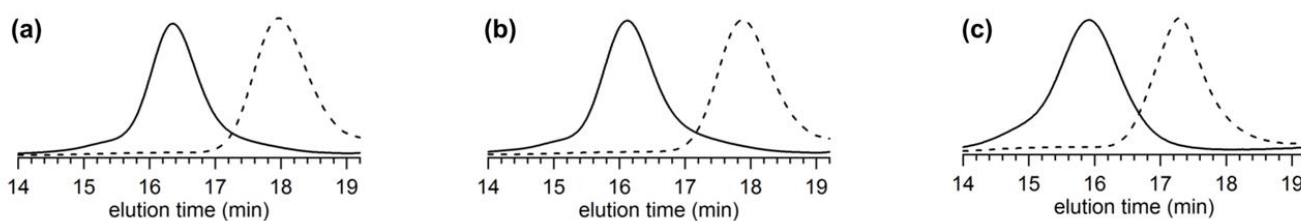


Figure 4-2. SEC traces of obtained block copolymer ($\text{PHIC-}b\text{-PMeEO}_4\text{IC}$) (solid line) and corresponding PHIC segment (dashed line) with (a) $\text{PHIC}_{13}\text{-}b\text{-PMeEO}_4\text{IC}_{41}$, (b) $\text{PHIC}_{22}\text{-}b\text{-PMeEO}_4\text{IC}_{36}$, and (c) $\text{PHIC}_{31}\text{-}b\text{-PMeEO}_4\text{IC}_{31}$ in THF.

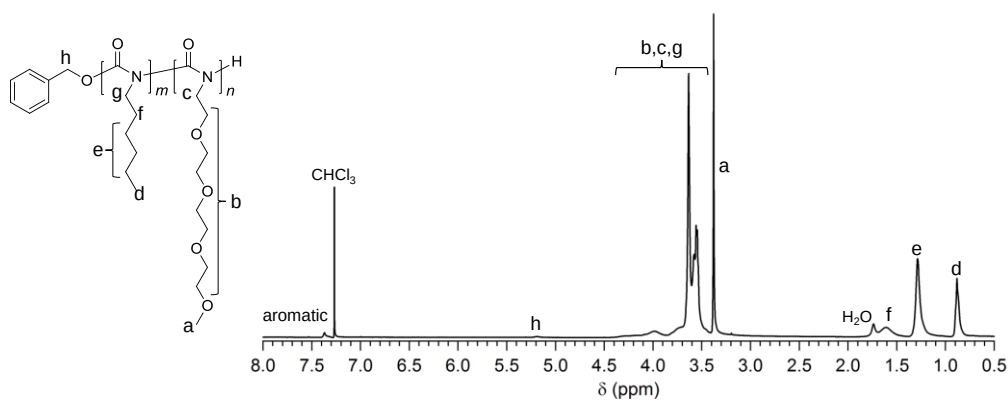


Figure 4-3. ^1H NMR spectrum of $\text{PHIC}_{22}\text{-}b\text{-PMeEO}_4\text{IC}_{36}$ in CDCl_3 at ambient temperature.

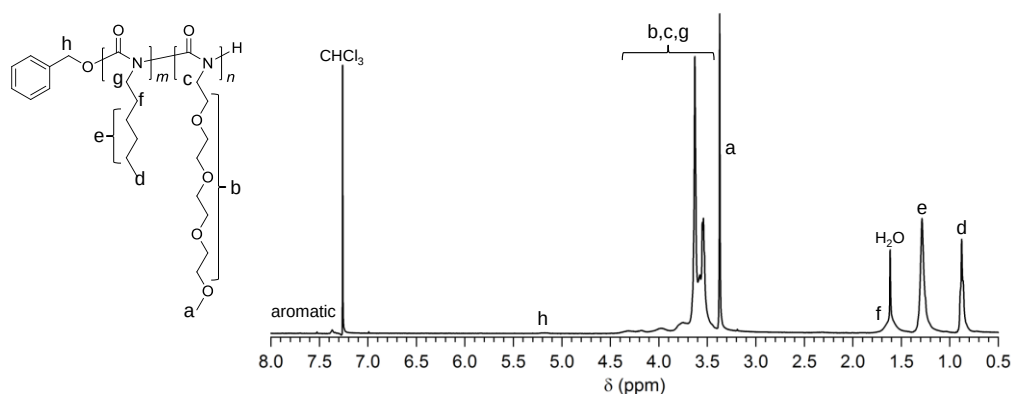


Figure 4-4. ^1H NMR spectrum of $\text{PHIC}_{31}\text{-}b\text{-PMeEO}_4\text{IC}_{31}$ in CDCl_3 at ambient temperature.

