博士論文

Study of polyrotaxane synthesized via reversible addition-fragmentation chain transfer polymerization

（可逆的付加開裂連鎖移動重合を用いたポリロタキサンの研究）

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Chapter 1 Introduction

1.1 Rotaxane

Rotaxane is one of the supramolecule that composed of liner molecule threaded by cyclic molecule. Supramolecule including catenane, daisy and rotaxane have drawn lots of attention for novel properties originate from structural behavior. In rotaxane, there is no chemical bonding between cyclic molecule and linear main chain. Cyclic molecule was confined in the linear molecule from the steric hinderance on the chain ends. As a result, sliding behavior became possible for the cyclic molecule on the linear molecule. Common preparation method of rotaxane including three methods, threading, slipping, and clipping as shown in Fig. 1.1. This concept has developed into many applications and rewarded a Nobel chemical price for the outstanding work of three researchers as the name of molecular machine.

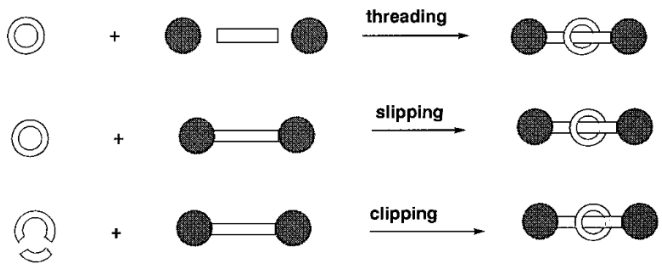


Fig. 1.1 Preparation of rotaxane.[1]

Stoddart et al. prepared [2]rotaxane composed of a polyether chain intercepted by a centrally-located π-electron rich hydroquinol ring and terminated by admantoyl groups and a tetracationic cyclophane constructed by two π-electron deficient bipyridinium units linked by paraphenylenedimethyl residues using the clipping method that reconnects the ring after the parts were electronically attracted to the center of dumbbell shape molecule. [2] With the stimulation of the pH or the light, the cyclic molecule changes the position based on the corresponding affinity as shown in Fig. 1.2. The molecular shuttle or molecular switch is one

of the frontier technologies with a great potential for many applications.

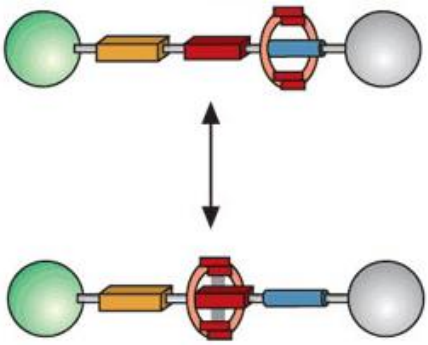


Fig. 1.2 Scheme of the molecular switch.[3]

For the cyclic molecules in a rotaxane preparation, cyclodextrin is one the common candidates. A cyclodextrin (CD) is composed of cellulose units that were enzymatically modified into a cyclic molecule.[4] Most commonly used CD are alpha CD (αCD),beta CD (βCD) and gamma CD (γCD) corresponding to the number of repeating units of cellulose units for 6, 7, and 8 respectively. In general, a cyclodextrin is hydrophilic on the outside and hydrophobic in the inside with the structure as shown in Fig. 1.3.[5] Because of this property, CD has been used as a host to encapsulate hydrophobic drugs in water.[6] This guest-host behavior of CD has been investigated for the drug delivery control researches. The sizes of the cavity for different type of CD are shown in Table 1.1. With different cavity sizes, cyclodextrins are applied as a carrier for various types of molecules.

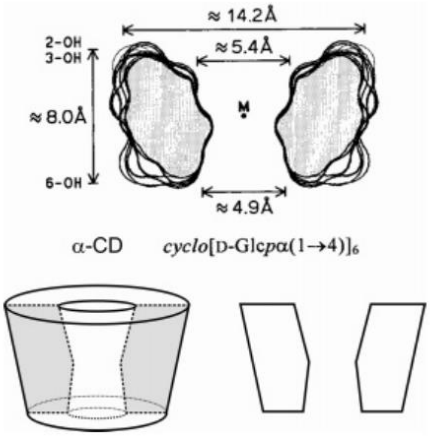


Fig. 1.3 Structure of alpha cyclodextrin.[5]

Table 1.1 Cavity sizes (d_{min}) and intersection sizes (A_{min}) of cyclodextrins.[5]

CD	d_{min}/Å	A_{min}/Å^2
α-CD	4.4	15
β-CD	5.8	26
γ-CD	7.4	43

1.2 Polyrotaxane

Notation of a rotaxane is known as a bracket in front of the rotaxane. For instance, [2] rotaxane represents that there are two components in the rotaxane (1 ring/1 axis). As another example of [3]rotaxane, there are three components in the rotaxane (2 ring/ 1 axis or 1 ring/ 2 axis). For the case that many cyclic molecules were threaded on the main chain polymer, this supramolecule is called polyrotaxane for the structure shown in Fig. 1.4. Harada et al reported inclusion complex between polyethylene glycol (PEG) and αCD as a pseudo polyrotaxane.[7] When PEG and αCD were mixed in water, linear PEG was gradually threading through cyclodextrin spontaneously because of the affinity between PEG and αCD. As a result, the precipitation occurred after a few days as inclusion complexes of ring and linear molecules coagulated. In a pseudo polyrotaxane, there is no end cappers on the chain ends. When a pseudo polyrotaxane dissolved in a good solvent for both component (DMSO, for instance), ring molecules are dethreading out of the main chain polymer. In 2001, polyrotaxane were prepared with an end capping on the polymer ends in the work of Okumura and Ito.[8] The polyrotaxane gel prepared from the polyrotaxane showed outstanding swelling behavior that able to absorb 400 times of its original weight. In the preparation scheme of polyrotaxane shown in Fig. 1.5, end capping on the chain ends is needed to prevent cyclic molecules from dethreading. As a result, ring molecules can slide along the linear main chain without detach from the supra molecular structure.

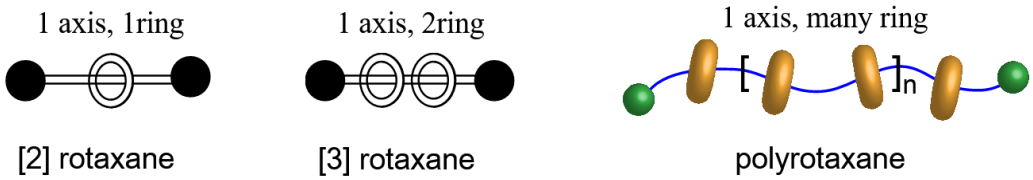


Fig. 1.4 Nomenclature of rotaxane to polyrotaxane

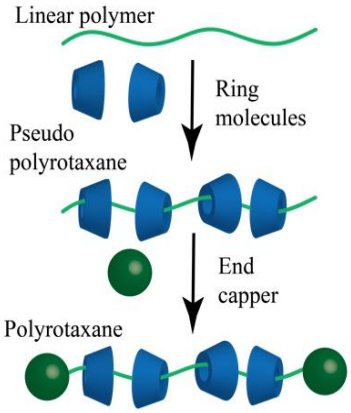


Fig. 1.5 preparation of polyrotaxane

As for the pseudo polyrotaxane, many polymer-cyclodextrin combination were discovered. In the report of Wenz, polyrotaxane of a linear polyurethane and cyclodextrin was prepared from a polycondensation with complexes of amino acids and cyclodextrins as shown in Fig. 1.6. For another instance, polyester was complexed with cyclodextrins in hot water and precipitated when cooling to obtain pseudo polyrotaxane in Harada's report.[9] In these studies, many approaches to thread cyclodextrins on to the linear chain were applied. Such as mixing solvent,[10] temperature control.[11] As a result, many types of the pseudo polyrotaxane were prepared.

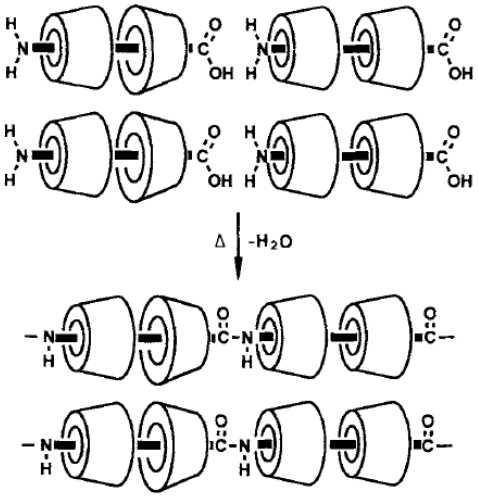


Fig. 1.6 Preparation of polyrotaxane composed of polyurethane.[12]

In the case of polyrotaxane, the most common polyrotaxane is composed of polyethylene glycol (PEG) and αCD as reported in Ito's group.[8] The procedure of this type of polyrotaxane is well developed to be commercially available nowadays. In the end capping process, solvent replacement is needed for the modification of the chain ends into the end capper group. The solubility difference of the cyclodextrins and the linear main chains in the solvent may cause massive dethreading that failed to prepare polyrotaxane before end capping. In Kato's report,[13] alternative types of the polyrotaxane composed of a polybutadiene or a polydimethylsiloxane were successfully prepared in an one-pot method to prevent the dethreading in the solvent change. The main idea of this research is using the cyclodextrins as the sliding components on the main chain and end cappers on chain ends of linear polymer at the same time to reduce the steps of preparation. The scheme is shown in Fig. 1.7.

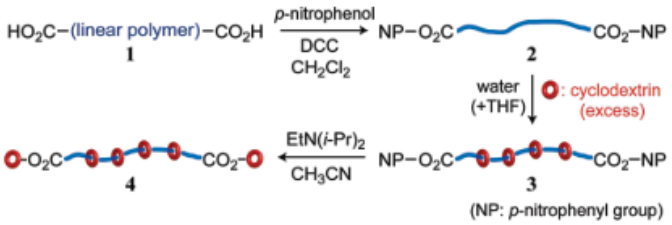


Fig. 1.7 Preparation of polyrotaxane using cyclodextrins as ring molecules and end cappers. [13]

Polyrotaxane has been focused increasingly on many research fields for the recent discoveries of the possible applications. For a polyrotaxane end capped with biodegradable functional groups, the drug delivery in the cell via a biochemical process is realized. In the delivery system of cell, when the end groups of polyrotaxane works as a key to the acceptors on the mebrane, the component covered by cyclodextrin can be carried into the cell. As the end groups disociated during the process, the guest molecules were released into the cell as shown in Fig. 1.8. For one alternative application, empty cyclodextrins can work as carriers to bring other molecules inside the cell out of the system and lowering the concentration for target component. Because of these functions, a polyrotaxane has many potential for the medical applications. Originated from the special strucutre of polyrotaxnae, the drug or gene delivery in the biochemical consideration are under various attention and research ongoing.[14]

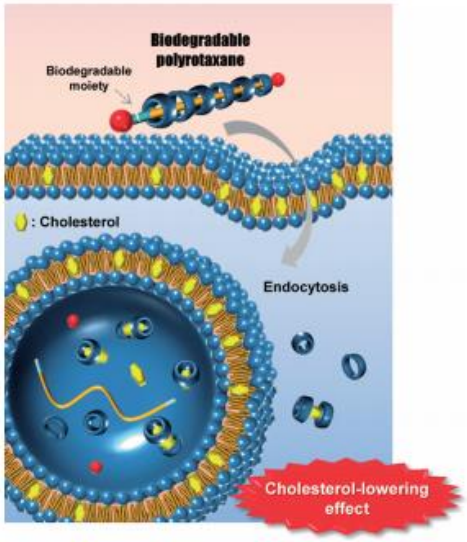


Fig. 1.8 Scheme of a polyrotaxane interaction with a cell for drug delivery application.[15]

If the ring molecules on the polyrotaxane were connected via crosslinking or hydrogen bonding, slide-ring is prepared as one of the most impactful application of polyrotaxane. The crosslinking points on the ring molecules can slide along the main chain polymer. As a result, the force can be released and dissipated through the process of the sliding behavior. This is

known as the pulley effect. Originated from this phenomena, slide-ring material can distribute the force equivalently in the material. The extra extensibility and resilience properties was observed from the gel and elastomer[16] prepared from polyrotaxane as shown in Fig. 1.9.

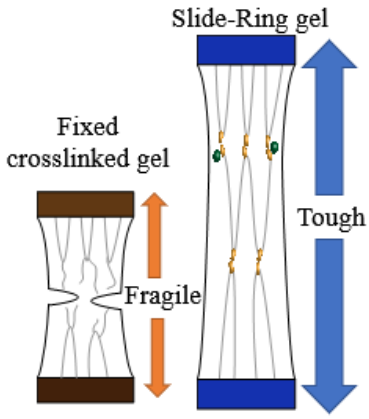


Fig. 1.9 Illustration of tough mechanical properties in the slide-ring gel compare to a fixed crosslinked gel.

For the polyrotaxane applied in the slide-ring gel, the coverage ratio plays an important role in the mechanical properties. In Jiang's report, slide-ring gel prepared from low coverage PR exhibited outstanding extensibility that up 1300% strain as shown in Fig. 1.10.[17] This considered that sliding distance is shorter for higher coverage polyrotaxane because of the hinderance between cyclodextrins on main chain polymer. On the other hand, the investigation about strain rate to the mechanical properties of slide-ring gel has found that pulley effect were not effective in the slide-ring material if movement of total polyrotaxane is much faster than sliding movement of cyclodextrin on the main chain.[18]

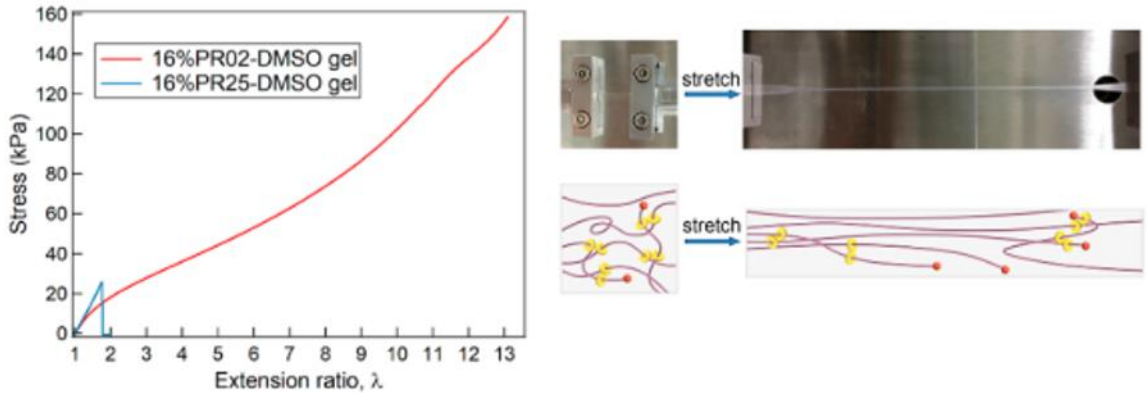


Fig. 1.10 (left) strain-stress curve of high and low coverage SPR (right) pictures of tensile tests.[17]

The idea of movable crosslinking points is available in other materials with a proper experimental design. In the report of Takata and Aoki, [19] a rotaxane crosslinker is proposed as a crosslinker with a movable point as shown in Fig. 1.11. The mechanical properties of a material can be enhanced by addition of rotaxane with small amount of 0.5% rotaxane crosslinker in the polymerization. With only a few of movable points in the material, the force dissipation become more equivalently distributed. As the result, more toughness and resilience were realized in traditional materials via introducing the sliding properties into the material.

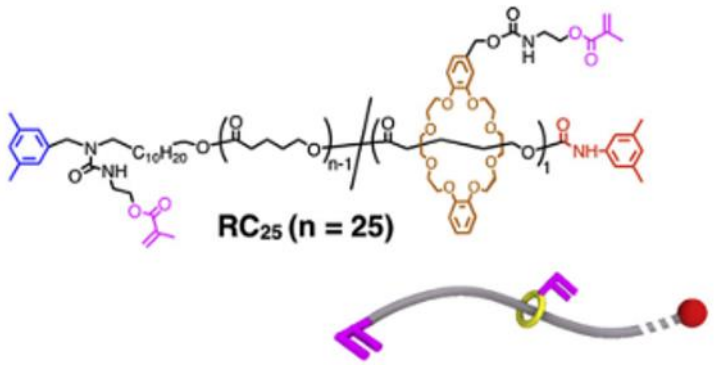


Fig. 1.11 Structure of a rotaxane crosslinker (RC).[19]

1.3 Reversible addition-fragmentation chain transfer radical polymerization

In this 20 year, there is a new energy poured into the polymerization technic researches as controlled polymerization developments. Known as living polymerization as well, the possibility to a better control of the polymerization and a molecular design from a synthetic approach has drawn many attentions in the field. There are two main features of a controlled/ living polymerization: (1) A well-controlled polymer with a narrow distribution of the molecular weight. (2) A resulting polymer is available for a further polymerization with other monomer as recognized as "living" polymer.[20] For polymers synthesized from this genre of process, block copolymer, end functionalized polymer, grafting polymer on the surface with desired nano layers, various of polymer design based on molecular level become possible as shown in Fig 1.12. IUPAC has announced a recommend nomenclature for this genre of polymer as reversible deactivation radical polymerization (RDRP) to avoid confusion for too many variation naming in the same research field.[21]

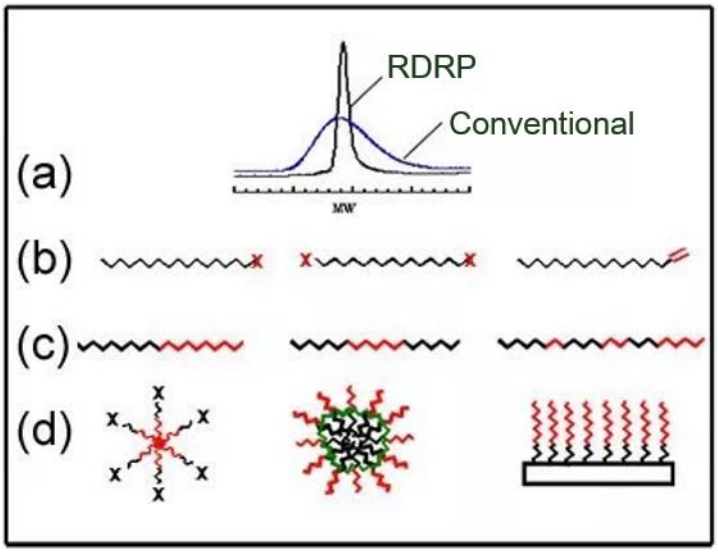


Fig 1.12 Possible molecular design from RDRP :(a) Mw control (b) End functionalization (c) Block copolymer (d) star/ micelle/ grafting copolymer

There are three main approach for RDRP developed so far as shown in Fig. 1.13. Dissociation-combination mechanism is protecting the radical in the process of radical polymerization using an electron acceptor. One of the examples is using 2,2,6,6-tetramethyl-1-piper-idinoxyl (TEMPO) for this mechanism.[22] This is one of the first mechanism proposed in RDRP. Polymer with narrow distribution was successfully synthesized with limited selection based on the affinity between TEMPO and reactive monomers. In the atom transfer mechanism, radicals on the propagating polymer chain is stabilized with transition metal complex. Meta stable complex of transition metal atom and radical prolonged the lifetime of radicals. As the result, polymerization with narrow distribution of molecular weight is realized as well.[23] In the case of a transitional metal complex, more types of polymer were able to be synthesized using RDRP. However, a metal involved process was not preferable for the application related to the human bodies or daily usages. The third mechanism is the degenerate transfer mechanism, also known as the reversible addition-fragmentation chain transfer (RAFT). In this mechanism, a chain transfer agent is applied into the conventional radical polymerization. The chain transfer reaction was considered as the side reaction to lower the molecular weight of resulting polymer. Nowadays this process has become one of the main ways to control polymerization using proper chain transfer agent that able to remain reactive after receiving the radical. [24]

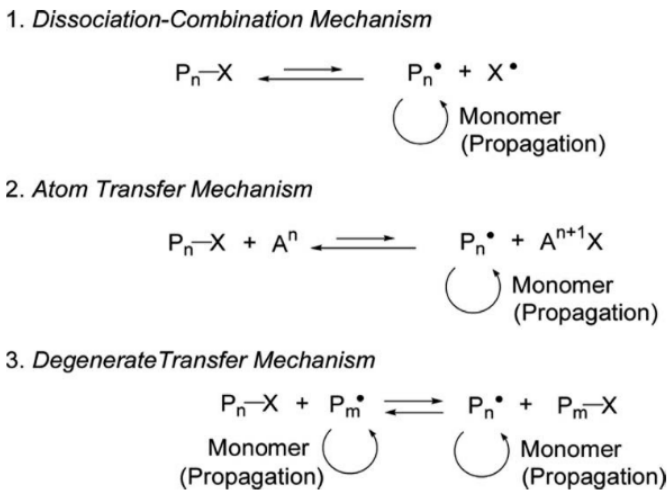


Fig. 1.13 Scheme of recent RDRP mechanisms.[25]

1.3.1 Mechanism of RAFT

The mechanism is shown as Fig. 1.14. the initiation followed conventional polymerization from initiator to produce the radicals. Then radicals reacted with chain transfer agent, and radicals were transfer to the leaving group of chain transfer. Polymerization propagates between the radical on the leaving group and monomer to be a propagating polymer chain. This is known that the radical returned to chain transfer agent and created new radical as a reversible addition-fragmentation process. The reactivity among chain transfer agent, monomer, and polymer chain controlled the processing of polymerization. As the propagating polymer chain only continuously reacted with chain transfer agent as losing the activity while chain growth, the polymerization is dormant. The resulting dormant polymer can be reinitiated again to react with another monomer to build up block copolymers.