Table 4-1. Synthesis of $\text{PHIC}_{13}\text{-}b\text{-PMeEO}_4\text{IC}_{41}$, $\text{PHIC}_{22}\text{-}b\text{-PMeEO}_4\text{IC}_{36}$, and $\text{PHIC}_{31}\text{-}b\text{-PMeEO}_4\text{IC}_{31}$ ^a

Run	$[\text{HIC}]/[\text{MeEO}_4\text{IC}]/[\text{CpTiCl}_2(\text{OBn})]$	$M_{n,\text{NMR}}$ (g mol^{-1}) ^b	M_w/M_n ^c	sample ^d
1	9/46/1	11,200	1.12	PHIC₁₃-<i>b</i>-PMeEO₄IC₄₁
2	19/41/1	11,200	1.14	PHIC₂₂-<i>b</i>-PMeEO₄IC₃₆
3	28/36/1	11,300	1.13	PHIC₃₁-<i>b</i>-PMeEO₄IC₃₁

^a Detailed polymerization procedures were described in Supporting Information. ^b Determined from ^1H NMR spectra in CDCl_3 . ^c Determined by SEC in THF using polystyrene standards. ^d The number average degrees of polymerization determined from ^1H NMR spectra.

4.2.2 Self-Assembling Property of Amphiphilic Diblock Polyisocyanate in Water

The critical aggregation concentration (CAC) was determined by the titration experiment using 1-anilino-8-naphthalene sulfonate (ANS) as the fluorescence indicator (2.0×10^{-4} M) to estimate the suitable condition for the aggregating property of PHIC-*b*-PMeEO₄IC in water. The fluorescence spectra of ANS were measured using various PHIC-*b*-PMeEO₄IC concentrations (Figure 4-5). The CAC values decreased with the increasing hydrophobic segment of PHIC in the order of 0.135 g L^{-1} for PHIC₁₃-*b*-PMeEO₄IC₄₁, 0.0442 g L^{-1} for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 0.0114 g L^{-1} for PHIC₃₁-*b*-PMeEO₄IC₃₁.

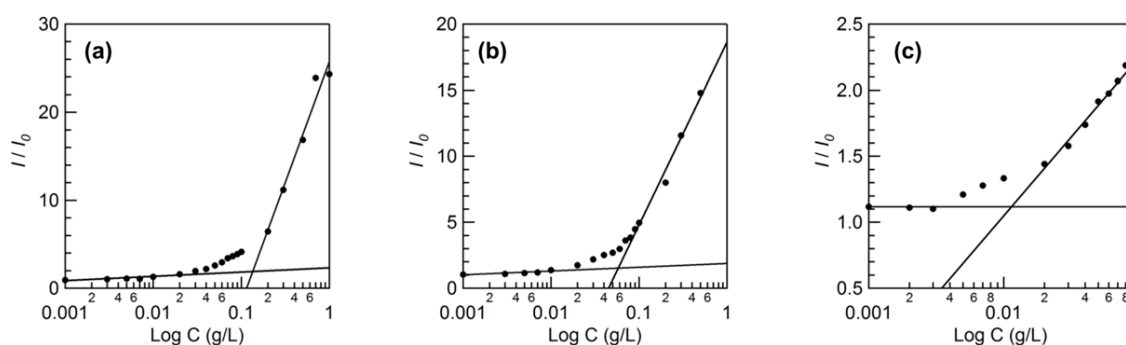


Figure 4-5. Fluorescence intensity of ANS versus concentration curves for (a) PHIC₁₃-*b*-PMeEO₄IC₄₁, (b) PHIC₂₂-*b*-PMeEO₄IC₃₆, and (c) PHIC₃₁-*b*-PMeEO₄IC₃₁.

In addition, the ^1H NMR spectrum of PHIC₁₃-*b*-PMeEO₄IC₄₁ above the CAC in D₂O was measured, as shown in Figure 4-6. Although the proton signals for the PMeEO₄IC segment were clearly observed in the range from 3.2 to 3.8 ppm, the intensity of the PHIC segment had

significantly decreased and broadened due to the restriction of the PHIC chain mobility, suggesting that PHIC-*b*-PMeEO₄IC aggregated with a PHIC inner part.²⁹ The aggregation behavior was also supported by the disappearance of the benzyloxy protons at the α -chain end group. These results clearly indicated the formation of the self-assembled structure consisting of the PHIC inner and PMeEO₄IC outer parts.