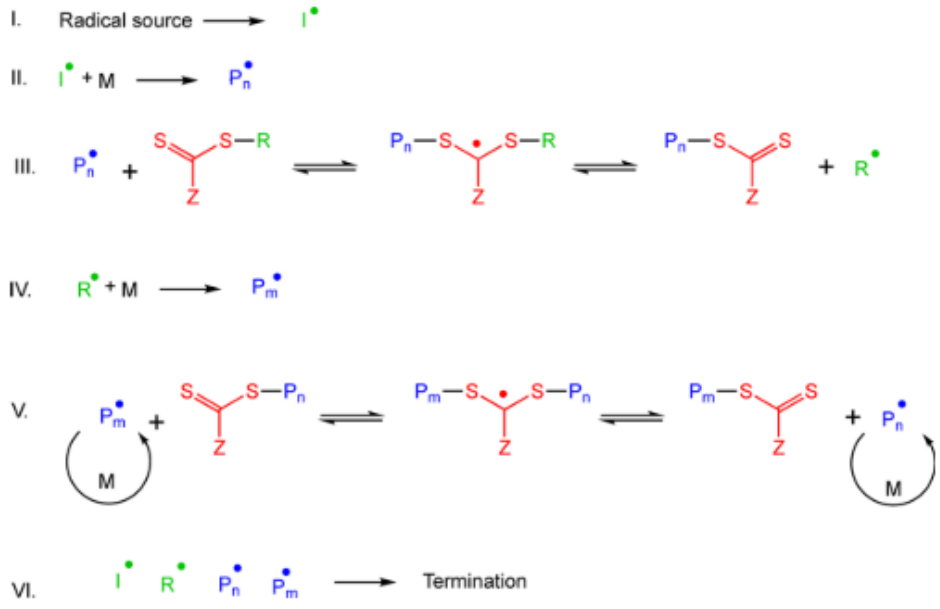


Fig. 1.14 Mechanism of RAFT.[20]

Determination of chain transfer constant

In the RAFT polymerization, proper choice of the chain transfer agent is one of the important factors in the process. In Mayo's report, the method to evaluate the chain transfer constant is

proposed as Mayo method.[26] In the polymerization, the degree of polymerization (DP) can be noted as the ratio of rate of propagation and rate of termination. Listing the parameter of possible termination mechanism including recombination, termination to impurities, and chain transfer. The equation can be noted as Eq. 1.1:

$$DP = \frac{R_p}{R_t} = \frac{k_p[R\cdot][M]}{k_{rc}[R\cdot][R\cdot] + k_i[R\cdot][i] + k_c[R\cdot][CTA]} \quad (1.1)$$

Taking reciprocal of DP and the equation can rewrite into Eq. 1.2:

$$\frac{1}{DP} = \frac{k_{rc}[R\cdot][R\cdot] + k_i[R\cdot][i]}{k_p[R\cdot][M]} + \frac{k_c[R\cdot][CTA]}{k_p[R\cdot][M]} \quad (1.2)$$

Noting the C_{tr} as k_c/k_p and DP_0 as the degree of polymerization without any addition of chain transfer agent, the function can be found as Eq. 1.3:

$$\frac{1}{DP} = \frac{1}{DP_0} + C_{tr}\frac{[CTA]}{[M]} \quad (1.3)$$

By plotting the reciprocal of DP of polymer synthesized in various condition of chain transfer addition to the ratio of chain transfer to monomer, the chain transfer constant to specific monomer can be found. If the chain transfer constant is high, the polymerization might no progress because radical would only react with chain transfer agent. On the other hand, polymerization would not be well controlled if chain transfer is too low because radical would only react with monomer. Proper selection of chain transfer for the RAFT system is important for the molecular design.

1.3.2 Examples of RAFT

In the recent development of RAFT polymerization, lighting initiation is one of the

approaches to synthesized precise polymers via RAFT. Liu et al. [27] prepared a block copolymer composed of polystyrene-b-poly(4-vinylpyrdine) using the light initiation as shown in Fig. 1.15. The radical was produced rapidly in the light initiation as one condition that fits the criteria of RDRP (fast initiation). In the case that initiation radicals were capture with chain transfer agent, the controllability of RAFT was improved. The self-assembly behavior originated from block copolymer design formed a micelle as an aqueous solution. This is known as polymerization induced self-assembly (PISA) as one efficient way to prepare nano particle as desired molecular structure. In the research of Sumerlin's group, UV light stimulation was directly applied to chain transfer agent to produce radical. In this case, the reaction is well-controlled with chain transfer agent without any side reaction from initiator and a controlled polymer with ultra-high molecule weight was prepared.[28] For the sequential polymerization in the second segment of monomer, direct reinitiation from macro chain transfer also prevent from any homopolymerization from initiator to the second monomer.

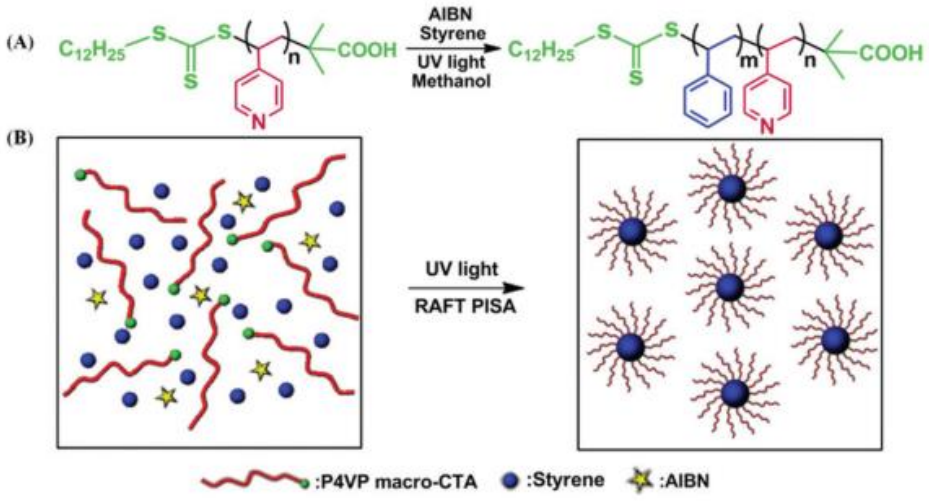


Fig. 1.15 Scheme of PISA via light-initiated RAFT.[27]

In Kamigaito's work, the cation polymerization has combined with RAFT polymerization using thioester and thioether as shown in Fig. 1.16. By switch the activity of chain transfer agent

via pH and environmental condition, the block copolymer of vinyl ether and acrylate was realized.[29] For the polymer preparation so far, there are various type of polymer which were only can be synthesized in limited method. By the combination of different polymerization mechanism, the possible selection of block copolymer has been widened. As a result, more potential application can be expected.

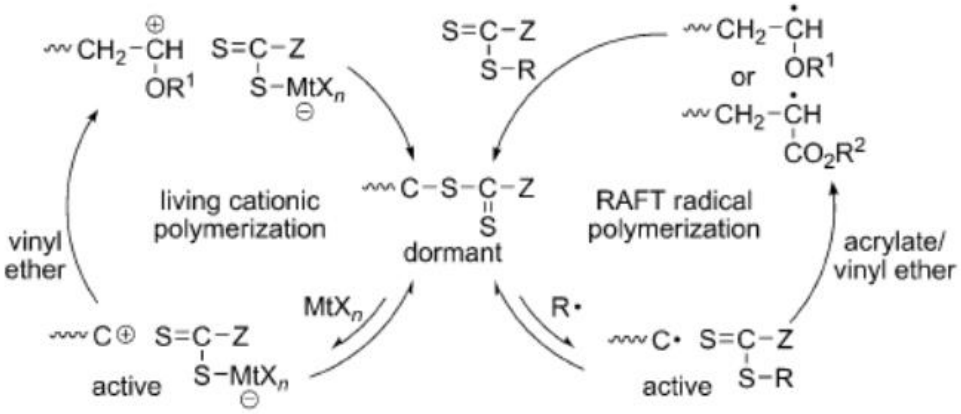


Fig. 1.16 Combination of cationic polymerization and RAFT radical polymerization.[29]

1.4 Polymerization using cyclodextrin

In many applications of the cyclodextrin, it has been applied as an additive for some polymerization as well. In Ritter's study, hydrophobic monomers were synthesized in water with help of methylated beta cyclodextrin as shown in Fig. 1.17. [30] The hydrophobic monomers were tended to self-terminated when polymerized in water because they were insoluble and easily coagulated in an aqueous solution. With the help of cyclodextrin, the hydrophobic monomer can be separated into water phase as inclusion complexes with cyclodextrin. During the polymerization, cyclodextrin detached with growing polymer chain and homopolymers of hydrophobic monomers were obtained. One of the merits in this method is that the cyclodextrin can be recycled for no consumption of cyclodextrin in the process.

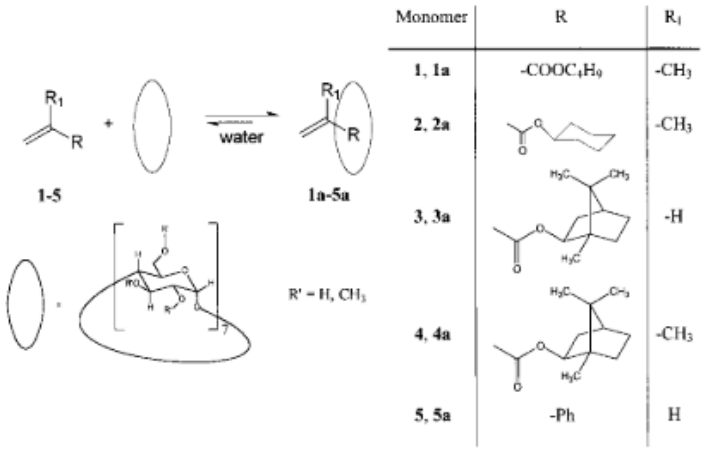


Fig. 1.17 Scheme of synthesis of hydrophobic monomer in a cyclodextrin aqueous solution. [30]

In Wenz's study, a method called rotaxanation[31] was developed using inclusion complexes as monomer units in the polymerization as shown in Fig. 1.18. the rotaxanation involved the inclusion complexes and a stopper monomer with a bulky side to prevent cyclodextrin from dethreading. As the inclusion complexes polymerized with the stopper, cyclodextrins on the segment of linear polymer were kept by the side chain of polystopper. As a result, a polyrotaxane was established in an alternative way. The polyrotaxane composed of polyisoprene as linear main chain polymer and methylated beta cyclodextrin as ring molecule was successfully prepared with proper stopper monomers involved in the system.

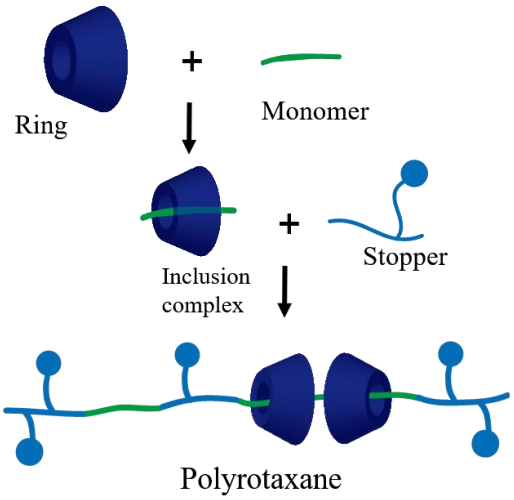


Fig. 1.18 Scheme of rotaxanation

1.5 Motivation and purpose

For a polyrotaxane, there are many potential applications originated from its supramolecular structure. However, the synthesis of polyrotaxane using main chain polymer other than PEG is still challenging. In rotaxanation, polyrotaxane were prepared from vinyl monomer but the linear segment in the polymer was hard to determined. In this study, a novel type of polyrotaxane was prepared via RAFT. MMA was chosen as one of the common monomers that widely applied to many materials for its thermal and chemical resistivity. The properties of polyrotaxane prepared from PMMA as main chain polymer is expected to show the strong properties from PMMA and resilience properties from the supra structure of polyrotaxane. To achieve the purpose, polystopper were synthesized with proper stopper via mediation of trithiocarbonate as a chain transfer agent. After that, the polystopper was applied as the macro chain transfer agent in the polymerization of inclusion complex of MMA and γCD. From the mechanism of RAFT, the second segment of inclusion complex is synthesized between polystopper segment. As a result, the γCDs on the PMMA main chain were kept by the side group on the polystopper and the structure of polyrotaxane with well-defined linear segments was established as shown in Fig. 1.18. In this study, proper stopper candidates were evaluated via synthesis of statistical polyrotaxane to confirm the ability of preventing CD from dethreading. Then block copolymer of polyrotaxane was synthesized and main parameters including the feed ratio of MMA, CD, and macroCTA were investigated to regulate the properties of resulting polyrotaxane. Finally, slide-ring gel was prepared from PMMA based polyrotaxane and mechanical properties were analyzed in comparison of PEG based polyrotaxane and polyrotaxane with various molecular weight.

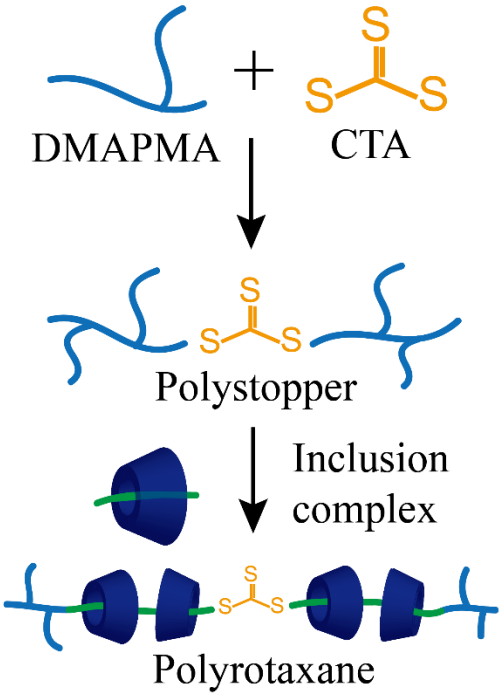


Fig. 1.18 Scheme of the synthesis of polyrotaxane via RAFT polymerization

Chapter 2 Statistical polyrotaxane synthesized via RAFT

2.1 Introduction

In a rotaxanation, stopper monomers and inclusion complexes of ring molecules and monomers were synthesized into a polyrotaxane as a statistical polymer. The space hinderance of bulky side chains on the stoppers plays an important role for PR preparation to keep cyclodextrins in the PR molecules.

The stopper on the chain end of PR main chain varies with the cavity size of ring molecule selections. In Araki 's report, the PRs with αCD threaded were stopped by adamantane groups.[32] The cavity size of cyclodextrin depends on the number of repeat units. For instances, βCD and γCD have 7 and 8units, of which the cavity sizes are 0.70nm and 0.88nm, respectively. When using cyclodextrin with bigger cavity, stoppers with bulkier side chains are needed. In this chapter, statistical polyrotaxane was synthesize by the scheme showed in Fig 2.1. The evidence of threaded CD is found from the analytical data of GPC and NMR. Three kinds of stoppers including PEGMA, DMAPMA and HEMA were tested for the efficiency of preventing CD from dethreading.

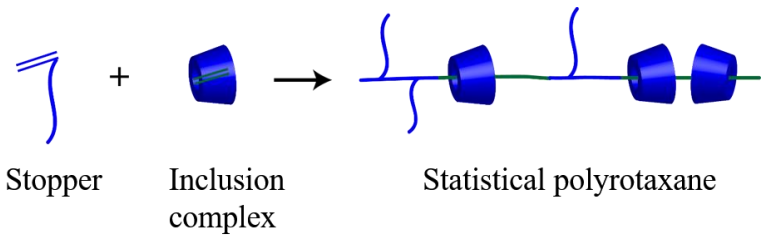


Fig 2.1 Scheme of synthesis of statistical PR

2.2 Experimental

2.2.1 Material

Chain transfer agent preparation

Acetone (>99.5%), carbon disulfide (>99.0%), tetrabutalammonium hydrogen sulfate (>98.0%), sodium hydroxide (50wt% aqueous solution), hydrochloric acid (35-37wt%) were purchased from Wako Chemicals and used as received. Deionized water was obtained from an Organo Purelite PRB.

Synthesis of statistical polyrotaxane

N-[3-(dimethylamino)propyl] methacrylamide (DMAPMA) (>98.0%, stabilized with monomethyl ether hydroquinone, MEHQ), was purchased from Tokyo Chemical Industry. Poly(ethylene glycol) methyl ether methacrylate (PEGMA) (contains 100 ppm MEHQ and 300 ppm BHT as inhibitor) and hydroxyethyl methacrylate (HEMA) (contains 100 ppm MEHQ as inhibitor) were purchased from Wako Chemicals. DMAPMA, PEGMA and HEMA were passed through a column filled with inhibitor remover (for MEHQ/HQ) purchased from Sigma Aldrich before use. Methyl methacrylate (MMA) (>99.0%, stabilized with 0.005% hydroquinone, HQ) was purchased from Wako Chemicals and distillated to remove impurities before use. Gamma cyclodextrin (γCD) was provided by Wacker Chemie. Urea (biochemistry grade), 2,2'-azobis[2-(2-imidazolin-2-yl) propane] dihydrochloride (VA44) (>97.0%) and dimethyl sulfoxide (>99%) were purchased from Wako Chemicals. Deuterium water (99.9%D) was purchased from Sigma Aldrich. D_6-dimethyl sulfoxide (99.9%D) was purchased from Kando chemicals. Lithium bromide (>99.0%) was purchased from Tokyo Chemical Industry.

Reagents and solvents mentioned above were analytical grade and used as received unless otherwise noted.

2.2.2 Synthesis of chain transfer agent

The chain transfer agent, S,S-Bis(α,α'-dimethyl-α"-acetic acid)-trithiocarbonate (BDATC), was synthesized according to a previous report.[33] 5.23g Acetone (0.09mole), 10.75g chloroform (0.09mole), 2.74g carbon disulfide (0.036mole) and 2.41g tetrabutylammonium hydrogen sulfate (0.71mmole) were mixed in 120ml hexane under N_2 purge for 30min. 20.16g sodium hydroxide (50% aqueous solution) was slowly added into the solution throughout 30 mins in cold water bath to prevent temperature from rising over 30℃ and react for 24hrs. 90ml H_2O was then added into solution to dissolve the solid and followed by 12ml of concentrated HCl to acidify the aqueous layer. The mixture was then stirred for 15 minutes and the precipitated product was gathered by vacuum filtering and rinsing with water. Brownish powder was obtained after dried to constant weight about 3.8g (Yield: 37.4%). The powder was further purified by recrystallization from acetone to afford a yellow crystalline solid; melting point: 173-8 °C (decomposed). IR spectrum (cm^{-1}): 802(C-S), 1060(C=S), 1710(C=O, carboxyl acid). ^1H NMR (DMSO-d_6, ppm from TMS): 1.59 (s, 12H), 12.91 (s, 2H). ^{13}C NMR (DMSO-d_6, ppm from DMSO): 24.9, 56.2, 173.1, 219.0.

2.2.3 Synthesis of polyrotaxane

γCD was dissolved in 8M urea solution and stirred for 10 mins till solution became clear. MMA was then added into the solution and solution became turbid after 30 min stirring. The mixture was moved to three-necked reactor and heated to 50℃ in oil bath. VA44 as an initiator

was dissolved in water and added into the mixture when solution temperature reached to 50℃ to trigger the reaction. Resulting products was purified via centrifugation and washed with water for 3 times. PEGMA/DMAPAM/HEMA were used as stopper monomers.