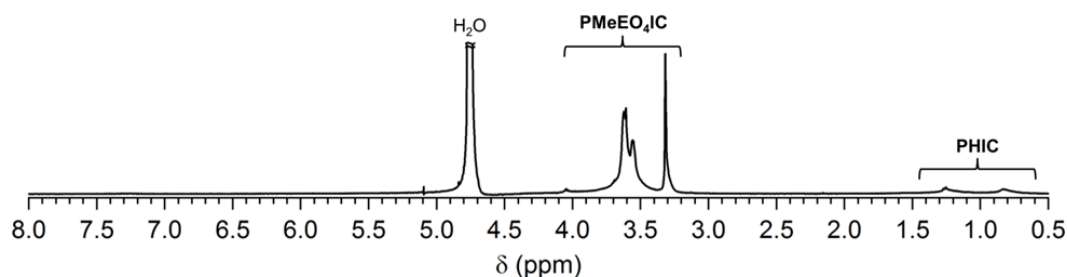


Figure 4-6. ¹H NMR spectrum of PHIC₁₃-*b*-PMeEO₄IC₄₁ in D₂O at ambient temperature [PHIC₁₃-*b*-PMeEO₄IC₄₁] = 1.0 g L⁻¹).

A dynamic light scattering (DLS) measurement was performed in order to investigate the hydrodynamic radius (R_h) and polydispersity for the aggregation of PHIC-*b*-PMeEO₄IC in water. The DLS plots of PHIC-*b*-PMeEO₄IC at $\theta = 90^\circ$ exhibited a monomodal shape with a polydispersity of ca. 0.2, as shown in Figure 4-7(a). In addition, the relaxation frequency (Γ) obtained from the DLS measurements at different angles is plotted as a function of the square of the scattering vector (q^2), as shown in Figure 3-7(b). The diffusion coefficient (D) values were estimated from the slopes of the Γ versus q^2 plots,

$$\left. \frac{\Gamma}{q^2} \right|_{q \rightarrow 0} = D$$

such as 4.72×10^{-6} , 3.48×10^{-6} , and $2.44 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ for PHIC₁₃-*b*-PMeEO₄IC₄₁ (0.2 g L⁻¹), PHIC₂₂-*b*-PMeEO₄IC₃₆ (0.1 g L⁻¹), and PHIC₃₁-*b*-PMeEO₄IC₃₁ (0.1 g L⁻¹), respectively. The hydrodynamic radius (R_h) is usually calculated from the Stokes-Einstein relation using the obtained D values,

$$R_h = \frac{k_B T}{6\pi\eta D}$$

where k_B is the Boltzmann constant, T is the temperature, and η is the viscosity of water. The R_h values were determined to be 51.9 nm for PHIC₁₃-*b*-PMeEO₄IC₄₁, 70.4 nm for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 101 nm for PHIC₃₁-*b*-PMeEO₄IC₃₁, indicating that the PHIC-*b*-PMeEO₄IC with a higher fraction of the PHIC segment formed a larger aggregate in water. In addition, the stability of the aggregated PHIC-*b*-PMeEO₄IC was estimated using the R_h values at various polymer concentrations, as shown in Figure 4-8. The R_h values are practically constant in measured concentration ranges, suggesting that each PHIC-*b*-PMeEO₄IC formed the very stable aggregate with a similar aggregation number (N_{agg}). These results lead to the conclusion that PHIC-*b*-PMeEO₄IC formed a self-assembled structure with the PHIC segment as a core and the PMeEO₄IC segment as a surface in water, and the self-assembled size increased with the increasing hydrophobic PHIC segment.

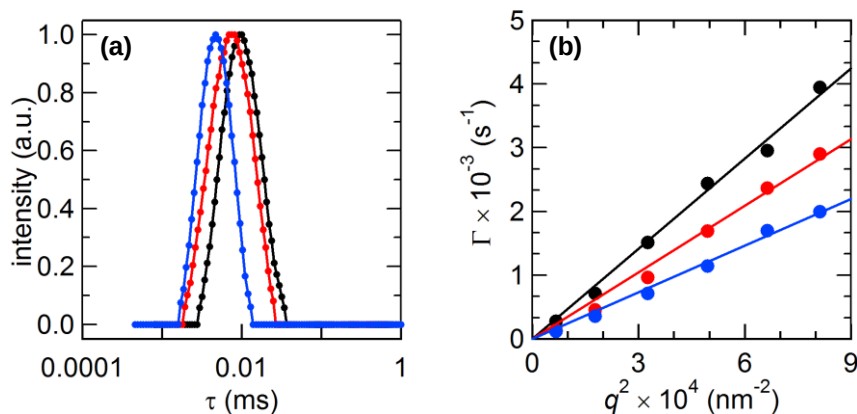


Figure 4-7. (a) DLS relaxation time distributions at scattering angle $\theta = 90^\circ$ and (b) relationship between relaxation frequency (Γ) and square of the scattering vector (q^2) at $\theta = 30\text{--}100^\circ$, for PHIC₁₃-*b*-PMeEO₄IC₄₁ (●), PHIC₂₂-*b*-PMeEO₄IC₃₆ (●), and PHIC₃₁-*b*-PMeEO₄IC₃₁ (●) in water at 25 °C.