2.2.4 Analysis of infrared spectrum

Infrared spectrum was recorded on Thermol Scientific NICOLET iS50 FT-IR spectrometer in room temperature using Attenuated Total Reflection (ATR) method by SENSIR DuraSampl IR II as an accessory set on FI-IR spectrometer.

2.2.5 Analysis of gel permeation chromatography

Gel permeation chromatography (GPC) was recorded on Shodex OHpac SB-G columns using 10mM LiBr in DMSO as eluent with flow rate of 0.4ml/min at 333K. Signal was received using RI detection and molecular weight was calculated based on PEG standards.

2.2.6 Analysis of nuclear magnetic resonance

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded at 400 MHz on a JEOL JNM-AL400 spectrometer under temperature of 298 K in d_6-DMSO or D_2O as the solvent. Diffusion order spectroscopy (DOSY) analysis was performed on JEOL ECS-400 using bpp_ste as analysis sequence and the parameters were applied as follow: relaxation time: 7ms, diffusion times: 0.6s, delta: 6ms, gradient pulse magnetic field: 0.3mT-300mT, steps: 64 steps. 2D DOSY spectrum were plotted using SPLMOD simulation module with following parameters: start: 0.01 ($\mu m^2/s$), stop: 1000 ($\mu m^2/s$), interp: 3, species: 2, peaks: 2, ratio:3, error: 0.2, Maxima: enabled, scale: 0.2.

2.2.7 Test of the inclusion complex formation

γCD was dissolved in 8M urea solution and stirred for 10 mins till being clear. Then stopper monomer was added into the solution and kept stirring for another 30 mins. The appearance of the solution was observed as an evidence of the formation of inclusion complexes. If the solution turned from clear to turbid, it suggests that the packing structure of inclusion complexes were formed.

2.3 Result and discussion

2.3.1 Synthesis of the chain transfer agent

The chain transfer agent used in this work in synthesized based on the previous report.[33] A trithiocarbonate was prepared from the reaction of carbon disulfide with hydroxide ion through the phase transfer catalyzed process. During the reaction, the mixture was clear at first. After addition of sodium hydroxide solution, it became yellowish color and turbid. For the reaction processed in 1hr, the mixture became viscous. For the best efficiency of phase transfer catalyzed process, a steady mechanical stirring was needed during the viscosity changed in the reaction. After the acidification by the addition of hydrochloric acid, the mixture had the phase separated into clear liquid layer and brown yellow precipitation. The precipitation was obtained by the vacuum filtering washed with water and recrystallized with acetone. The NMR and the IR spectrum of the final product were shown in Fig. 2.1 (13C NMR), Fig. S2.1 (1H NMR), and Fig. S2.2 (IR spectrum), the characteristic peaks of the BDATC were found as the result for the confirmation of the trithiocarbonate structure.

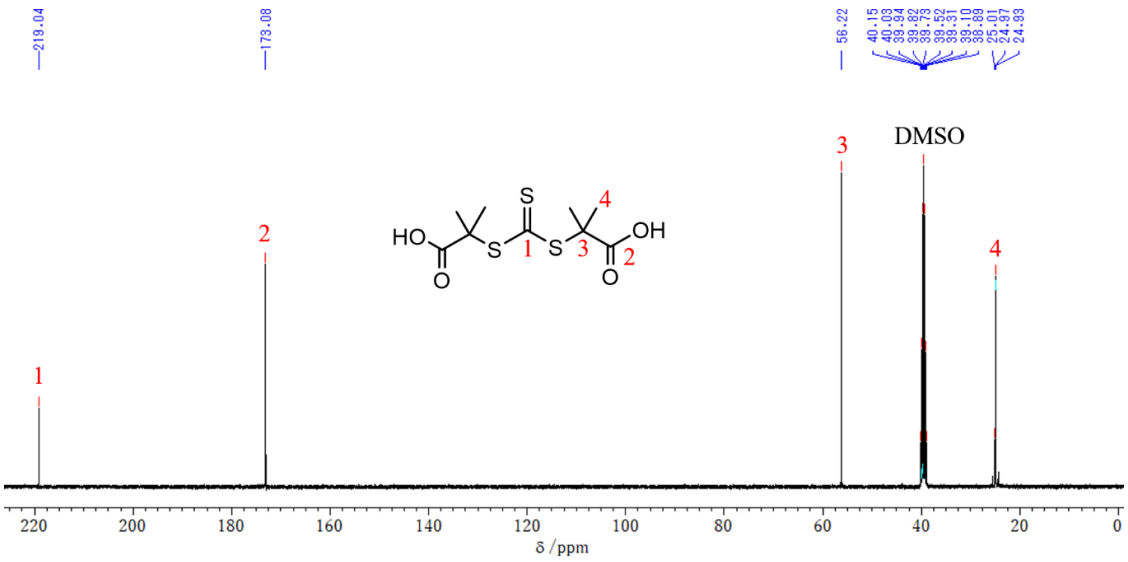


Fig. 2.1 ^{13}C NMR spectrum of BDATC. (solvent: d6-DMSO, temperature: 25°C)

2.3.2 Polyrotaxane synthesis with chain transfer agent

The reaction scheme is shown as Fig.2.2. For the reaction mechanism proposed in this work to synthesize polyrotaxane via RAFT polymerization, a suitable stopper to prevent γCD from dethreading is important. In this chapter, three kinds of the monomers were investigated whether they can build up a polyrotaxane for different side group attached on these candidates.

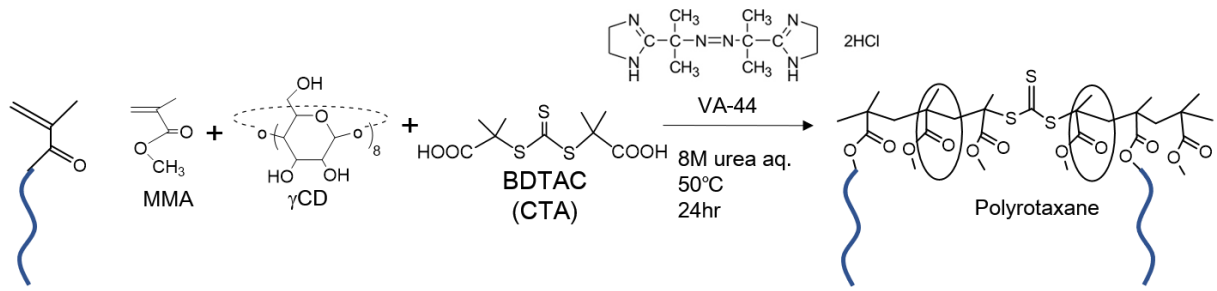


Fig. 2.2 Scheme of statistical polyrotaxane synthesis

In the GPC curve of these polymers, a polymer peak over molecular weight 10k was identified while the peak of free CD was also observed as shown in Fig.2.3 for one example. The product was purified by centrifugation and washed with water for 3 times. However, free

γCD was not fully removed as the peak at 39-42 mins represented in the GPC curve. This suggests that empty γCD was included in the packing structure forming from the inclusion complexes and hard to remove while washing with water. The PDI of the polymer peak is more than 2.0, which is not ideal for a controlled polymerization. This suggests that the reactivity of inclusion complexes was hindered by γCD, so the addition-fragmentation process was not ideally processed.

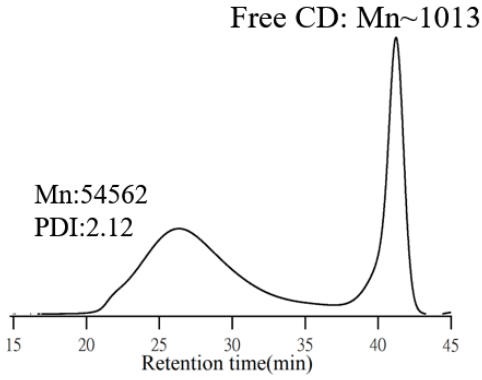


Fig. 2.3 GPC curve of PR synthesis using PEGMA as a stopper

The wt% of free γCD in the PR was calculated from the GPC result using the calibration curve method. The γCD solution in DMSO with concentration of 5mg/ml to 20mg/ml were prepared and their GPC curves were obtained. In the GPC analysis, the intensity of the peak at the retention time is proportional to the concentration of corresponding component in the solution. As the result, the calibration curve of the γCD concentration to the peak height in GPC curves was established from this series of analysis as shown in Fig.2.4. Applying this calibration curve to the measurement of unknown sample, the concentration of the free γCD could be evaluated from the peak height of the γCD at corresponding retention time.

Multiple purification methods were used in this study. The solution was first dialysis with a dialysis bag (MWCO=5-6k) in water for 24 hours, precipitated by centrifugation, and washed by water for 3 times. The sample was further purified by dissolving it into DMSO and reprecipitated in water for 2 times to remove free γCD as much as possible. The evolution of

GPC curves in the purification steps was shown in Fig.2.5. The peak of free γCD was weakened throughout the purification process while the peak of polymer remained unchanged. This suggests that only free γCD was removed, and little γCD was dethreaded during the purification process.

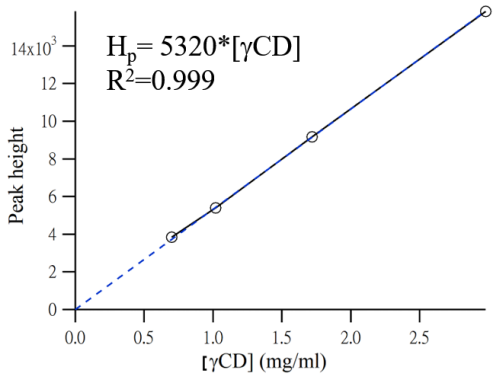


Fig.2.4 Calibration line of the peak height in GPC result to γCD concentration

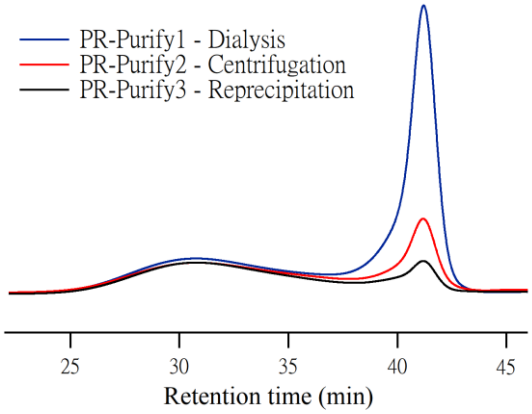


Fig.2.5 Peak evolution of residual free γCD in the polyrotaxane during purification process

2.3.3 Evidence for γCD existence

To find the evidence of threaded γCD in the PR, GPC and NMR analysis were applied. From the GPC result, MW was found as the peak of the free γCD was also presented. On the other hand, the total composition of PR was obtained by the analytical result of the NMR spectrum. From the NMR spectrum shown in Fig.2.5, characteristic peaks of each component were found as follow: 0.8-1.1ppm (-CH3, a, A), 1.7-2.1ppm (-CH2, b, B), 3.3-3.8ppm (-CH, 2-6, c, C, E, F), 4.0-4.2ppm (-CH, D), 4.4-4.6ppm (-OH, 6), 4.8-5.1ppm (-CH, 1), 5.6-5.9ppm(-OH, 2, 3).

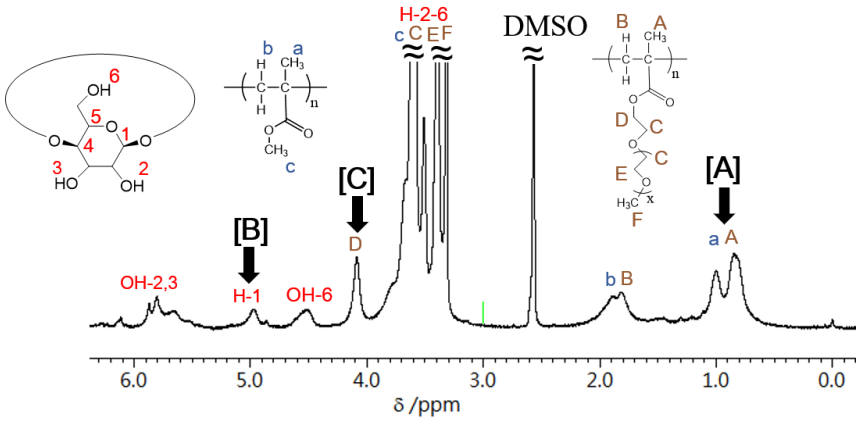


Fig.2.5 Assignment in NMR spectrum of polyrotaxane using PEGMA as a stopper

In the NMR spectrum, the integral area of the peak corresponds to the amount of the component. According to the peak assignment of each component, the molar ratio of components in the compound was calculated as following forms:

$$A = 3 * (\mathrm{MMA} + \mathrm{PEGMA}) \qquad (2.1)$$

$$B = 8 * \gamma\mathrm{CD} \qquad (2.2)$$

$$C = 2 * \mathrm{PEGMA} \qquad (2.3)$$

$$\text{Total CD(wt\%)} = \frac{\gamma\mathrm{CD}}{\gamma\mathrm{CD+MMA+PEMGA}} * 100\% \qquad (2.4)$$

Noted the γCD weight percentage calculated in NMR spectrum included free and threaded γCD. As the result, the threaded γCD amount of γCD was obtained by subtracting free γCD wt% from total wt% of γCD. For the evaluation of the coverage ratio as γCDs covered on the main chain of PMMA, one cyclodextrin was considered to cover 2.5 units of MMA as described in Kida's report.[34]

As a further confirmation for the existence of threaded γCD in PR, diffusion ordered spectroscopy (DOSY) was applied as one of the advanced functions in NMR analysis. In DOSY experiment, the gradient pulse of magnetic field was applied to the sample. The decay of peak intensity is correlated to the mobility of the components. As a result, the diffusion coefficients of the components were calculated based on the simulation for the change of peak intensities.

Given γCD as a molecule with smaller molecular weight, mobility is higher than the polymer with larger molecular weight. However, in the DOSY spectrum shown in Fig.2.6, the diffusion coefficient of γCD was aligned with polymer main chain peak. This suggests that γCDs were threaded on the main chain polymer for their mobility was fixed to the same. From this series of analytical method, the CD existence in the polyrotaxane was found and the coverage ratio of CD on the main chain was also evaluated.

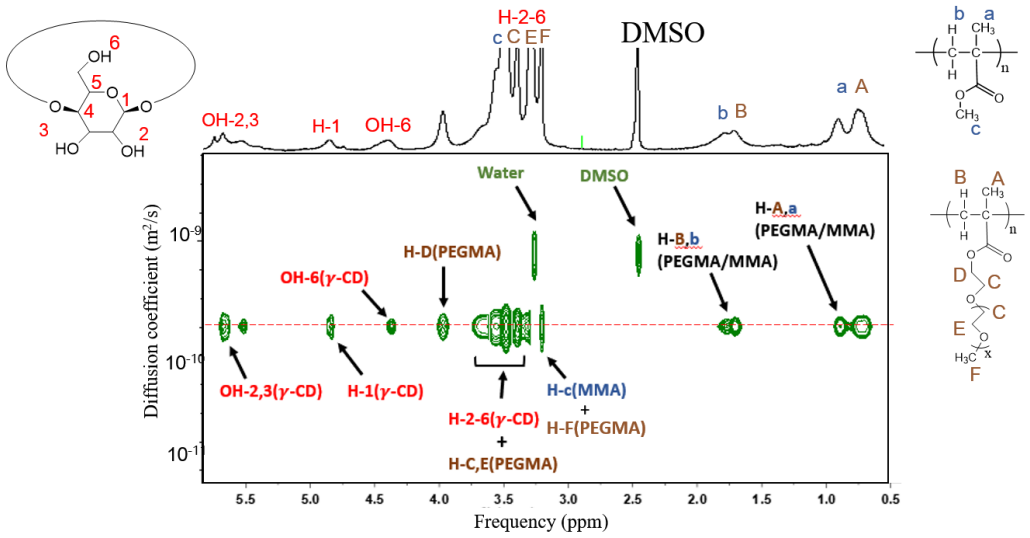


Fig.2.6 DOSY spectrum with reference of NMR spectrum of the polyrotaxane.

2.3.4 Properties of PR from different stoppers

A stopper is the component that prevents γCD from dethreading on the chain ends of the polymer. To achieve this, a hydrophilic monomer with bulky side chain is needed. PEGMA, DMAPMA and HEMA were chosen as candidates that fitted the criteria with various bulkiness of their side chains as shown in Fig.2.7. Among three stopper candidates, PEGMA has the bulkiest side chain while HEMA has the least bulky side group.

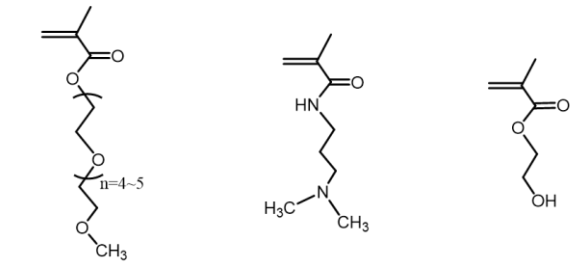


Fig. 2.7 Molecular structure of stoppers investigated in this study

The recipe and the result are shown in Table2.1 with the coverage ratio of the PR using PEGMA as stopper was 58.3%. This suggests that the bulky side chain of PEGMA was able to keep γCD in the polymer. On the other hand, less γCDs were found from the PR using HEMA as stopper for the coverage ratio calculated as 2%. Since HEMA has shorter side chain group, γCD was possible to dethread during the reaction and purification. In the previous study in Feng's group, a PR was built from γCD using N-isopropylacrylamide (NIPAAm) as a main chain polymer.[35] In that case, γCD is considered possible to slide alone on the PNIPAAm polymer chain. For HEMA bearing shorter side chain than NIPAAm, the result showed that HEMA did not effectively prevent γCD from dethreading.

Table 2.1 Polyrotaxane synthesize with various of stoppers.

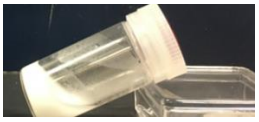
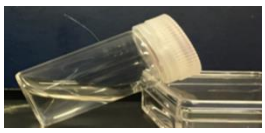
MMA	γCD	Stopper	Amount	Yield[1]	Mn[2]	PDI	Coverage ratio
300mM	300mM	PEGMA	100mM	34.5%	59k	1.99	58.3%
300mM	300mM	DMAPMA	100mM	42.45%	58k	1.65	17.7%
300mM	300mM	HEMA	100mM	49.7%	17k	1.97	>2%

[BDATC] = 10mM, [VA44] = 5mM, synthesized in 10ml 8M urea solution under 50°C.
[1]: Yield=Wpolymer/Wmonomer (γCD not involved). [2]: Obtained from GPC result.

2.3.5 Inclusion complex with side chain

From the discussion above, PEGMA and DMAPMA are considered able to stop γCD from dethreading. However, the side chain itself might form the inclusion complexes with γCD. A test for the stoppers and γCD was conducted to check the affinity between the stopper and γCD as the condition shown in Table 2.2. In the case of DMAPMA, the mixture with γCD solution was kept clear. However, for PEGMA mixed with γCD solution, the mixture was clear at first and turned into turbid solution after stirring for 30 mins. This suggests that inclusion complexes were formed between stopper monomer and γCD. Considering it might cause the bias for the coverage ratio calculation. DMAPMA was chosen as the stopper for further investigation of block polyrotaxane.

Table 2.2 Mixture of γCD and stoppers after stirring for 30mins.

γCD	Stopper	Amount	8M urea solution	Mixture state	Description
0.39g (0.03mmole)	PEGMA	0.03g (0.01mmole)	1ml		Turbid
0.39g (0.03mmole)	DMAPMA	0.017g (0.01mmole)	1ml		Clear

2.4 Summary

The synthetic mechanism of PR preparation via RAFT has been proven from the series of analytical method including GPC, NMR and DOSY analysis. In the DOSY result, the mobility of γCD was aligned with the mobility of the main chain polymer, which is considered as the evidence of threaded γCD in the PR molecule. For stoppers with different side chains,

DMAPMA and PEGMA showed better capability of preventing γCD from dethreading for the coverage ratio of 17%, 58%, respectively. However, in the test of mixing the stopper monomer with γCD solution, the inclusion complexes were recognized in the case of PEGMA. This suggests that the polyethylene glycol side chains on the PEGMA monomer tend to form inclusion complexes with γCD. As the result, a part of the γCD might be threaded on the side chain and dethreaded after the reaction because only one end was capped on the side chain. For cationic DMAPMA, no obvious complex was observed. This suggests that DMAPMA is better stopper to prepare PR and that γCD would be mainly threaded on the main chain polymer.

2.5 Supporting information

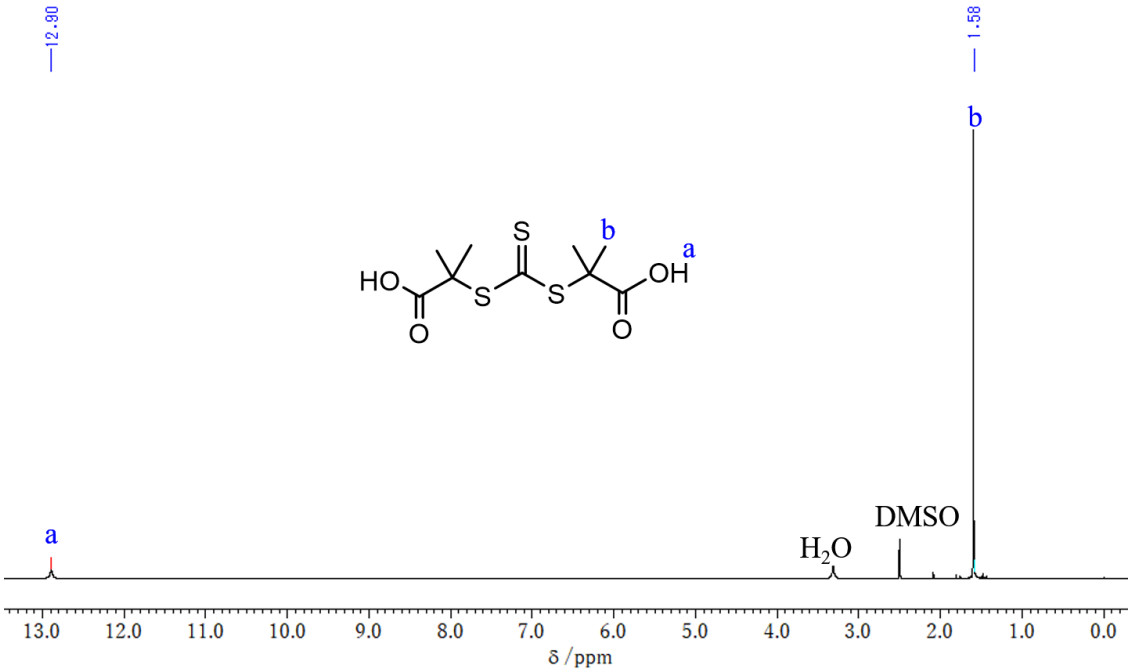


Fig S2.1 1H spectrum of BDATC (solvent: d6-DMSO, temperature: 25℃).

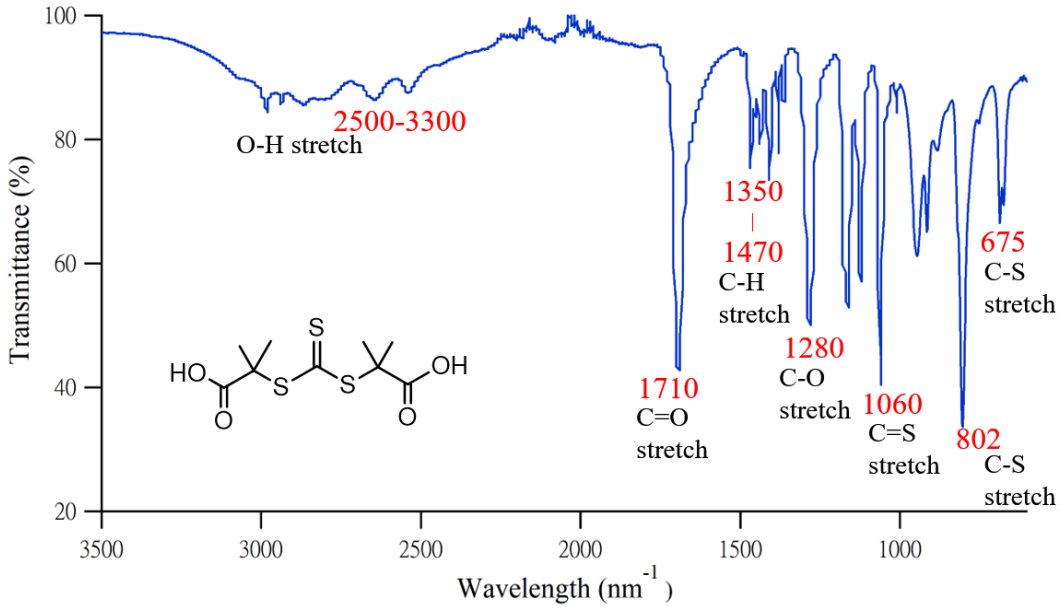


Fig S2.2 IR spectrum of the BDATC.

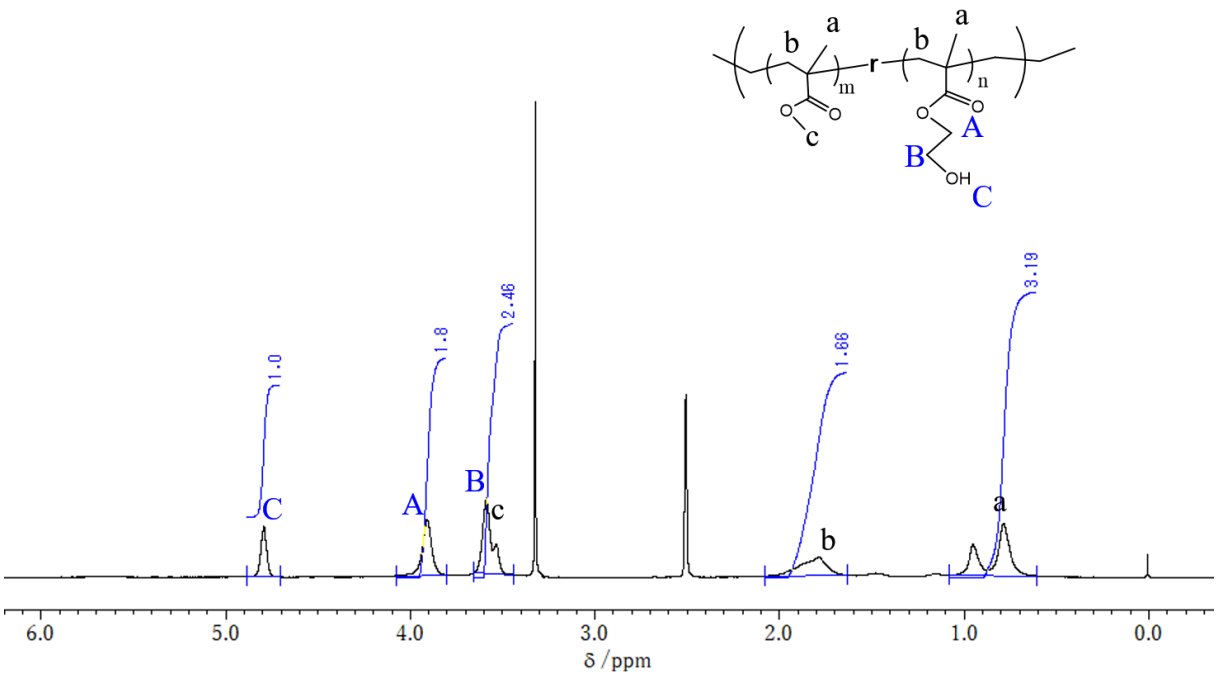


Fig. S2-3 NMR spectrum of poly(HEMA-r-(MMA+γCD)) copolymer. The signal peaks of the cyclodextrin were barely found.

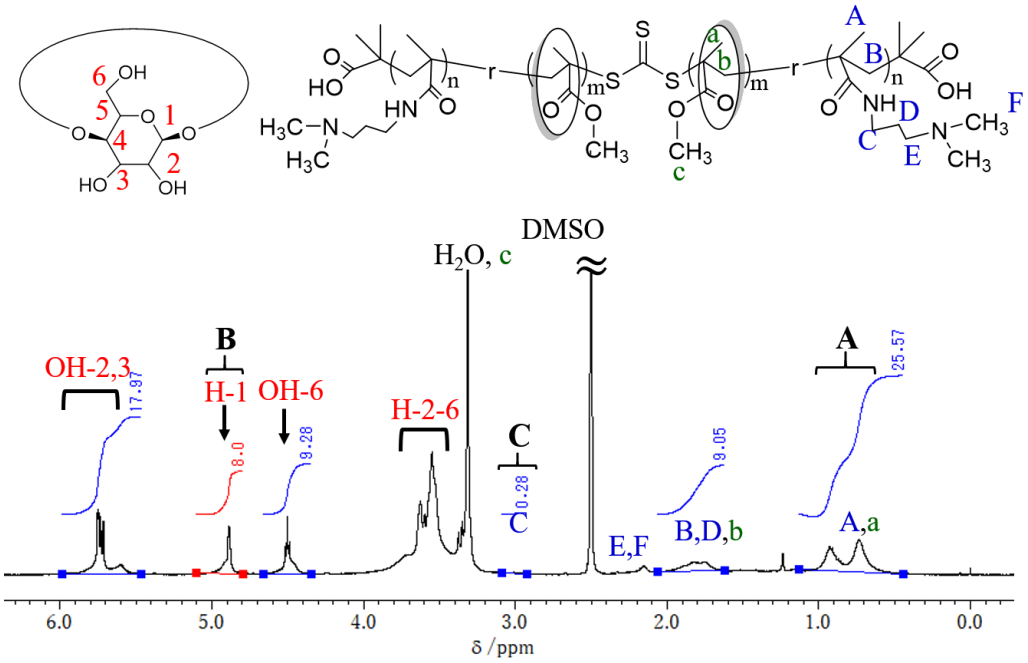


Fig. S2-4 NMR spectrum of poly(DMAPMA-r-(MMA+γCD)) copolymer. The wide peaks of the cyclodextrin were the evidence that CDs were threaded so that the peaks were affected.

Chapter 3 Block polyrotaxane synthesized via RAFT

3.1 Introduction

In the previous chapter, the evidence of the γCD existence in the PR synthesis via RAFT polymerization was obatined. Stoppers were evaluated as candidates for the polyrotaxane synthesis and DMAPMA was chosen as the proper stopper monomer. For PR synthesized as a statistical copolymer, the sliding distance was hard to determine because the linear segments were randomly distributed between stopper segments. In the case of the controlled polymerization, it becomes possible to build a block copolymer from the sequential polymerization. For instance, homopolymer synthesized with mediation of chain transfer agent in RAFT polymerization can be applied as a macro chain transfer agent for the polymerization of another polymers. As a result, segments of the second polymer chain were synthesized with the first segments connected. In this chapter, a symmetrical thioester chain transfer agent was applied in the polymerization of the stopper. Then polystopper was used as a macroCTA mediating the polymerization of the inclusion complexes of γCD and MMA. Because of the mechanism of RAFT polymerization, the second segment was synthesized between the stopper segments in the addition-fragmentation process and the polyrotaxane structure was established with a well-defined length of the linear segment. In the polymerization, the stability of complexes and controllability was related to various parameters condition in the system. The main parameters including amount of MMA, γCD, polystopper and temperature were investigated. From the evaluation of these results, the method to arrange the coverage ratio and the molecular weight in the PR synthesis was proposed.

3.2 Experimental

3.2.1 Material

Chain transfer agent preparation

Acetone (>99.5%), carbon disulfide (>99.0%), tetrabutalammonium hydrogen sulfate (>98.0%), sodium hydroxide (50wt%, aqueous solution), hydrochloric acid (35-37wt%, aqueous solution) were purchased from Wako Chemicals and used as received. Deionized water was obtained from an Organo Purelite PRB reverse osmosis/filtration unit (resistivity 14.6 MΩ).

PolyDMAPMA preparation as a polystopper

N-[3-(dimethylamino)propyl] methacrylamide (DMAPMA) (>98.0%, stabilized with monomethyl ether hydroquinone, MEHQ) was purchased from Tokyo Chemical Industry and passed through a column filled with inhibitor remover (for MEHQ/HQ, purchased from Sigma Aldrich) before use. 4,4'-azobis (4-cyanovaleric acid) (ACVA) (>98.0%), Isopropyl alcohol (>98.0%) was purchased from Wako Chemicals.

Polyrotaxane preparation

Methyl methacrylate (MMA) (>99.0%, stabilized with 0.005% hydroquinone, HQ) was purchased from Wako Chemicals and distillated to remove ingredients before use. Gamma cyclodextrin (γCD) was kindly provided by Wacker Chemie. (2-Hydroxypropyl)-γ-cyclodextrin (0.6 molar substitution, average Mw= 1580) (HP-γCD) was purchased from Sigma Aldrich. Urea (biochemistry grade), 2,2'-azobis[2-(2-imidazolin-2-yl) propane] dihydrochloride (VA44) (>97.0%), maleic acid reference Material and dimethyl sulfoxide (>99%) were purchased from Wako Chemicals. PR05 as PEG based polyrotaxane with coverage ratio of 5% was prepared according to the previous report.[17] Deuterium water

(99.9%D) was purchased from Sigma Aldrich. D_6-dimethyl sulfoxide (99.9%D) and lithium bromide (>99.0%) were purchased from Kando Chemicals. Reagents and solvents mentioned above were analytical grade and used as received unless otherwise noted.

3.2.2 Synthesis of chain transfer

The chain transfer agent, S,S-Bis(α,α'-dimethyl-α"-acetic acid)-trithiocarbonate (BDATC), was synthesized according to the previous literature[33]. 5.23g Acetone (0.09mole), 10.75g chloroform (0.09mole), 2.74g carbon disulfide (0.036mole) and 2.41g tetrabutylammonium hydrogen sulfate (0.71mmole) were mixed in 120ml hexane under N_2 purge for 30min. 20.16g sodium hydroxide (50% aqueous solution) was slowly added into the solution throughout 6 hours in cold water bath to prevent temperature from rising over 30℃ and react for 24hrs. 90ml H_2O was then added into solution to dissolve the solid and followed by 12ml of concentrated HCl to acidify the aqueous layer. The mixture was then stirred for 30 minutes and the precipitated product was gathered by vacuum filtering and rinsing with water. Brownish powder was obtained after dried to constant weight about 3.8g (Yield: 37.4%). The powder was further purified by recrystallization from acetone to afford a yellowish crystalline solid; melting point: 173-8 °C (decomposed). IR spectrum (cm^{-1}): 802(C-S), 1060(C=S), 1710(C=O, carboxyl acid). ^{1}H NMR (DMSO-d_6, ppm from TMS): 1.59 (s, 12H), 12.91 (s, 2H). ^{13}C NMR (DMSO-d_6, ppm from DMSO): 24.9, 56.2, 173.1, 219.0.

3.2.3 Synthesis of polystopper

DMAPMA and BDATC were dissolved in 9ml mix solvent of isopropyl alcohol and DI water with the weight ratio of 1:2. The solution was purged by N_2 for 30min. Then the solution was heated to 70℃ in oil bath. After temperature reach to 70℃ for 10 min, ACVA solution as dissolved in another 1 ml mixed solvent was dropped into reaction solution to trigger the

polymerization as an initiator solution and reacted for 6 hrs. After the polymerization, the sample was vacuum evaporated to concentrate the solution and precipitated in 10x amount of acetone to remove the residual monomer.

3.2.4 Synthesis of polyrotaxane

γCD was dissolved in 10ml of 8M urea aqueous solution and stirred till solution became clear. Then MMA was slowly dropped into the solution. The solution was a misty mixture at beginning. After stirring for at least 30min, the solution turned to milky mixture as the inclusion complex formed. After that, PDMAPMA was added into solution and vigorously stirred for another 30min. The solution was moved to a 3 necked reactor and purged with N_2 for 10 min while stirring. After the mixture was heated to 50℃ by an oil bath, the VA44 solution as dissolved in another 1ml 8M urea aqueous solution was added to trigger the polymerization and reacted for 24hrs. The resulting PRs were purified via centrifugation to collect the precipitated part. After the solution was repeatedly washed with water and precipitated by centrifugation for 3 times, white powder was obtained by lyophilization.

3.2.5 Gel permeation chromatography (GPC) analysis

GPC was recorded on Shodex OHpac SB-G columns using 10mM LiBr in DMSO as eluent with flow rate of 0.4ml/min at 333K. The signal was received using RI detection and molecular weight was calculated based on PEG standards.

3.2.6 Nuclear magnetic resonance (NMR) analysis

Regular measurement

^{1}H NMR spectra were recorded at 400 MHz on a JEOL JNM-AL400 spectrometer under temperature of 298 K in d_6-DMSO or D_2O as solvent. In the evaluation of residual γCD, coaxial cell for use in the external reference method was applied. Coaxial NMR tubes were purchased from SHIGAMEI (Outer tube: PS-001-07, inner tube: SP-402). Maleic acid was used as external reference to identify the relative concentration of γCD.

DOSY analysis

Diffusion order spectroscopy (DOSY) analysis was performed on JEOL ECS-400 using bpp_ste as analysis sequence and the parameters were applied as follow: relaxation time: 7ms, diffusion times: 0.6s, delta: 6ms, gradient pulse magnetic field: 0.3mT-300mT, steps: 64 steps. 2D DOSY spectrum were plotted using SPLMOD simulation module with following parameters: start: 0.01 ($\mu m^2/s$), stop: 1000 ($\mu m^2/s$), interp: 3, species: 2, peaks: 2, ratio:3, error: 0.2, Maxima: enabled, scale: 0.2.

3.2.7 Optical microscopy (OM)

OM pictures were taken with Nikon Eclipse Ts2R inverse research microscopy using CFI Plan Apo DM Lambda 100X Oil lens. Solution was dropped on the slide glass and covered with cover glass.

3.2.8 Wide angle X-ray scattering

Synchrotron wide-angle X-ray scattering (WAXS) measurements were conducted at the beamline BL-05SS at SPring-8 (Hyogo, Japan). The wavelength of the incident X-ray beam

was 1 Å, and the beam size was 0.1 mm (vertical) × 0.2 mm (horizontal). The sample-to-detector distance was 64 mm, and a CMOS flat-panel detector from Hamamatsu Photonics (C9728DK) was used as the 2D detector to collect the scattering profile.

3.2.9 Thermal gravimetrical analysis (TGA)

TGA analysis was performed on Thermo Plus EVO TG8120. Al_2O_3 was used as a reference sample. Measured samples were put in the Alumina pot and analyzed in air or N_2 atmosphere. The weight loss and the heat flow were recorded from room temperature to 500℃ with heat rate as 10℃/min.

3.3 Result and discussion

3.3.1 RAFT of polystopper

In Singhsa's work, PDMAPMA was synthesized in mixed solvent (isoprene: water=1:2) using 4-cyanopentanoic acid dithiobenzoate (CTP) as the chain transfer agent.[36] In this study, a trithiocarbonate (BDATC) was used as a CTA in the PDMAPMA synthesis to prepare a homopolymer with symmetrical structure as shown in Fig.3.1.

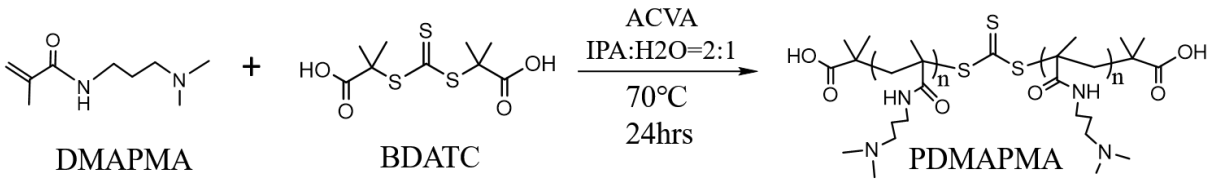


Fig. 3.1 Scheme of PDMAPMA synthesis

Evolution of molecular weight and polydispersity with the conversion of DMAPMA is displayed in Fig.3.2. As a result, the molecular weight is proportional to the conversion. This suggests that the reaction was regulated by the chain transfer agent from the mechanism of RAFT polymerization. Polydispersity index (PDI) of the polystopper slightly increased to 1.4 at the conversion about 80%. This result is due to possible decomposition of the thiocarbonate in the synthesis of polyacrylamide as illustrated in the previous study. [37]

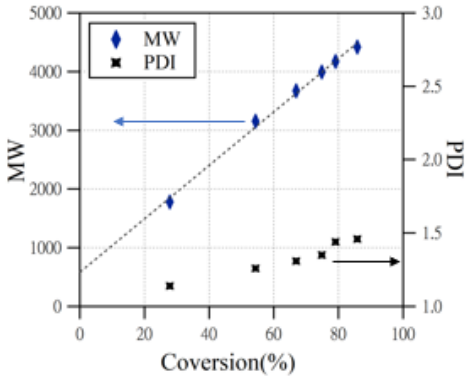


Fig.3.2 Evolution of molecular weight and polydiversity to the conversion of the PDMAPMA.