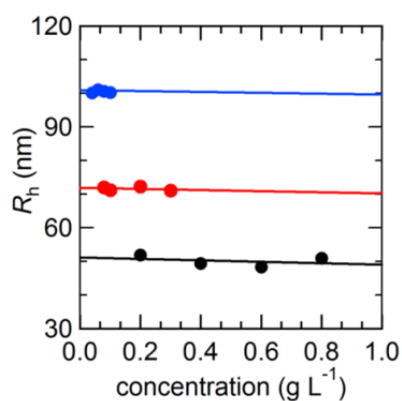


Figure 4-8. Plots of hydrodynamic radius (R_h) as a function of polymer concentration, for PHIC₁₃-*b*-PMeEO₄IC₄₁ (●), PHIC₂₂-*b*-PMeEO₄IC₃₆ (●), and PHIC₃₁-*b*-PMeEO₄IC₃₁ (●) in water at 25 °C ([PHIC₁₃-*b*-PMeEO₄IC₄₁] = 0.2–0.8 g L⁻¹, [PHIC₂₂-*b*-PMeEO₄IC₃₆] = 0.08–0.3 g L⁻¹, and [PHIC₃₁-*b*-PMeEO₄IC₃₁] = 0.02–0.08 g L⁻¹).

A static light scattering (SLS) measurement was carried out to obtain further information about the self-assembled PHIC-*b*-PMeEO₄IC structure, which could be estimated using the ρ parameter, *i.e.*, the ratio of R_g to R_h values (R_g/R_h). In general, for the ρ values of 0.7, 1, 1.7, and >2, the self-assembled structure in solution is a hard sphere, vesicle, cylinder, and rod structure, respectively.³⁰ The R_g value of the self-assembled PHIC-*b*-PMeEO₄IC was calculated from the $I(q)$ of the scattered intensity using the Guinier approximation as follows:

$$\ln I = \ln I_0 - \frac{1}{3} q^2 R_g^2$$

where I is the scattering intensity and I_0 is the scattering intensity at $q = 0$. Here, the R_g values are 84.4 nm for PHIC₁₃-*b*-PMeEO₄IC₄₁, 76.6 nm for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 110 nm for PHIC₃₁-*b*-PMeEO₄IC₃₁, estimated from the slope of the Guinier plots, *i.e.*, $\ln I$ versus q^2 , as shown in Figure 4-9. There is no relation between the R_g value and the fraction of the hydrophobic PHIC segment in comparison to that for the R_h value, meaning that different self-assembled structures were formed from the amphiphilic polyisocyanates with different PHIC/PMeEO₄IC ratios. The ρ values are 1.67 for PHIC₁₃-*b*-PMeEO₄IC₄₁, 1.09 for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 1.09 for PHIC₃₁-*b*-PMeEO₄IC₃₁, meaning that PHIC₁₃-*b*-PMeEO₄IC₄₁ self-assembled as a cylindrical micelle structure and PHIC₂₂-*b*-PMeEO₄IC₃₆ and PHIC₃₁-*b*-PMeEO₄IC₃₁ as spherical vesicle structures, as listed in Table 4-2. The volume fractions of the hydrophilic PMeEO₄IC segment ($f_{\text{PMeEO}_4\text{IC}}$) were calculated to be 0.85 for PHIC₁₃-*b*-PMeEO₄IC₄₁, 0.75 for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 0.65 for PHIC₃₁-*b*-PMeEO₄IC₃₁. In general, amphiphilic BCPs with a hydrophilic segment of > 0.5 are

expected to form spherical and cylindrical micelles according to the typical relation between the self-assembled structure and the f_{PEOIC} . Although PHIC₁₃-*b*-PMeEO₄IC₄₁ agreed with this relation, PHIC₂₂-*b*-PMeEO₄IC₃₆ and PHIC₃₁-*b*-PMeEO₄IC₃₁ formed vesicles, which should be caused by the rod structure of the polyisocyanates backbone.¹² In addition, the weight average molecular weight ($M_{\text{w,SLS}}$) of self-assembled PHIC-*b*-PMeEO₄IC were calculated from the SLS measurement. The aggregation number (N_{agg}) for the self-assembled PHIC-*b*-PMeEO₄IC was calculated from the ratio of $M_{\text{w,SLS}}$ and M_{w} of the unimer ($M_{\text{w,unimer}}$). The $M_{\text{w,unimer}}$ values were estimated from the $M_{\text{n,NMR}}$ and $M_{\text{w}}/M_{\text{n}}$ values as 12500 g mol⁻¹ for PHIC₁₃-*b*-PMeEO₄IC₄₁, 12800 g mol⁻¹ for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 12800 g mol⁻¹ for PHIC₃₁-*b*-PMeEO₄IC₃₁. The $M_{\text{w,SLS}}$ and N_{agg} values increased with the increasing hydrophobic segment of PHIC, such as 19200 kg mol⁻¹ and 1520 for PHIC₁₃-*b*-PMeEO₄IC₄₁, 28200 kg mol⁻¹ and 2200 for PHIC₂₂-*b*-PMeEO₄IC₃₆, and 62600 kg mol⁻¹ and 4890 for PHIC₃₁-*b*-PMeEO₄IC₃₁, respectively.

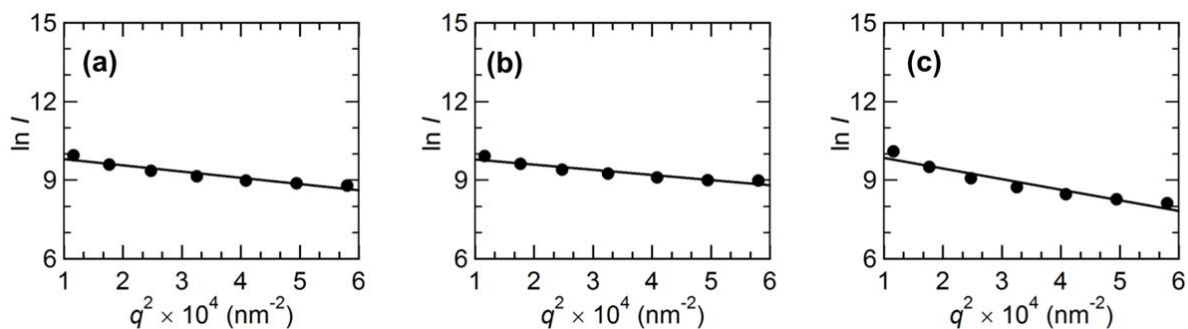


Figure 4-9. Guinier plots calculated from the static light scattering intensity for (a) PHIC₁₃-*b*-PMeEO₄IC₄₁ ($c = 0.2 \text{ g L}^{-1}$), (b) PHIC₂₂-*b*-PMeEO₄IC₃₆ ($c = 0.2 \text{ g L}^{-1}$), and (c) PHIC₃₁-*b*-PMeEO₄IC₃₁ ($c = 0.08 \text{ g L}^{-1}$) in water at scattering angles between 40° and 100°.

Table 4-2. Self-assembling properties of the PHIC-*b*-PMeEO₄ICs in water

Polymer	$f_{\text{PMeEO}_4\text{IC}}^a$	$R_h \text{ (nm)}^b$	$R_g \text{ (nm)}^c$	ρ^d	Macromolecular architecture ^d
PHIC₁₃-<i>b</i>-PMeEO₄IC₄₁	0.85	51.9	84.4	1.63	cylindrical micelle
PHIC₂₂-<i>b</i>-PMeEO₄IC₃₆	0.75	70.4	76.6	1.09	spherical vesicle
PHIC₃₁-<i>b</i>-PMeEO₄IC₃₁	0.65	101	110	1.09	spherical vesicle

^a The volume fraction of the PEOIC segment was calculated from (M.W. of PMeEO₄IC) / (M.W. of PHIC-*b*-PMeEO₄IC). ^b Determined from DLS measurement. ^c Determined from SLS measurement. ^d Calculated from (R_g/R_h) . ^d Observed by TEM measurement.

The self-assembled PHIC-*b*-PMeEO₄IC structure is directly confirmed using transmission electron microscope (TEM) measurement, as shown in Figure 4-10. A cylinder-like micelle structure is observed for PHIC₁₃-*b*-PMeEO₄IC₄₁ with a length of *ca.* 404 nm and a width of *ca.* 45 nm. On the other hand, spherical vesicles are observed with a diameter of *ca.* 163 nm for PHIC₂₂-*b*-PMeEO₄IC₃₆

and *ca.* 226 nm for PHIC₃₁-*b*-PMeEO₄IC₃₁, which agreed with the R_g values obtained from the SLS measurements. In addition, the TEM images fairly agreed with the self-assembled structures expected from the ρ values.