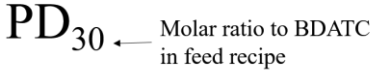
The theoretical molecule weight of polymer synthesized via RAFT is determined in the condition that all the chain transfer agent was reacted to become the macro CTA. The molecular weight is evaluated by the number of chains that from CTA and the initiator. Thus, the theoretical molecular weight, $M_{n,th}$, follows the eq 3.1:

$$M_{n,th} = \left(\frac{pM_M\,[M]_0}{[CTA]_0 + 2f[I]_o(1 - e^{-k_d t})}\right) + M_{CTA} \qquad (3.1)$$

Here $[M]_0$, M_M, p, $[CTA]_0$, f, $[I]_0$, k_d, t and M_{CTA} represent the initial monomer concentration, molecular weight of the monomer, conversion, initial CTA concentration, constant of initiator decomposition, time and the molecular weight of CTA. If the amount of the chains from the initiation is much smaller than CTA ($[I]_0 << [CTA]_0$), eq 3.1 can be simplified to eq 3.2.

$$M_{n,th} = pM_M \frac{[M]_0}{[CTA]_0} + M_{CTA} \qquad (3.2)$$

PDMAPMA as polystopper was synthesized from the various ratio of [DMAPMA] to [CTA] with notation shown in Fig. 3.3 and the results are shown in Table 3.1. The resulting molecular weight is close to the theoretical one. This suggests that the polymerization was mediated with the chain transfer agent for the RAFT process. In a RAFT polymerization, the resulting polymer of higher molecular weight is more stable and considered to be less active for the copolymerization with other monomers. However, enough bulkiness from the segment length of polystopper is needed to prevent γCD from dethreading for the polyrotaxane preparation. Given the tradeoff between bulkiness and chain transfer efficiency, PD_{30} was chosen for the synthesis of polyrotaxane in the following investigation. Peak list for NMR assignment (Fig.S3.1): δ/ppm=0.8-1.0(-CH3, A), 1.4-1.8(-CH2, B, D),2.1-2.4(-CH2, -CH3, E, F), 2.9-3.1(-CH2, C)



PD: PolyDMAPMA

Fig 3.3 Example of the nomenclature for the polystopper.

Table 3.1 PolyDMAPMA synthesized via RAFT polymerization with medication of BDATC as a chain transfer agent.

Entry	DMAPMA	BDATC	ACVA	[M]/[CTA][1]	Solvent[2]	Yield[3]	Mn[4]	$M_{n,th}$[5]	PDI
PD_{50}	1.914g	63mg	31mg	50	10ml	61.2%	3021	5467	1.46
PD_{30}	1.914g	105mg	31mg	30	10ml	49.0%	2574	2781	1.42
PD_{20}	1.914g	145mg	31mg	20	10ml	47.1%	1977	1880	1.42

Reaction Temperature:70℃. Time:24hrs. [1]: Molar ratio of DMAPMA and BDATC amount in the recipe. [2]: Mixed solvent of isopropyl alcohol and H_2O (1:2 in volume ratio). [3]: Yield= $W_{polymer}/W_{DMAPMA+BDATC}$ where $W_{polymer}$ was measured from sample weight after purification via precipitation in acetone and $W_{DMAPMA+BDATC}$ were the weight amount in the recipe. [4]: Obtained from GPC analysis. [5]: Theoretical molecular weight.

3.3.2 Initiation effect to the coverage ratio

Packing structure

Since PDMAPMA was synthesized via RAFT process as a polystopper, polyrotaxane was prepared by applying polystopper as a macro CTA in various conditions. In this reaction mechanism, inclusion complexes were polymerized as monomer units with the macroCTA. At room temperature, the mixture of γCD and MMA is turbid. This suggests that the inclusion complexes formed a structure that packed into a larger scale. For further investigation for the packing structure of inclusion complexes as monomers in the polymerization, WAXS analysis was performed. In the scattering pattern shown in Fig. 3.4, no obvious peaks were observed for the γCD solution in 8M urea and polyrotaxane solution after reaction. However, the scattering

pattern of mixture of MMA and γCD showed the specific pattern of peaks. These peaks are recognized as a channel structure for one of the structures can be found from the inclusion complex with γCD.[38] In the channel structure, the cavity of γCDs were aligned with a channel like structure as shown in Fig.3.5. This structure implied that the propagation of polymer chain is possible in the channels of γCD packings. On the other hand, the inclusion complexes in the cage structure are hard for the reaction propagation for the hinderance between the wells of CD for guests was encapsulated be the surrounding host molecules.

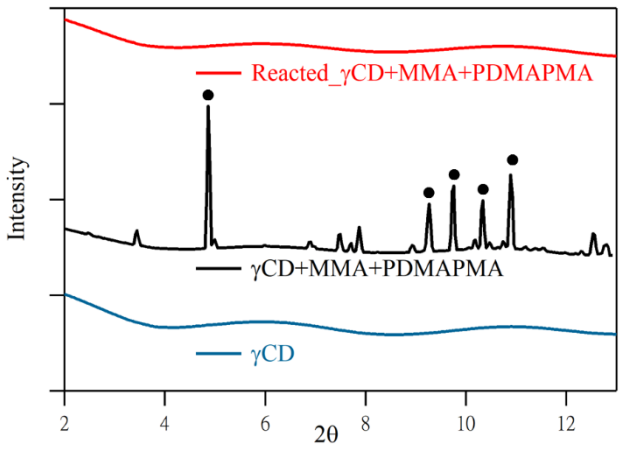


Fig. 3.4 WAXS pattern of the γCD MMA mixtures. Solvent: 8M urea. [γCD] = 300mM, [MMA]= 300mM, [PDMAPMA]= 10mM.

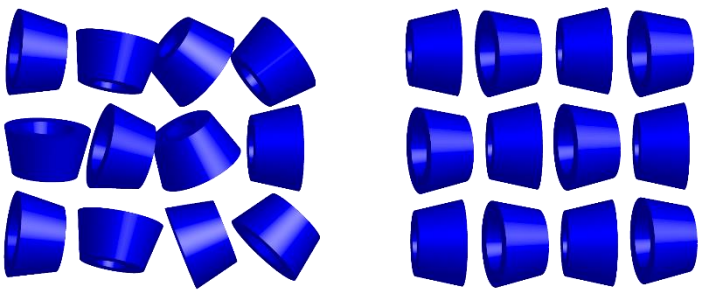


Fig.3.5 Scheme of possible packing structure of inclusion complexes of γCD.

When heated to 60℃ for 30min, the mixture became clear again by the dissolution of the packing structure. To investigate the initiation effect for the reaction, PR syntheses under various initiation condition were performed. The feed of monomer, γCD and polystopper were fixed as the recipe shown in Table 3.2. The coverage ratio of PR reacted under 50℃ was about 4%. However, for the PR synthesized in higher temperature as 70℃, only 0.8% of the coverage ratio was found. This result suggests that stability of the inclusion complexes decreased because molecular vibration increased and dethreading happened as MMA became more volatile under higher temperature. Although the inclusion complexes were able to equivalently react with propagating polymer chain at higher temperature as the homogenous system when reaction started, dethreading occurred as polymer chain propagated. As the result, the solution became turbid as reaction processed and the final product included less γCD inside the polymer. On the other hand, inclusion complexes are more stable incorporated at lower temperature so that more CDs were kept in the resulting polyrotaxane. The result also implied that polymerization could propagate in the channel structure of inclusion complexes.

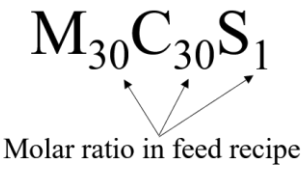
Table. 3.2 Recipe of PR synthesis for investigation of temperature factor.

MMA	γCD	PD30	VA044	Temp	Time	Mn	PDI	Coverage
300mM	300mM	10mM	10mM	50℃	24hr	32800	1.93	4.2%
300mM	300mM	10mM	10mM	70℃	24hr	28441	1.51	0.8%

3.3.3 Nomenclature of the polyrotaxane

Since PDMAPMA was synthesized via RAFT process as a polystopper, polyrotaxane is synthesized by applying polystopper as a macro CTA in various condition to discuss related

factors in the following discussion. For series of PR synthesized in this chapter, samples were noted as MxCySz for *x: y: z*=MMA: CD: polystopper as the feeding molar ratio in the recipe as shown in Fig 3.6 for instance. The feed ratios of MMA, cyclodextrin, and polystopper were investigated for their relationship to the resulting polyrotaxane. The list of the experiments and result are shown in Table S3.1.



M: MMA C: Cyclodextrin S: Polystopper

Fig 3.6 Example of the nomenclature for the polyrotaxane discussed in this work.

3.3.4 RAFT properties in the polyrotaxane synthesis

The general synthetical scheme of polyrotaxane in this study is shown in Fig. 3.7. As symmetrical polystopper applied as a macroCTA, inclusion complexes were polymerized between stopper segments and the structure of polyrotaxane was established with γCD being kept in the PR via bulky side groups on the polystopper.

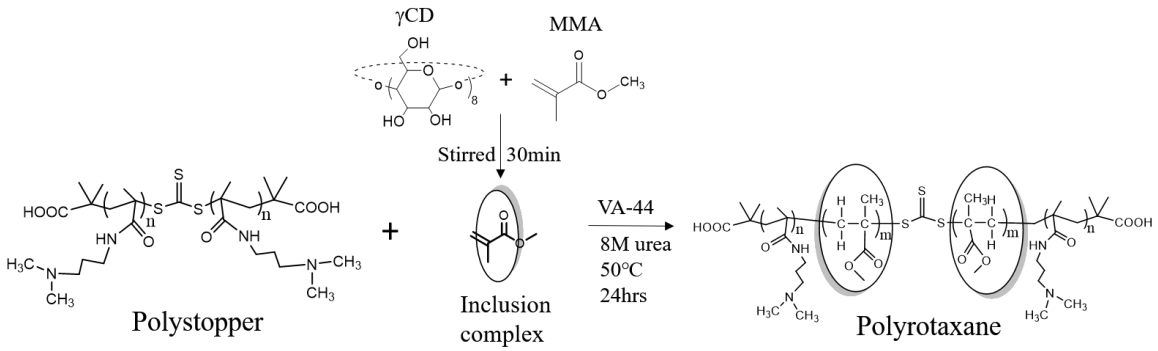


Fig.3.7 Scheme of polyrotaxane synthesis.

GPC curves of $M_{60}C_{30}S_1$ and PD_{30} are showed in Fig.3.8. For PR synthesized PD_{30} as the polystopper, the evolution of molecular weight is observed. This suggests that PR was synthesized based on the polystopper as the molecular weight grew. The unimodal peak indicated that the copolymerization between polystopper and inclusion complex was dominant as homopolymerized PMMA peak was not found in the chromatography. The residual free γCD peak was found in 39-41 min for the polyrotaxane is evaluated as the same method illustrated in Chap. 2. DOSY spectrum of this polyrotaxane is shown in Fig. S3.2 for polyrotaxane using polyDMAPMA as polystopper.

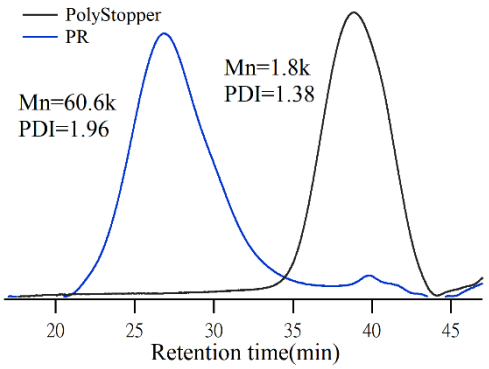


Fig.3.8 GPC curve of polystopper(PD30) and PR($M_{60}C_{30}S_1$)

Evaluation of chain transfer constant via Mayo method

In a RAFT polymerization, radical produced from initiator is first reacted with the chain transfer and the reaction is regulated through reversible addition-fragmentation process. In this case, the activity of CTA to the propagating radical and monomer is one of the main factors known as the chain transfer constant to evaluate the efficiency of a RAFT reaction. To investigate the RAFT behavior in this reaction, PDMAPMA as the polystopper was applied for various molar ratio in feed recipe to synthesize PRs while [MMA] and [VA44] were fixed as

300mM and 10mM as shown in Table 3.3.

Table 3.3 PR synthesize with different polystopper feeding.

Entry	MMA	γCD	PDMAPMA	[MMA]/[CTA][1]	Mn	PDI	Coverage
$M_{30}C_{30}S_1$	0.3g	3.9g	0.2g	30	32800	1.93	4.0%
$M_{30}C_{30}S_2$	0.3g	3.9g	0.4g	15	17300	1.69	5.5%
$M_{30}C_{30}S_3$	0.3g	3.9g	0.6g	10	7500	1.84	9.8%

Initiator: VA44= 32mg. Reacted in 8M urea aqueous solution under 50℃.

The apparent chain transfer constant ($Ctr_{(app)}$) of PMMA radicals to polystopper as marcoCTA was determined by Mayo method[26] as Eq. 3.3.

$$\frac{1}{\mathrm{DP}} = \frac{1}{\mathrm{DP}_0} + C_{\mathrm{tr(app)}} \frac{[\mathrm{CTA}]}{[\mathrm{M}]} \qquad (3.3)$$

From the plot of reciprocal of degree of polymerization (1/DP) to the molar ratio of polystopper to monomer in Fig.3.9, this method gave Ctr(app) = 0.1 as the slope of the regression line. The result value was lower than the chain transfer constant of dithiocarbonate reported in other publication.[39] This implied that the reactivity of chain carriers to macroCTA was weakened by the hinderance of γCD as the reaction occurred inside the channels composed of the γCD cavities. However, the polymerization was still under control of RAFT mechanism for chains propagated between macroCTA and PMMA chains because the propagation polymer chain only reacted with monomer without prominent termination to γCD according to the previous literature[30]. From the discussion above, PR was recognized to be synthesized by the mediation of polystopper as a macro chain transfer agent.

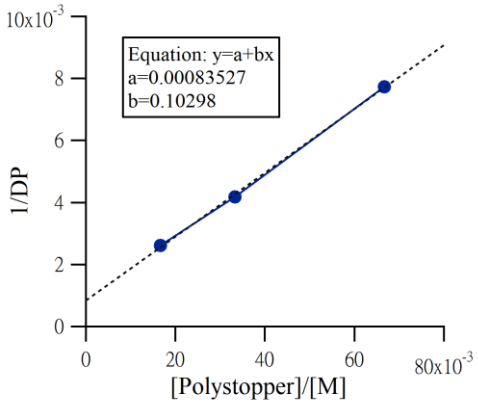


Fig.3.9 Mayo plot of PR synthesized with medication of polystopper as macro CTA

3.3.5 Effect of the CD concentration to the coverage ratio

To investigate the CD effect to the coverage ratio of resulting polyrotaxane, various concentrations of CD in the recipe were applied in the PR synthesis. The result was listed as shown in Table 3.4.

Table 3.4 PR synthesized with various concentration of γCD.

Entry	MMA	γCD	PDMAPMA	[MMA]/[γCD]	$Mn_{(MMA)}$ [1]	PDI	Coverage
$M_{30}C_{50}S_1$	0.3g	6.5g	0.2g	0.6	37131	1.98	21.8%
$M_{30}C_{30}S_1$	0.3g	3.9g	0.2g	1	26953	1.93	4.0%
$M_{30}C_{15}S_1$	0.3g	1.95g	0.2g	2	25460	2.15	1.3%
$M_{30}C_{07}S_1$	0.3g	0.93g	0.2g	4	27590	2.49	0.7%

Solvent: 10ml of 8M urea aqueous solution. Initiator: VA44 = 32mg. Temperature: 50℃. Reaction time: 24hr. [1]: Calculated from the Mn from GPC subtracted with the weight percentage of threaded γCD. $Mn_{(MMA)}=Mn_{(total)}*(1\text{-}wt\%_{(\ CD)})$

In the case of PMMA synthesized as main chain polymer, the molecular weight was 25k-

30k for the PRs synthesized under the same ratio of [MMA] to [PDMAPMA]. This suggests that the molecular weight is controlled via RAFT process without obvious effects from γCD. However, when higher [γCD] was applied, PR with higher coverage ratio was obtained according to the result of $M_{30}C_{50}S_1$. In the polymerization process with inclusion complexes, the tendency toward inclusion complexes is higher in the case of higher γCD concentration considered the equilibrium between the complex and the monomer as Eq. 3.4:

$$[\mathrm{M}] + [\gamma\mathrm{CD}] \rightarrow [\mathrm{IC}] \qquad (3.4)$$

Here [M] and [IC] represent for the monomer concentration and inclusion complex concentration. As a result, γCD was more steadily threaded on the polymer main chain during the polymerization in the case of higher [γCD] added in the system. As the aspect of the coverage ratio of the PRs, this result suggests that γCD was involved in the reaction for a topological connection other than chemical bonding.

Modified γCD for PR synthesis

When MMA was added, the mixture solution turned from clear to turbid as native γCD was dissolved in the solution. The reaction was performed in emulsion, which was considered as a reaction in a heterogeneous solution. To testify for the reaction in a homogenous state, HP-γCD was applied in replacement of native γCD. In the case of HP-γCD, less hydrogen bonding exists between molecules, so that inclusion complexes were more steadily separated in the solution without further coagulation happened. As a result, the solution remained clear after addition of MMA. With excess amount of MMA added to the mixture to [MMA]/[HP-γCD] = 2, small droplet of MMA can be observed in solution as partially escaped MMA in the system. The recipe that [MMA]/[HP-γCD] = 1 was chosen to compare with PR synthesized with the native γCD. After reaction, the mixture of polymer and HP-γCD turned into a milky emulsion as the similar behavior to the case of the recipe using the native γCD. As the result, the coverage

ratio of PR synthesized with HP-γCD was found around 0.2% as shown in Table 3.4. Low coverage ratio found in the PR synthesized with HP-γCD suggests that most of the HP-γCD were dethreaded during the reaction as similar condition elaborated in other publication using methylated βCD for synthesis of PMMA in aqueous solution.[40] These results implied that the reaction propagating in the channel structure of the γCD facilitated the threading behavior of the main chain polymer into the ring molecules.

Table 3.4 PR synthesized with HP-γCD and native γCD.

Entry	MMA	γCD[1]	PDMAPMA	Mn	PDI	Coverage ratio
HP-γCD PR	0.3g	4.7g (HP-γCD)	0.2g	37k	1.97	0.2%
γCD PR	0.3g	3.9g (Native γCD)	0.2g	27k	1.93	4.0%

Initiator: VA44 = 32mg. Reacted in 10ml of 8M urea aqueous solution under 50°C. [1]: [γCD] is fixed as 300mM.

3.3.6 MMA-γCD inclusion complexes

Stoichiometry of γCD to MMA in the inclusion complex

The solubility of γCD in water is about 200mM (0.249g/ml).[41] To increase the efficiency for cyclodextrin threading in the system, γCD with higher concentration was needed. To achieve this, 8M urea aqueous solution was used for higher solubility to dissolve γCD as a clear solution in high concentration for 500mM. When MMA was slowly added into the solution, the mixture became misty at first, and gradually turned into a milky solution during continuously stirring within 30mins. γCD is known as being able to covered 2.5 units of MMA as in the inclusion complexes with PMMA polymer.[34] In the case of the inclusion complex with MMA monomer, the stoichiometry (the molar ratio of γCD to MMA units) was investigated. To analyze the actual ratio in the inclusion complex, precipitation of inclusion complex was obtained by

centrifugation with the upper solution removed. The precipitated cake was then redissolved in DMSO and analyzed via NMR as shown in Fig.3.10. For excessed MMA added, the upper layer of monomer was observed as free monomers, not complexed with γCD. In the case of the precipitation, peaks of γCD and MMA were found in the spectrum. From the assignment of these peaks, the ratio of MMA to γCD was calculated from the integral are as Eq. 3.5.

$$\text{MMA}:\ \gamma\text{CD} = \frac{\text{B}}{3} : \frac{\text{A}}{16} \qquad (3.5)$$

As a result, MMA: γCD was found as 3.14: 1. This suggests that the capacity of γCD to monomer is higher than the polymer for thr higher degree of freedom for monomer molecules to fit into the cavity of γCD or be trapped in the gaps between the inclusion complexes.