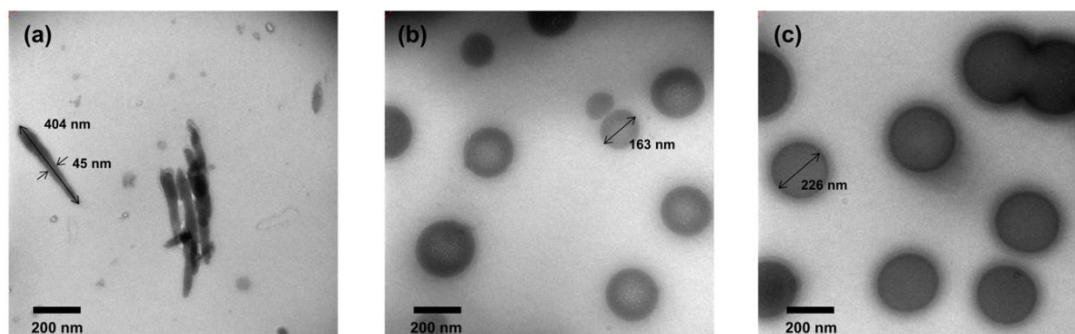


Figure 4-10. TEM images of assembled PHIC-*b*-PMeEO₄IC formed from (a) PHIC₁₃-*b*-PMeEO₄IC₄₁ ($c = 0.2 \text{ g L}^{-1}$), (b) PHIC₂₂-*b*-PMeEO₄IC₃₆ ($c = 0.1 \text{ g L}^{-1}$), and (c) PHIC₃₁-*b*-PMeEO₄IC₃₁ ($c = 0.08 \text{ g L}^{-1}$).

4.3 Conclusions

In conclusion, the self-assembling property of novel amphiphilic rod-rod diblock polyisocyanates has been demonstrated. The hydrodynamic radius (R_h) increased with the increasing fraction of the hydrophobic PHIC segment, whereas the radius of gyration (R_g) exhibited a different relation. The difference between the R_h and R_g values meant the formation of different self-assembled structures from PHIC-*b*-PMeEO₄IC in water. The ρ parameter (R_g/R_h) strongly suggested that the self-assembled structures were cylindrical micelle for PHIC₁₃-*b*-PMeEO₄IC₄₁ and vesicle for PHIC₂₂-*b*-PMeEO₄IC₃₆ and PHIC₃₁-*b*-PMeEO₄IC₃₁, which should be one of the characteristics for the rod-rod polyisocyanate amphiphile. We are focusing on the study of the design, synthesis, and self-assembling structure for amphiphilic BCPs based of rod polyisocyanates from the viewpoint of self-assembly science.

4.4 Experimental Section

Materials. Tetrahydrofuran (THF) for the polymerization was purchased from Kanto Chemicals Co., Inc., and distilled in the presence of sodium benzophenone ketyl under an Ar atmosphere. Benzyl alcohol was purchased from Kanto Chemicals Co., Inc., and distilled in the presence of CaH₂ under an Ar atmosphere. 1-Anilino-8-naphthalene sulfonate (ANS) was purchased from Wako Pure Chemical Industries, Ltd., and used without further purification. *n*-Hexyl isocyanate (**HIC**) was purchased from Tokyo Kasei Kogyo Co., Ltd., and distilled in the presence of CaH₂ under an Ar atmosphere. Dichloromethane (CH₂Cl₂) and methanol (MeOH) for the termination reaction were purchased from Kanto Chemicals Co., Inc., and used as received. (η⁵-Cyclopentadienyl)trichlorotitanium(IV) (CpTiCl₃, 99%) was purchased from Acros Organics Co., and used as received. The synthesis of 2,5,8,11-tetraoxadtriacyl isocyanate (MeEO₄IC) used a previously reported technique.³¹

Instruments. The ¹H NMR spectra were recorded using a JEOL ECS400 instruments. The polymerization was carried out in an MBRAUN stainless steel glovebox equipped with a gas purification system (molecular sieves and copper catalyst) and a dry argon atmosphere (H₂O, O₂ < 1 ppm). The moisture and oxygen contents in the glovebox were monitored by an MB-MO-SE1 and an MB-OX-SE 1, respectively. Size exclusion chromatography (SEC) was performed at 40 °C in THF (1.0 mL min⁻¹) using a Jasco GPC-900 system equipped with a set of Waters Ultrastaygel 7mm

columns (linear, $7.8 \times 300 \text{ mm}^2$) and two Shodex KF-804L columns (linear, $8 \times 300 \text{ mm}^2$). The molecular weight distribution (M_w/M_n) of the polymers was calculated on the basis of a polystyrene calibration. The preparative SEC was performed in CHCl_3 (3.5 mL min^{-1}) at room temperature using a JAI LC-9201 equipped with a Shodex GPC K-2004 column ($20 \times 300 \text{ mm}^2$; exclusion limit, 400,000) and JAI RI-50s refractive index detector. The critical aggregation concentration (CAC) of PHIC-*b*-PMeEO₄IC was determined using ANS as a fluorescent probe. The fluorescence emission spectra of ANS were obtained at various polymer concentrations. The ANS concentration remained constant at $2.0 \times 10^{-4} \text{ M}$. The fluorescence emission spectra (excitation at 355 nm) were recorded by a FP-5500 spectrofluorometer. The value of dn/dc was determined using an Otsuka Electronics Photal DRM-1021 differential refractometer at 632.8 nm.