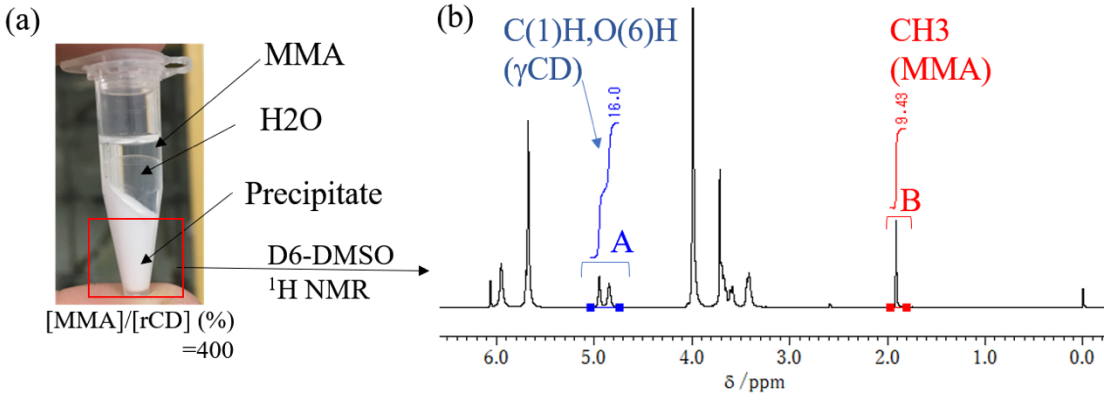


Fig. 3.10 Investigation of inclusion complexes of γCD and MMA. (a) picture of the mixture after centrifugation. (b) NMR spectrum of the precipitated part.

In the NMR analysis, the γCD signal in the inclusion complexes would not be detected because of the precipitation. Based on this phenomenon, the consumption of γCD because of the MMA addition in the D_2O solution was evaluated for the investigation of stoichiometry of γCD and MMA in the inclusion complex. Using maleic acid as an external reference with coaxial NMR tubes, relative concentration of γCD was traced. In the samples added with various amount of MMA, the residual amount of γCD in the system was calculated as Eq. 3.6.

$$\gamma\mathrm{CD}_{\mathrm{residual}} = \frac{[\gamma\mathrm{CD}]_0 - [\gamma\mathrm{CD}]_\mathrm{M}}{[\gamma\mathrm{CD}]_0} \qquad (3.6)$$

Here $[\gamma CD]_0$, $[\gamma CD]_M$ are the concentrations of dissolved γCD before and after addition of MMA, respectively. The result is shown in Fig.3.11. For [MMA]/[γCD] = 25%, the inclusion complexes were dispersed in the solution and less precipitation was observed. With increasing MMA concentration, the precipitation increased and corresponding signal of γCD was dramatically dropped. This suggests that 1 γCD trapped 3 units of MMA in an inclusion complex as the result roughly fitted the theoretical line of [γCD] = 3[MMA].

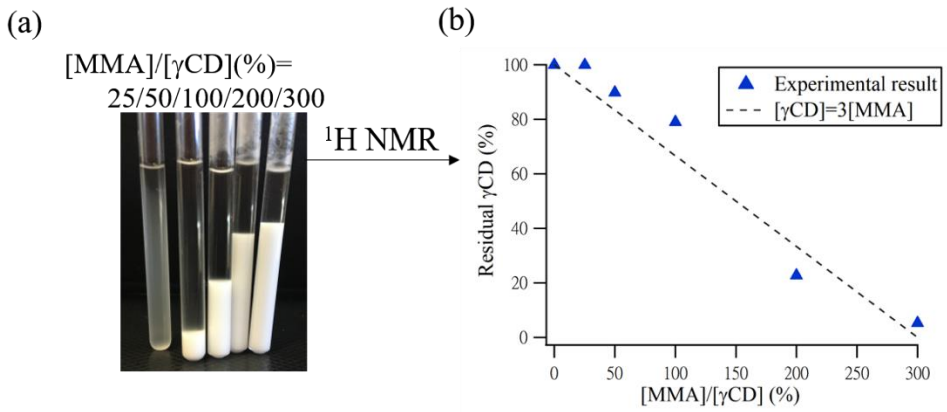


Fig.3.11 Evaluation of γCD consumption with MMA addition. [γCD]=300mM. (a) The mixture of MMA and γCD in D_2O solution. (b) Concentration plot of residual γCD from NMR analysis.

Mixture prepared from various concentration of MMA with fixed [γCD] =300mM was observed by optical microscope as in pictures showed in Fig.3.12. In the case of [MMA]= 150mM, the inclusion complexes were observed as a square shape. However, as concentration of MMA increased, droplets were observed to be surrounded by square shaped inclusion complexes. This suggests that excessed MMA was stabilized by inclusion complexes as a role like a surfactant. In other words, CD emulsion was formed in the mixture when high concentration of MMA was applied.[42]

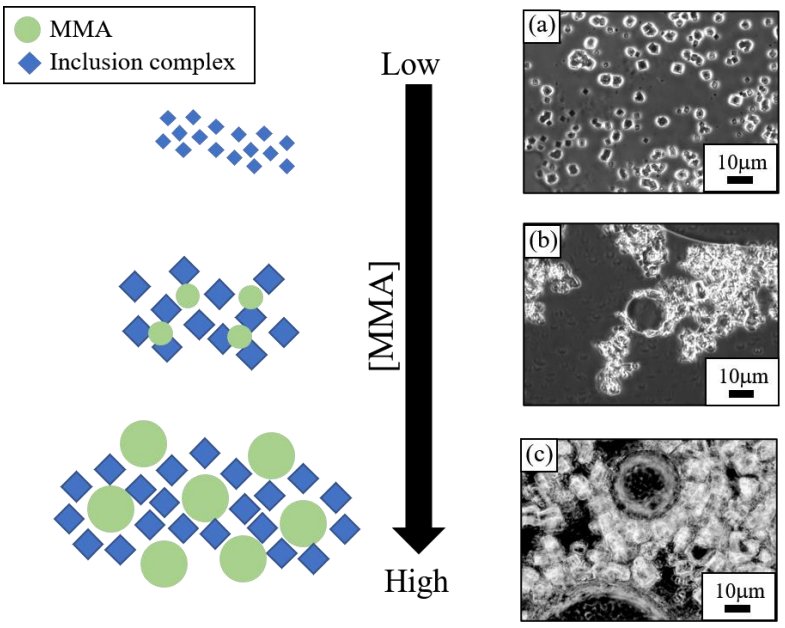


Fig. 3.12 Illustration of MMA droplets stabilized by inclusion complexes as increasing amount of MMA added and pictures under OM observation for the mixture of γCD solution in 300mM with various MMA concentration: (a) 150mM (b) 300mM (c) 600mM.

MMA feed ratio to the coverage ratio of polyrotaxane

Coverage ratio and molecular weight for PR synthesized in variety amount of [MMA] was investigated. [γCD] and [PDMAPMA] were fixed as 300mM and 10mM, respectively, and PR was prepared from the different amount of MMA feed. Mn and the coverage ratio are listed in Table.3.5 for $M_{15}C_{30}S_1$, $M_{30}C_{30}S_1$ and $M_{60}C_{30}S_1$ as corresponding [MMA] feed.

Table 3.5 PR synthesized with various of MMA feeding concentration.

Entry	MMA	γCD	PDMAPMA	[MMA]/[CD]	$Mn_{(MMA)}$ [1]	PDI	Coverage
$M_{60}C_{30}S_1$	0.6g	3.9g	0.2g	2	50.1k	1.96	4.5%
$M_{30}C_{30}S_1$	0.3g	3.9g	0.2g	1	26.9k	1.93	4.0%
$M_{15}C_{30}S_1$	0.15g	3.9g	0.2g	0.5	15.6k	1.63	12.1%

Reacted in 10ml of 8M urea solution with initiator of 32mg VA44 under 50℃ for 24hrs. [1]: $Mn_{(MMA)} = Mn_{(PR)}*(1\text{-}wt\%_{(\gamma CD)})$.

Molecular weight increasing linearly with [MMA] shows that the reaction was regulated through RAFT mechanism to achieve the molecular weight control. On the other hand, the coverage decreased with increasing feeding of [MMA]. With this result, the scheme of the reaction is proposed as shown in Fig. 3.13, where [IC], [PIC], and [P] represent the concentration of inclusion complex, polymer inclusion complex and polymer, resecitively. In the beginning of the mixing, inclusion complexes were formed form guest-host betwen MMA and CD. As excessed MMA was added over the capacity of CD, CD emulsion was formed as an alternative route to stabilize MMA droplets. When the chain propagation occurred within a monomer droplet, those segments of polymer were synthesized without γCD covered. As a result, the coverage ratio became lower in the PR synthesized under high [MMA] conditions.

$$[\mathrm{MMA}] + [\mathrm{CD}] \rightarrow [\mathrm{IC}] \rightarrow [\mathrm{PIC}] \rightarrow [\mathrm{PR}]$$
$$\text{MMA droplets} \downarrow \qquad \downarrow \text{ Dethreading}$$
$$[\text{CD emulsion}] \rightarrow [\mathrm{P}] + [\mathrm{CD}]$$

Fig. 3.13 Scheme of inclusion complexes and possible route for PR synthesis.

The highest coverage ratio of PR synthesized in this study was found to be 15% for $M_{15}C_{30}S_1$. In the case that molar ratio feed of MMA to γCD was smaller than 2.5 (for the ideal case that every MMA was covered by γCD to become inclusion complexes before reaction). It was considered that γCD could cover 2.5 units of MMA monomer in the inclusion complex with PMMA polymer, so that theoretical 100% coverage was expected. However, only 5%-15% of the coverage ratio was found in the PR synthesized in this work, which was much lower than expected even for the sample with excessed γCD applied. According to a previous report, the affinity of polymer to ring molecular is dependent on the molecular weight of the polymer.[7] In the result plotted as shown in Fig. 3.14, low coverage ratio for the PR with higher molecular

weight suggests that the dethreading occurred in beginning of PR synthesis because the polymer inclusion complex was not stable enough for polymer with a low molecular weight as a propagating chain. As the polymerization propagated, γCD was complexed more steadily when hydrophobicity of polymer chain increased with the growth of molecular weight. As the result, some of the γCD remained threaded on the polymer main chain when the polymerization ended, and finally PR structure was formed.

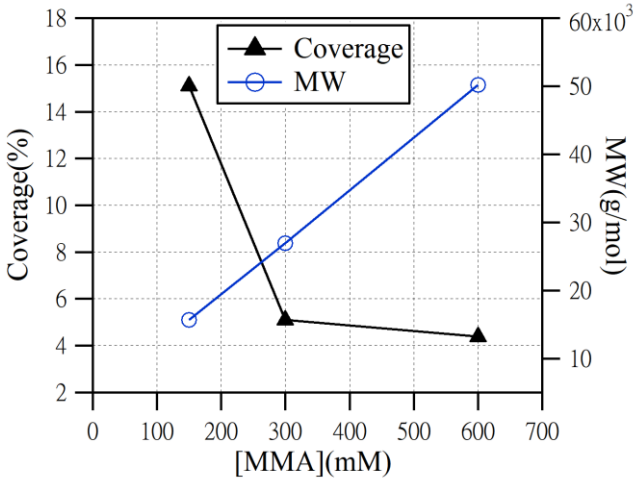


Fig. 3.14 Evolution of coverage and molecular weight on the concentration of MMA feed.

3.3.7 Thermal properties

For the polyrotaxane using PMMA as the main chain polymer, good thermal resistance is expected because of good thermal properties from PMMA homopolymer.[43] In order to investigate the thermal properties of PMMA based PR, thermogravimetric analysis (TGA) was performed to compare PMMA based polyrotaxane (PMMA-PR) prepared in this study ($M_{60}C_{30}S_1$) with a PEG based polyrotaxane (PEG-PR) with coverage ratio of 5% prepared in other work.[17] TGA and differential thermal analysis (DTA) curves were shown in Fig.3.15 (air atmosphere) and Fig. 3.16 (N2 atmosphere). In the air condition, PEG-PR showed a thermal degradation at 190℃ for the oxidation of PEG[44] shown as an exothermic peak in the DTA curve

and the weight loss in the TGA curve. The resulting TGA curve is considered as the emerging curve of γCD and PEG. On the other hand, PMMA-based PR showed better thermal resistance as almost no degradation occurred during the heating process and 90% weight lost at 410℃ as originated from the thermal durability of the PMMA main chain. In the case of N_2 condition, oxidation with oxygen was avoid and both PR started to degrade at higher temperature than the air condition. Among these results, PMMA based PR showed better thermal resistance than PEG based PR as durability for higher temperature and oxidation. The gel of elastomer prepared from PR prepared in this study is expected to show high heat resistance, which is planned to investigate as the future work.

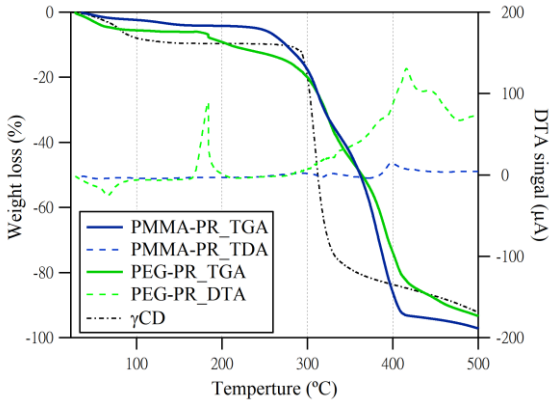


Fig. 3.15 TGA and DTA curves of PMMA-PR and PEG-PR under air atmosphere.

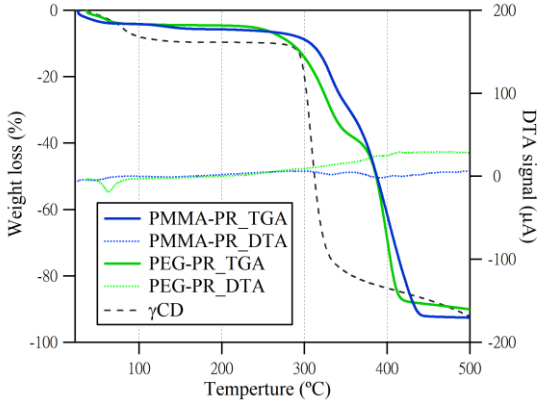


Fig. 3.16 TGA and DTA curves of PMMA-PR and PEG-PR under N_2 atmosphere.

3.4 Summary

BDATC as a CTA was applied to synthesize PDMAPMA in the condition of controlled polymerization. The PDI of the PDMAPMA was about 1.4 with molecule weight of 4.5k g/mol, which was closed to theoretical value. Using the PDMAPMA as polystopper, polyrotaxane composed of poly(DMAPMA-(MMA+γCD)-DMAPMA) as a PMMA based PR was successfully prepared. As the concentration of γCD feed in the recipe raised, the coverage ratio of resulting PR is higher because of the higher tendency toward inclusion complexes considered the equilibrium of the system. From the observation of optical microscope and NMR analyses, the behavior of hydrophobic MMA monomer in the mixture was recognized to be complexed with γCD or emulsified into a CD emulsion with the help of inclusion complexes. As the result, PR with the coverage ratio about 4%-5% was prepared for higher molecular weight of PMMA applied and about 12% of the coverage ratio was found for PR synthesized with smaller molecular weight. The resulting PR showed thermal resistance better than PEG-based PR, which can endure high temperature condition within 400℃.

3.5 Supporting information

Table S3.1 Recipe of PR synthesized via RAFT.

Entry	MMA	γCD	PDMAPMA	[MMA]/[CTA][1]	[MMA]/[CD]	VA44
$M_{60}C_{30}S_1$	0.6g	3.9g	0.2g	30	2	32mg
$M_{30}C_{30}S_1$	0.3g	3.9g	0.2g	30	1	32mg
$M_{15}C_{30}S_1$	0.15g	3.9g	0.2g	30	0.5	32mg
$M_{30}C_{30}S_2$	0.3g	3.9g	0.4g	15	1	32mg
$M_{30}C_{30}S_3$	0.3g	3.9g	0.6g	10	1	32mg
$M_{30}C_{50}S_1$	0.3g	6.5g	0.2g	30	0.6	32mg
$M_{30}C_{15}S_1$	0.3g	1.95g	0.2g	30	2	32mg
$M_{30}C_{07}S_1$	0.3g	0.93g	0.2g	30	4	32mg

Solvent: 8M urea aqueous solution. Reaction temperature: 50℃. Reaction time: 24hrs.

Table S3.2 Results of PR synthesized via RAFT.

Entry	Yield	Mn	PDI	Wt% of γCD[1]	Mn of MMA[2]	# of γCD[3]	Coverage[4]
$M_{60}C_{30}S_1$	46.4%	60695	1.96	17.3%	50184	45	4.5%
$M_{30}C_{30}S_1$	31.3%	32800	1.93	17.9%	26953	12	4.0%
$M_{15}C_{30}S_1$	4.6%	24500	1.63	36.0%	15658	34	12.1%
$M_{30}C_{30}S_2$	49.4%	17300	1.69	15.0%	14742	2	5.5%
$M_{30}C_{30}S_3$	41.4%	7500	1.84	21.2%	5917	2	9.8%
$M_{30}C_{50}S_1$	62.0%	63531	1.98	41.5%	37131	82	21.8%
$M_{30}C_{15}S_1$	43.7%	27500	2.15	7.4%	25460	8	1.3%
$M_{30}C_{07}S_1$	28.3%	28500	2.49	3.2%	27590	4	0.7%

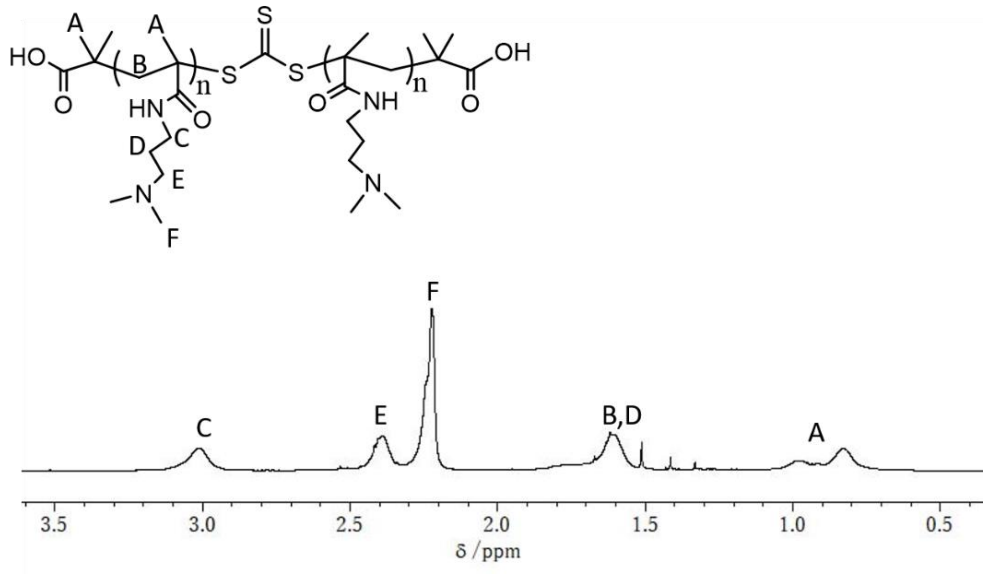


Fig. S3.1 NMR spectrum of PD_{30}. Solvent: d-DMSO. Temperature: 25°C.