General procedure of synthesis of diblock copolymer (PHIC-*b*-PMeEO₄IC). To a solution of (η^5 -cyclopentadienyl)titanium(IV) trichloride (CpTiCl_3) (20.5 mg, 93.3 μmol) in dry THF (467 μL) in a Schlenk flask, benzyl alcohol (10.1 mg, 93.3 μmol) was added with stirring at room temperature for several hours, then the solvent was removed under vacuum. *n*-Hexyl isocyanate (HIC) (107 mg, 122 μL , 0.839 mmol) was added and stirred for 3 h at 0 °C. After consuming the monomer, MeEO₄IC (1.00 g, 917 μL , 4.29 mmol) was added as the second monomer with a small amount of THF. After 62.5 h at 10 °C, the polymerization was quenched by the addition of methanol/ CH_2Cl_2 . The crude product was purified by reprecipitation and then preparative size exclusion

chromatography (SEC) to remove any catalyst residues, residual monomer, and byproducts to afford PHIC₁₃-*b*-PMeEO₄IC₄₁ as a solid material. Yield: 36.9 %, dn/dc (water): 0.135 mL g⁻¹, $M_{n,PHIC}$: 1650 g mol⁻¹, $M_{n,PMeEO4IC}$: 9,560 g mol⁻¹, $M_{n,PHIC-b-PMeEO4IC}$: 11200 g mol⁻¹, ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.37 (br, 5H, C₆H₅CH₂O-), 5.19 (s, 2H, C₆H₅CH₂O-), 4.45–3.16 (br, 64H, -NCH₂-, -OCH₂- and -OCH₃), 1.60 (br, 26H, -CH₂CH₂(CH₂)₃CH₃), 1.28 (br, 78H, -(CH₂)₂(CH₂)₃CH₃), 0.881 (45H, -(CH₂)₅CH₃).

PHIC₂₂-*b*-PMeEO₄IC₃₆: Yield, 32.7 %; $M_{n,PHIC}$, 2840 g mol⁻¹; $M_{n,PMeEO4IC}$, 8400 g mol⁻¹; $M_{n,PHIC-b-PMeEO4IC}$, 11200 g mol⁻¹.

PHIC₃₁-*b*-PMeEO₄IC₃₁: Yield, 28.5 %; $M_{n,PHIC}$, 3970 g mol⁻¹; $M_{n,PMeEO4IC}$, 7280 g mol⁻¹; $M_{n,PHIC-b-PMeEO4IC}$, 11300 g mol⁻¹.

Dynamic light scattering (DLS) measurement.

The dynamic light scattering (DLS) measurement was performed using an Otsuka Electronics FDLS-3000 light scattering spectrophotometer equipped with a solid state laser (λ = 532 nm). Samples were filtered using a 0.45 μ m PTFE membrane filter to remove any dust. The obtained data were analyzed by the CONTIN program. The diffusion coefficient (D) of the PHIC-*b*-PMeEO₄IC

assembly was calculated from the relation between the relaxation frequency (Γ) and the square of the scattering vector (q^2).

$$q^2 = \left(\frac{4\pi n}{\lambda}\right)^2 \sin^2\left(\frac{\theta}{2}\right)$$

where λ is the light wavelength, θ is the scattering angle, and n is the refractive index of the solvent at 25 °C. The hydrodynamic radius (R_h) was determined from the Stokes-Einstein relation as a typical procedure using the obtained D value.

Static light scattering (SLS) measurement.

The static light scattering (SLS) measurement was performed at 25 °C using an Otsuka Electronics Phottal DLS-7000 light scattering spectrometer. The sample solutions were filtered using a 0.45 μm pore size membrane filter at the rate of 0.5 mL min⁻¹. A He-Ne laser ($\lambda = 632.8$ nm) was used as the light source. Toluene was used for the calibration of the instrument. The absolute weight average molecular weights ($M_{w,\text{SLS}}$) of the self-assembled PHIC-*b*-PMeEO₄IC were determined using the Zimm plot³²

$$\lim_{\substack{c \rightarrow 0 \\ \theta \rightarrow 0}} \frac{Kc}{R(\theta)} = \frac{1}{M_w}$$

where c is the polymer concentration, $R(\theta)$ is the Rayleigh ratio at the scattering angle θ , and K is the optical constant. The optical constant is

$$K = \frac{4\pi^2 n^2 (dn/dc)^2}{\lambda^4 N_A}$$

where N_A is Avogadro's number, λ is the light wavelength, n is the refractive index of the solvent, and dn/dc is the refractive index increment.