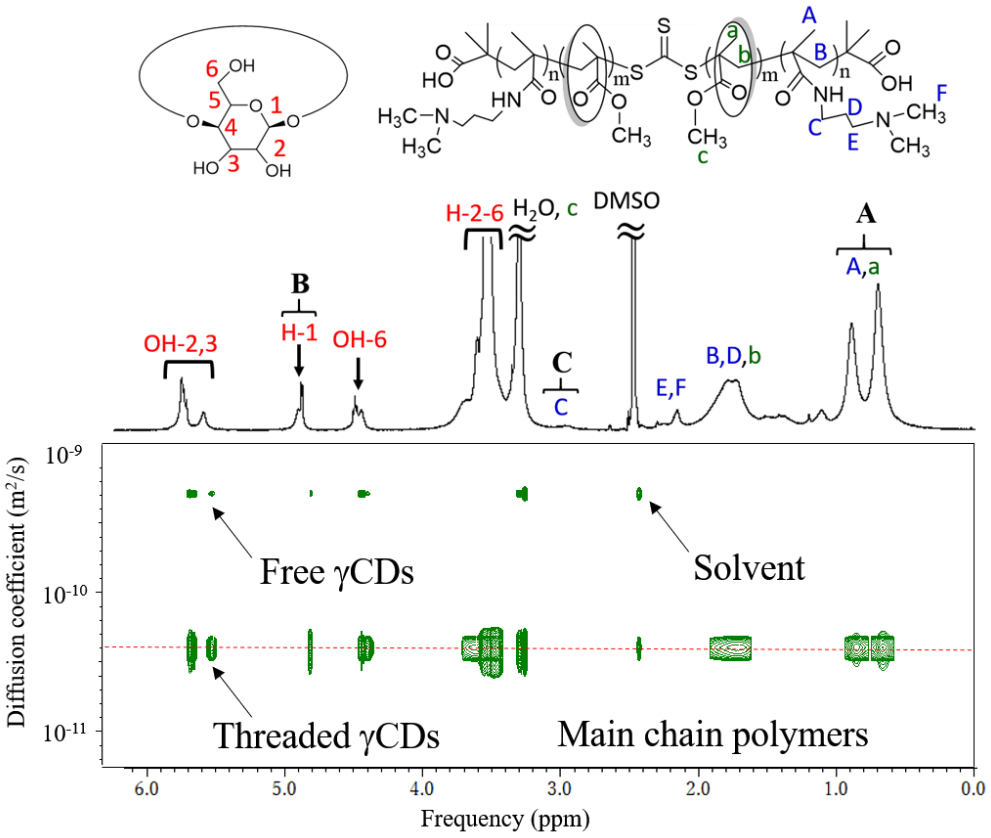


Fig. S3.2 NMR assignment and DOSY spectrum of PMMA based PR synthesized via RAFT ($M_{30}C_{30}S_1$). Solvent: d_6-DMSO, Temperature: 25°C.

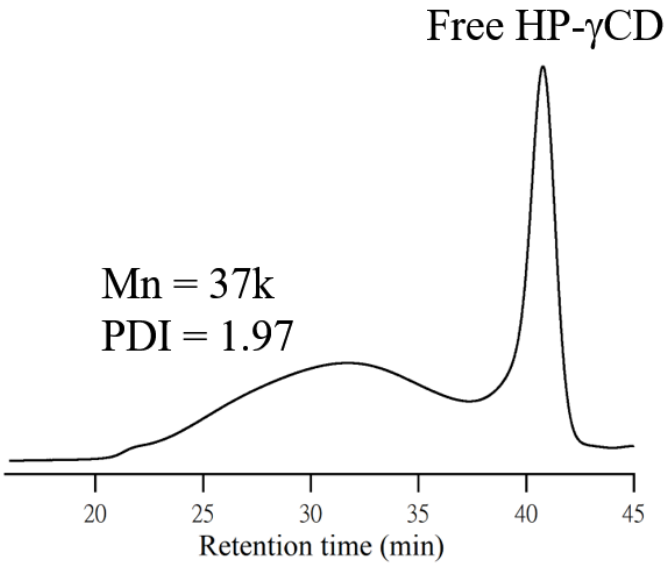


Fig. S3.3 GPC curve of PR synthesized with HP- CD. Eluent: DMSO (10mM LiBr) in 60°C. From the method elaborated in Chap. 2, amount of the free HP- CD was calculated from the calibration curve based on the peak height. As a result, weight percentage of the free HP-γCD was 17.5%.

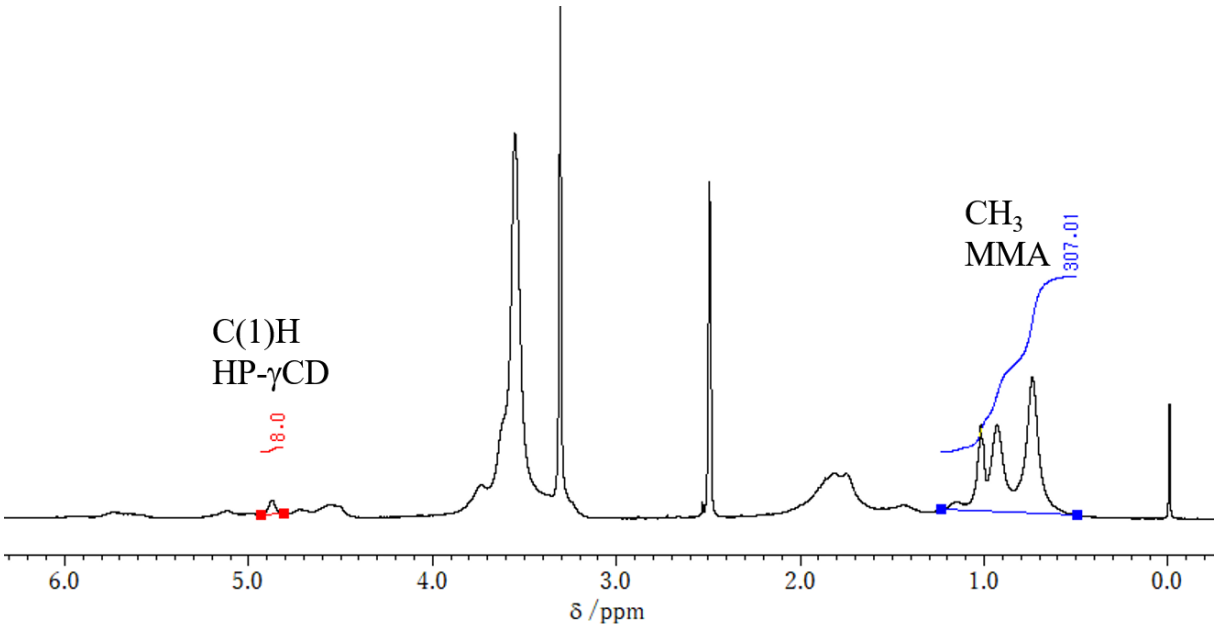


Fig. S3.4 NMR spectrum of PMMA based PR synthesized with HP- CD. Solvent: d_6-DMSO, Temperature: 25°C. From the method elaborated in Chap. 2, weight percentage of total amount of HP-γCD was 18.4%. As a result, the coverage ratio was calculated as 0.2%.

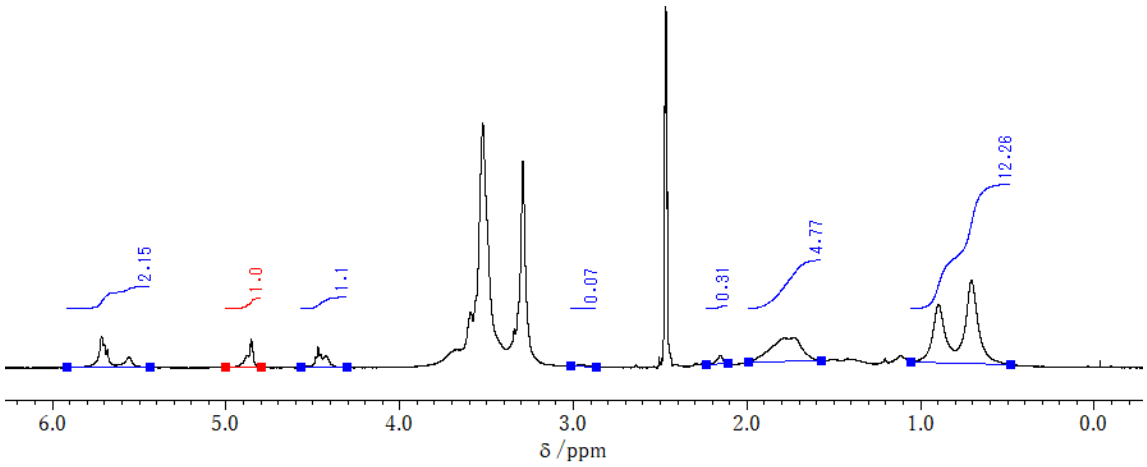


Fig. S3.5 NMR spectrum of $M_{30}C_{30}S_1$.

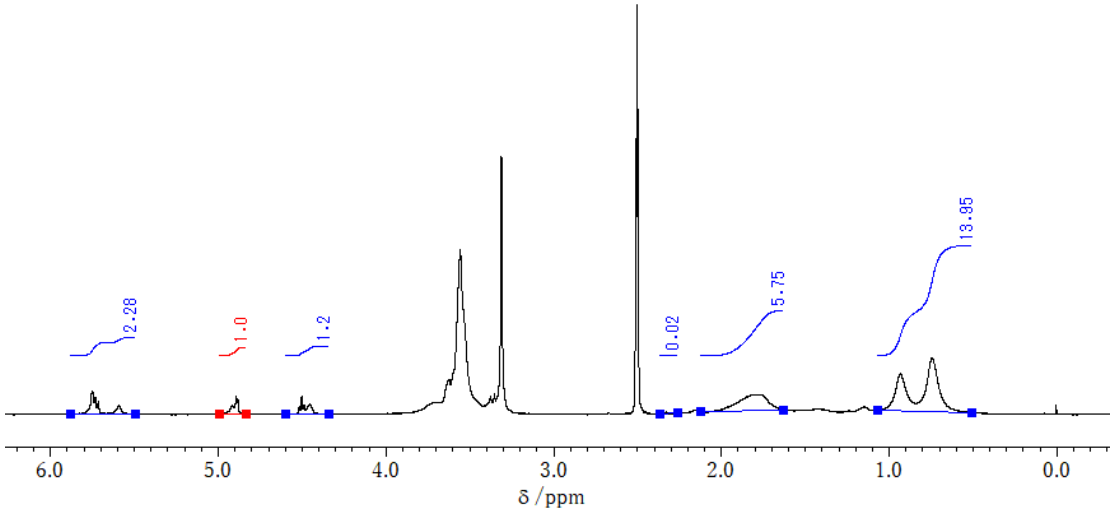


Fig. S3.6 NMR spectrum of $M_{60}C_{30}S_1$.

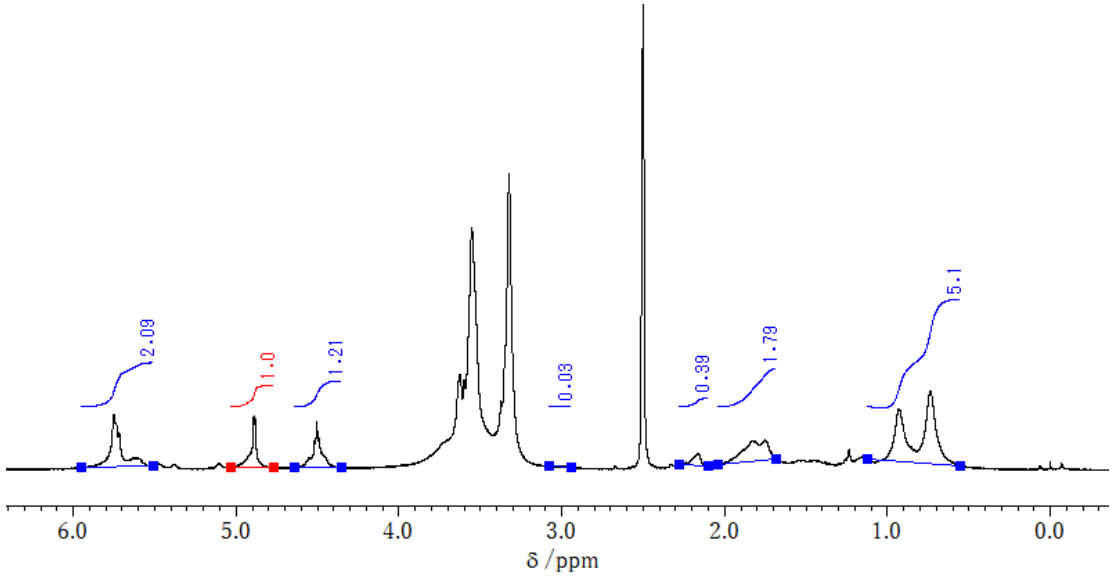


Fig. S3.7 NMR spectrum of $M_{15}C_{30}S_1$.

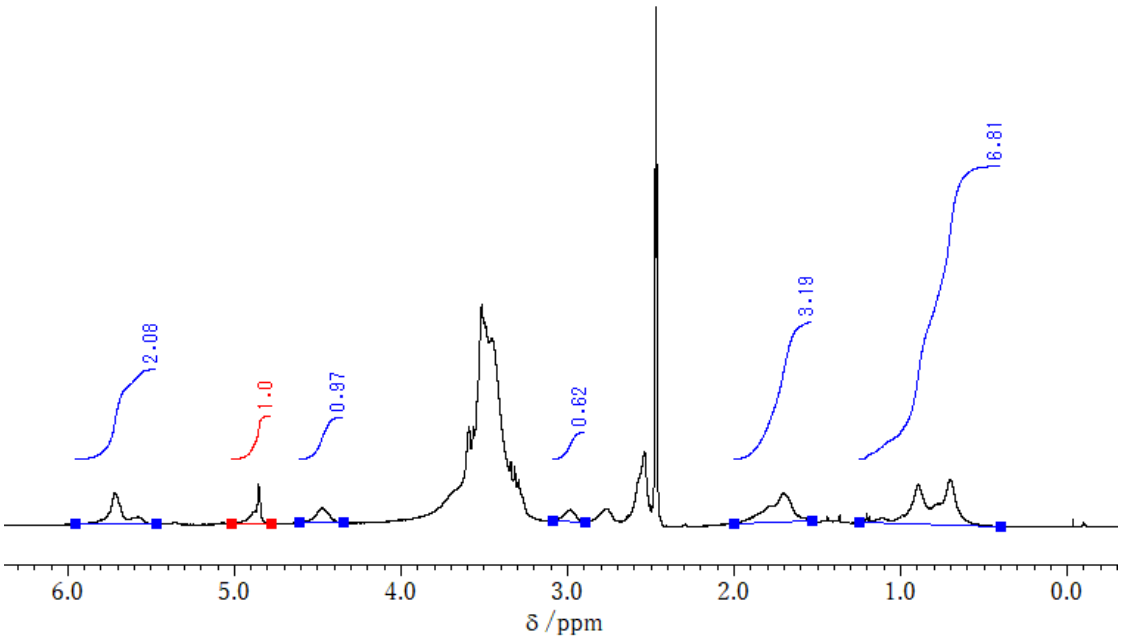


Fig. S3.8 NMR spectrum of $M_{30}C_{30}S_3$.

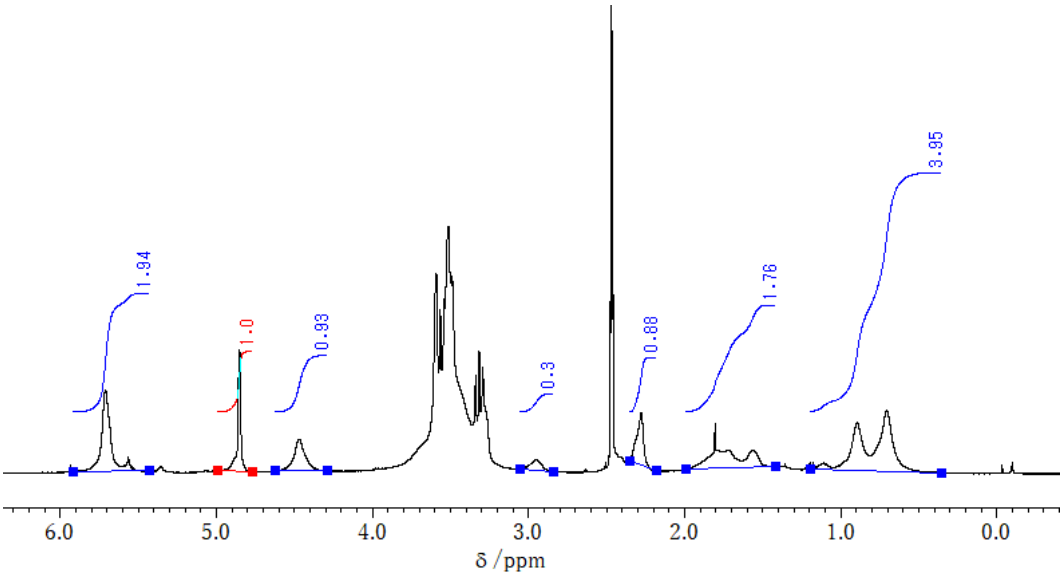


Fig. S3.9 NMR spectrum of $M_{30}C_{30}S_2$.

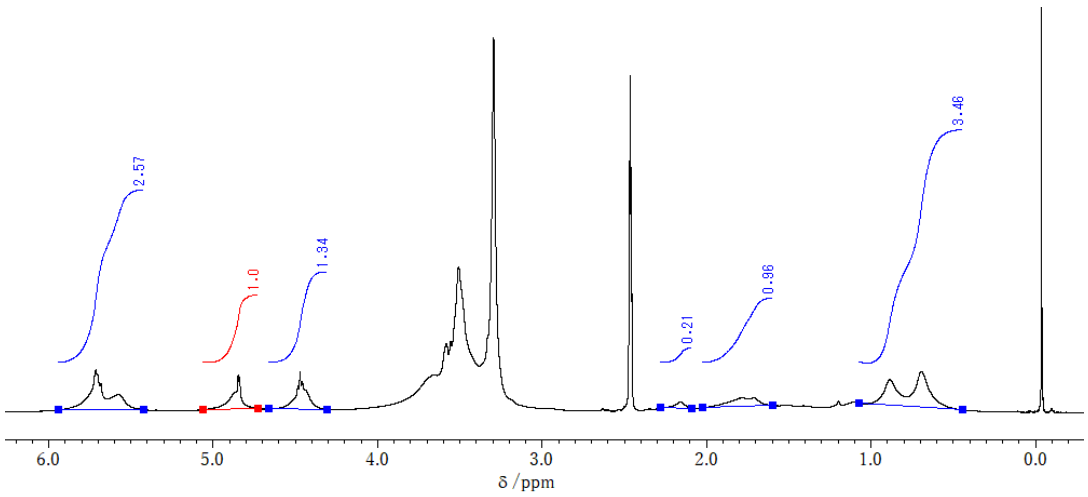


Fig. S3.10 NMR spectrum of $M_{30}C_{50}S_1$.

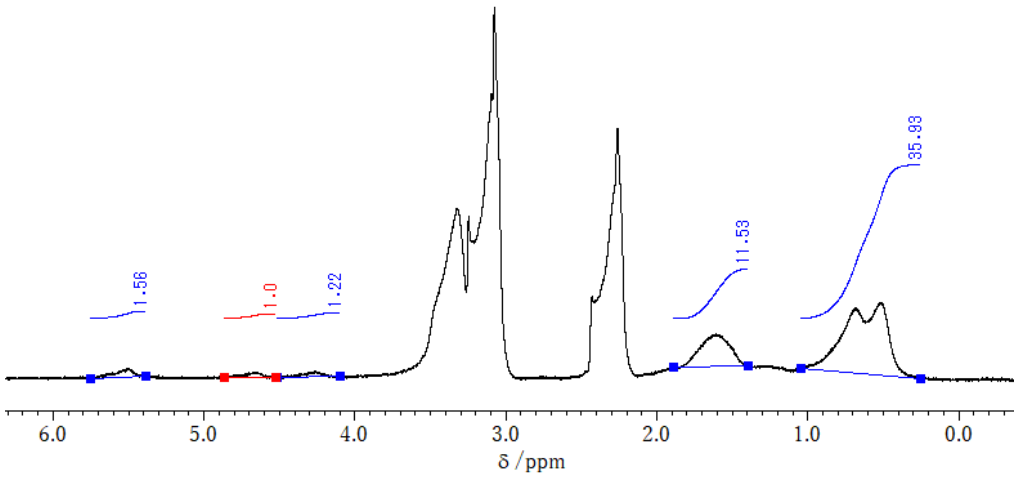


Fig. S3.11 NMR spectrum of $M_{30}C_{15}S_1$.