Transmission electron microscope (TEM) measurement.

The transmission electron microscopy (TEM) images were obtained using a JEM-2000FX (JEOL) operating at an 80 kV acceleration voltage. The sample solutions were filtered using a 0.45 μm PTFE membrane filter and cast on a carbon-coated copper grid without any staining and air-drying.

4.5 References and Notes

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Chapter 5

Conclusions

In this thesis, the author describes the molecular design and the precise synthesis of water-soluble rod-like polyisocyanates with the thermoresponsive property in aqueous solution. The thermal phase transition behavior of the polyisocyanates with an oligo(ethylene glycol) unit as the side-chain, which depends on the side-chain structure, chain-end structure, solution concentration, and molecular weight, was investigated for the rod-like polyisocyanate. Moreover, the rod-like amphiphile of diblock polyisocyanates was successfully synthesized by a coordination polymerization method, and the relation between the hydrophobic/hydrophilic ratio and the self-assembled structure was then clearly elucidated. Therefore, we believe that this investigation provides useful insights into molecular design of the self-assembled materials which have the potential applications such as drug carrier, reactor, and sensor materials.

A summary of this thesis is as follows:

In chapter 2, we have successfully synthesized well-defined PICs conjugated with 2,5-dioxaoctyl, 2,5,8-trioxadecyl, 3,6,9-trioxaundecyl, and 2,5,8,11-tetraoxatridecyl groups as side chains by the living coordination polymerization using the half titanocene catalyst, *i.e.* *n*-butoxy(η^5 -cyclopentadienyl)di-chlorotitanium(IV). The aqueous solutions of PICs exhibited phase transition behaviors due to the intermolecular aggregation. The phase transition temperature decreased with the increasing molecular weight of the PICs, which is a typical property of

thermoreponsive polymers. On the contrary, as an interesting feature for the obtained PIC, the side-chain group in the water-soluble PICs, particularly its chain-end group, significantly affected the thermoresponsive property. To the best of our knowledge, the present water-soluble PIC is a novel type of thermoresponsive polymers. Because PIC is generally expected to have a rod-like structure through the increasing polymerization degree, this may allow for the development of novel smart materials having stimuli-responsive properties, such as a sensory material, due to their unique properties like a main-chain stiffness.

In chapter 3, the phase transition behavior was elucidated for the well-defined α -end-substituted polyisocyanates with an *n*-alkyl chain (C_m -PMeEO₃IC). The phase transition temperature was significantly changed, which decreased with the increasing *n*-alkyl chain length. The intermolecular aggregation was observed as an endothermic enthalpy change due to the phase transition, which was caused by dehydration from the thermoresponsive 2-(2-methoxyethoxy)ethoxy side-chain unit. The aggregation behavior of C_m -PMeEO₃IC below and above the phase transition temperature was significantly changed depending on the *n*-alkyl chain length. The effect of the polymer chain-end groups on the thermoresponsive property was usual, whereas the phase transition temperature was independent of the molecular weight of C_m -PMeEO₃IC, which apparently differed from the usual thermoresponsive polymers. The interesting thermoresponsive characteristics of C_m -PMeEO₃IC should be caused by the stiffness of the polymer backbone, *i.e.*, the rod-like polyisocyanate. On the

basis of this demonstration, we should try to design, synthesize, and characterize the other rod-like polymers as smart-materials.

In chapter 4, the self-assembling property of novel amphiphilic rod-rod diblock polyisocyanates has been demonstrated. The hydrodynamic radius (R_h) increased with the increasing fraction of the hydrophobic PHIC segment, whereas the radius of gyration (R_g) exhibited a different relation. The difference between the R_h and R_g values meant the formation of different self-assembled structures from PHIC-*b*-PEOIC in water. The ρ parameter (R_g/R_h) strongly suggested that the self-assembled structures were cylindrical micelle for PHIC₁₃-*b*-PEOIC₄₁ and vesicle for PHIC₂₂-*b*-PEOIC₃₆ and PHIC₃₁-*b*-PEOIC₃₁, which should be one of the characteristics for the rod-rod polyisocyanate amphiphile. We are focusing on the study of the design, synthesis, and self-assembling structure for amphiphilic BCPs based on rod polyisocyanates from the viewpoint of self-assembly science.