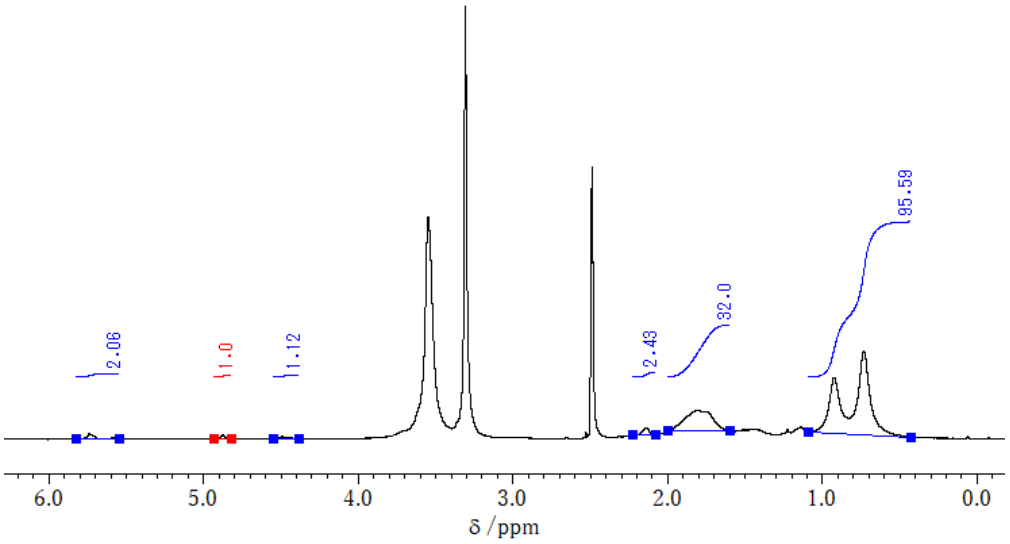


Fig. S3.12 NMR spectrum of $M_{60}C_{07}S_1$.

Chapter 4 Gel prepared from PMMA based polyrotaxane

4.1 Introduction

Slide-ring gel (SRG) is a gel prepared by crosslinking between ring molecules on the polyrotaxane. Since no chemical bonding between ring molecules and the main chain polymer, ring molecules can slide along the main chain. When a deformation is applied to SRG, the mechanical stress can equivalently distribute over the material via the sliding of movable crosslinking point. As the result, SRG shows better resilience and extensibility than conventional fixed crosslinked gel (FCG) as shown in Fig.4.1, known as the pulley effect. In 2001, Ito et al. first prepared SPR from polyrotaxane composed of PEG and αCD.[8] In Kato's report, the extensibility of SPR was found to be related to the coverage ratio.[45] The mechanical properties originated from the pulley effect are dependent on the interaction between ring molecules and main chain polymer. So far, the discussion and evaluation focused on the PR prepared from αCD-PEG combination. In this chapter, SRG prepared from PMMA-based PR synthesized in Chap.3 was investigated. The fixed crosslinked gel (FCG) was prepared from the copolymer involving hydroxyethyl methacrylate (HEMA) to compare with slide-ring gel. The PRs with various molecular weight were synthesized in Chap.3 via RAFT polymerization.

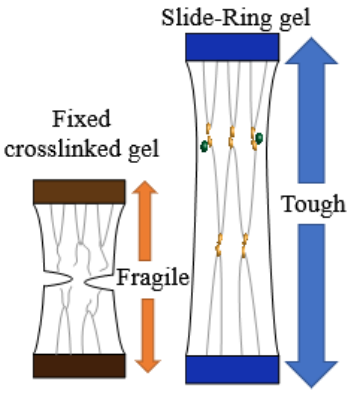


Fig. 4.1 Illustration for SRG and FCG under deformation.

4.2 Experimental

4.2.1 Material

Hydroxyethyl methacrylate (HEMA) (>95%, stabilized with monomethyl ether hydroquinone ,MEHQ), Dicyclohexylmethane 4,4'-Diisocyanate (DCDI) (>90%, mixture of isomers), and dibutyltin dilaurate (DBTBL) (>95%) were purchased from Tokyo Chemical Industry. 2,2'-azobis[2-(2-imidazolin-2-yl) propane] dihydrochloride (VA44) (>97.0%), methyl methacrylate (MMA) (>99.0%, stabilized with 0.005% hydroquinone, HQ), dimethyl formamide (DMF) (>99.5%, super dehydrated), and dimethyl sulfoxide (DMSO) (>99.0%, super dehydrated) were purchased from Wako Chemical. 1,1'-carbonyldiimidazole (CDI) (>90%) was purchased from Aldrich Sigma. Poly(N-[3-(dimethylamino)propyl] methacrylamide) (PDMAPMA) and PMMA based polyrotaxane (PMMA-PR) were prepared from the method elaborated in Chap. 3 noted as PD_{30}. Deionized water was obtained from an Organo Purelite PRB reverse osmosis/filtration unit (resistivity 14.6 MΩ).

4.2.2 Synthesis of poly(DMAPMA-(HEMA+MMA)-DMAPMA) block copolymer

HEMA, PD_{30} and MMA were mixed in deionized water and stirred for 30mins. The mixture was moved to a 3-necked reactor and put in an oil bath. VA44 was dissolved in another 1ml of deionized water and added to solution after the mixture was heated to 50℃ and reacted for 24hr. Resulting product was precipitated via centrifugation and washed with water for 3 times. White powder was obtained after lyophilization. The resulting copolymer prepared as triblock copolymer of poly(DMAPMA-(MMA+HEMA)-DMAPMA) is noted as PMMA-HEMA

4.2.3 Gel preparation

Sample for compression tests as a column shaped gel

The samples were dissolved in DMSO or DMF with the solid content of 10 wt% and stirred for 30 mins till fully dissolved. After degassed for 10 mins in a vacuum chamber, a prepolymer was prepared by adding CDI as the crosslinker into the mixture and stirring for 3 mins. The prepolymer was then moved to the mold with a column shape. For a prepolymer of 1ml mixture, the shape is shown in Fig. 4.2. The gelation processed as the prepolymer was put in a 70℃ oven overnight.

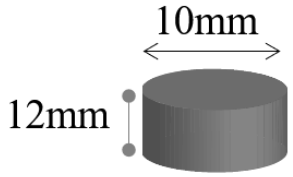


Fig 4.2 Shapes of the sample prepared for the compression tests.

Sample for tensile tests as a thin plate shaped gel

The samples were dissolved in DMSO or DMF with the solid content of 10 wt% and stirred for 30 mins till fully dissolved. For the samples used in tensile tests, the prepolymer was prepared by adding the DCDI as a crosslinker for 3wt% and DBTBL as a catalyst for 0.5wt% into the mixture. After degassed for 5 mins, a pregel was prepared for the preliminary gelation processed under room temperature for 24hrs. The pregel was then put in a vacuum chamber for another 24hrs to crosslink thoroughly. The plate shape gel was then cut with a cuter into the dumbbell shape as the criteria of JIS K6251 as shown in Fig. 4.3.

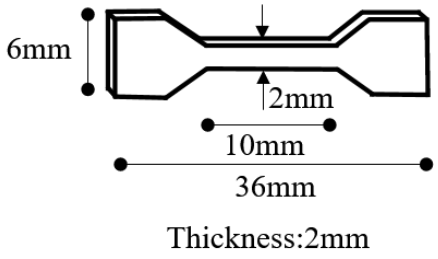


Fig 4.3 Shapes of the sample prepared for the tensile test.

4.2.4 Dynamic mechanical analysis (DMA)

Dynamic mechanical analysis was performed by Metravib DMA+300. The storage and loss moduli were measured in the frequency sweeping from 0.1hz to 30hz and the temperature sweeping from 25℃ to 80℃.

4.2.5 Compression test

Compression test was performed via Shimadzu-EZ-S universal tensile/compression machine using the column shape sample. Compression condition: 5mm/min in room temperature.

4.2.6 Tensile test

Tensile test was performed via Shimadzu-EZ-S universal tensile/compression machine using the dumbbell shape sample. Tensile condition: 5mm/min in room temperature.

4.3 Result and discussion

4.3.1 Chemical Gel confirmation from DMA analysis

The dynamic mechanical analysis result was shown in Fig. 4.4. There was no drastic change for the storage modulus (*E*') in the frequency range measured and slightly dropped with increasing temperature. This suggests that the bonding inside the gel remained in high T condition but some coagulation was collapsed for the reason of the dropping of *E*'. On the other hand, loss modulus (*E*") decreased gradually with increasing temperature. This suggests that the molecular friction was reduced at high temperature so that less energy was dissipated. From this result, the gel was confirmed to be chemically crosslinked for its sustainable mechanical properties during temperature change.

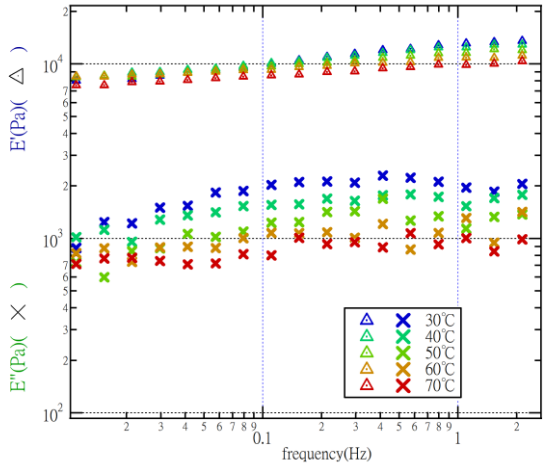


Fig. 4.4 DMA result of gel prepared from PMMA based polyrotaxane

4.3.2 Comparation with fixed crosslinking gel

Preparation of the copolymer for fixed crosslinking

In the preparation of slide-ring gel, hydroxyl groups on the CD molecules were crosslinked to build up movable crosslink points. In order to prepare copolymer with fixed hydroxyl groups

for the comparison, HEMA was applied as a hydroxyl resource in the block copolymer to be synthesized with PDMAPMA as shown in Table 4.1.

Table 4.1 Copolymer for FCG and PR for SRG

Entry	MMA	OH-source	macroCTA	Solvent	Mn	Mw	Coverage
PMMA-HEMA	0.25g	HEMA 0.065g	PDMAPMA 0.2g	H2O 10ml	17k	35k	N/a
PMMA-PR	0.6g	γCD 3.9g	PDMAPMA 0.2g	8M urea 10ml	61k	119k	4.5%

The molar ratio of MMA units to HEMA in the feed recipe was set as 50:1 to compare with the PMMA-PR because the molar ratio of MMA units to γCD was 50:1. The NMR spectrum of the resulting copolymer is shown in Fig 4.5 with the assignment of corresponding peaks. As the result, the molar ratio of MMA units to HEMA in the copolymer was 0.95:1. For the polymerization in the aqueous solution, HEMA as a hydrophilic monomer was miscible with marcoCTA. As a result, HEMA was more dominantly reacted and the molar ratio of MMA to HEMA in the copolymer was found higher than the expected result of 50:1.

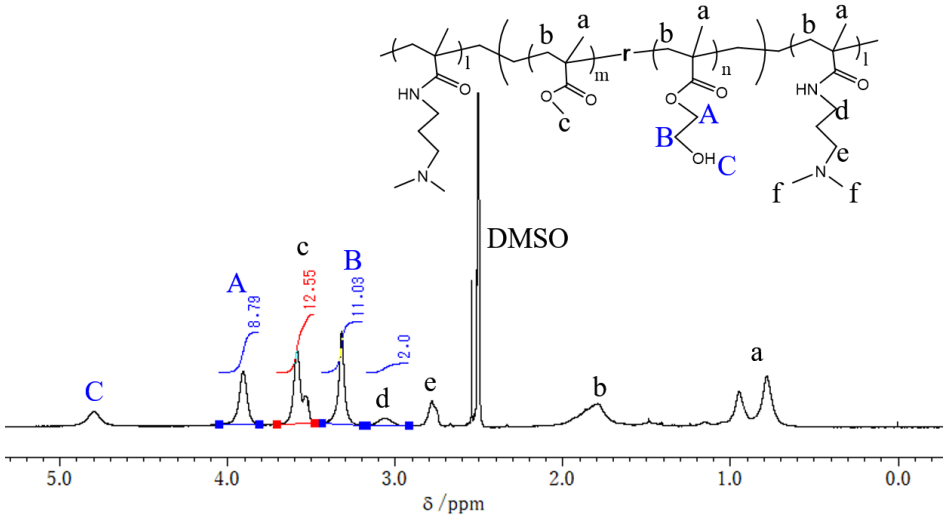


Fig 4.5 NMR spectrum of poly(DMAPMA-(MMA-r-HEMA)-DMAPMA) copolymer. Solvent: d6-DMSO. Temperature: 25°C.

Gel preparation

The crosslinking scheme is shown in Fig 4.6. Compared with movable crosslinking point existing in the slide-ring gel, fixed crosslinking gel was prepared by crosslinking the fixed hydroxyl groups on the HEMA segments in the copolymer. DMSO and DMF were used as the solvent to dissolve the polymer and crosslink the polymers. The results are shown in Table 4.2. The resulting polymer with HEMA can only dissolve in DMSO but is not soluble in DMF because of more hydrogen bonds in the polymer originated between hydroxyl groups. The PMMA-PR can dissolve in both DMSO and DMF to be a clear solution, but the resulting gels were slightly misty. For the PMMA-PR gel in DMSO, the gel was fragile and phased separated into two layers of gel and DMSO. For original homopolymer PMMA, DMSO is a theta solvent at 35℃ and becomes a good solvent in the condition of higher temperature.[46] In other words, DMSO is relatively a poor solvent for PMMA at room temperature around 25℃. In 70℃ as the crosslinking temperature, gel was swollen for DMSO, which is good solvent at high temperature. However, coagulation of PMMA occurred because of the high solid content in the mixture and the crosslinking was not equivalently reacted over the gel, which led to fragile gel. On the other hand, DMF gel was prepared using the solvent that can fully dissolve the sample and a compact gel was prepared and used for the mechanical tests in the next step.

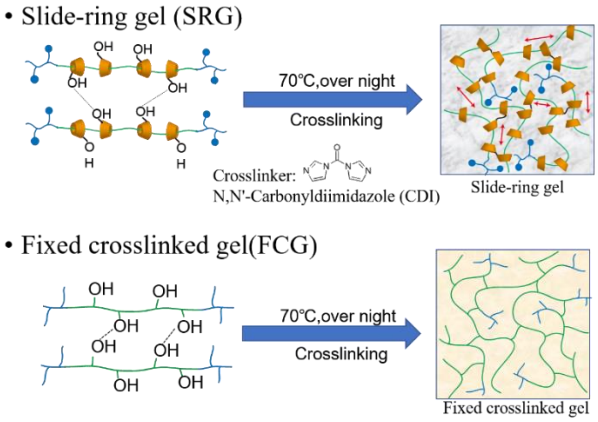


Fig4.6 illustration of the crosslinking process for SRG and FCG

Table 4.2 Gel prepared from PMMA-HEMA and PMMA-PR

Polymer	Solvent	Solid content	Crosslinker wt% (CDI)	Resulting gel
PMMA-HEMA	DMSO	10%	5%	O
PMMA-HEMA	DMF	10%	5%	X (Not soluble)
PMMA-PR	DMSO	10%	5%	X (Fragile)
PMMA-PR	DMF	10%	5%	O

Compression tests

For the compression tests, the Neo-Hookean model[47] was applied to evaluate the elastic properties in the curve fitting of the Eq. 4.1.

$$\sigma = \frac{E}{3}\left(\lambda - \frac{1}{\lambda^2}\right) \quad (4.1)$$

The result is shown in Fig. 4.7. In the initial strain at 1.0-1.2, the stress-strain curve can be fitted with the model. As more strain was applied to the gel, the hardening occurred because of the infinite extensibility in the crosslinking network. In the case of the gel from PMMA-PR as the slide-ring gel, the maximum strain reached over 90% of the original thickness and recovered after releasing the force as shown in Fig. 4.8. However, as the compression force was applied to the fixed crosslinked gel, the maximum strain was about 50% and the gel was broken into small pieces. For the Young's modulus of SRG and FCG, the moduli were close to each other for the condition of the solid content and the weight percentage of crosslinker fee was fixed as the same value. From the result of compression tests, the gel prepared from PMMA-PR showed higher toughness and better resilience than the fixed crosslinking gel. This suggests that the mechanism of the pulley effect is applicable for the polyrotaxane prepared in this study.

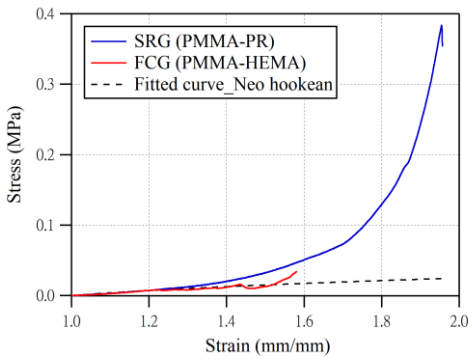


Fig. 4.7 Strain-stress curve of SRG and FCG. The fitted curve showed the Young's was about 46kPa for both gel

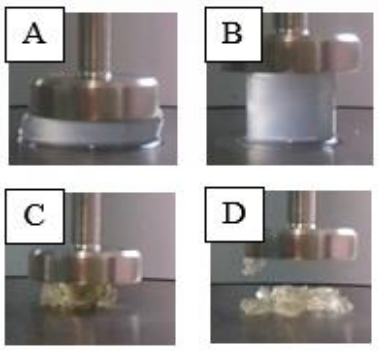


Fig. 4.8 Images of compression tests. SRG:(A) Under (B) After compression. FCG:(C) Under (D) After compression.

4.3.3 Mechanical properties for slide-ring gel prepared from PR of various molecular weight

From the synthesis method in chapter3, PRs with various molecular weights were obtained via corresponding recipe from the regulation of the RAFT polymerization. SPRs were prepared from theses PR to investigate the relationship of the mechanical properties to the molecular weight of PR. The list of PR applied is shown in Table 4.2.

Table 4.2 Polyrotaxane used for preparation of SRG from various MW polyrotaxanes

Entry	MMA	γCD	PDMAPMA	[MMA]/[PDMAPMA][1]	VA44	Mn	PDI	Coverage
$M_{60}C_{30}S_3$	0.6g	3.9g	0.2g	20	32mg	35165	1.74	5.2%
$M_{60}C_{30}S_2$	0.6g	3.9g	0.4g	30	32mg	44658	2.15	4.8%
$M_{60}C_{30}S_1$	0.6g	3.9g	0.6g	60	32mg	68907	2.53	4.9%

[1]: Ratio of MMA to PDMAPMA was calculated considered the DMAPMA with 2k molecular weight was applied in the reaction.

For the thin plate shape sample for the tensile tests, the gel prepared with CDI using $M_{60}C_{30}S_3$ from PR with lower MW was fragile. It can be considered that low reactivity of CDI and possible side reactions on the amide side chains on the PDMAPMA segments leaded to an inequivalent crosslinking. To prepare a contact gel for tensile tests, diisocyanate (DCDL) as another crosslinker with higher reactivity was applied. The SRGs were prepared from 10 wt% polymer solution of DMF and crosslinked with DCDL as crosslinker and DBTDL as catalyst. For the SRG prepared from PR with smaller MW, the extensibility reached to 150%. However, PR with higher MW showed more extensibility over 3 times of the original length as the curves shown in Fig. 4.9.

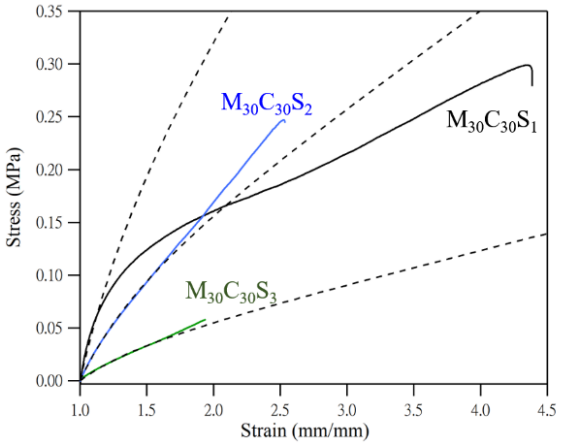


Fig. 4.9 Stress-strain curve of SRG from PR with various Mw. The Young's modulus evaluated by the Neo-Hookean model are 550kPa, 260kPa, 93kPa for $M_{30}C_{30}S_1$, $M_{30}C_{30}S_1$, $M_{30}C_{30}S_1$, respectively.

The main mechanism for the enhancement of a slide-ring gel may be the pulley effect. With the sliding movement during the application of outer force, the force can be equivalently distributed throughout the material. As the result, the material can exhibit the maximum mechanical properties. To achieve this property, enough sliding distance within the polyrotaxane is needed for ring molecules to slide. As PR with small molecular weight corresponding to shorter sliding distance, the behavior becomes more similar to fixed crosslinked gel because sliding distance cannot dissipate the force sufficiently. On the other

hand, the pully effect becomes more eminent for longer sliding distance in PR with higher molecular weight and higher extensibility was observed as shown in Fig 4.7. From a previous report, the extensibility of SRG prepared from PEG based polyrotaxane is related to the molecular weight of applied PR.[48] In that report, the Young's modulus was similar values for SRG from PEG based PR with various MW. In the case of PMMA based PR in this study, the Young's modulus showed positive relation to the molecular weight of applied PR. This might be considered as the interaction between the PMMA main chain increasing with PMMA segment in the PR. Since there are side chains on the PMMA segments as well, the silding behavior may be different from the PEG based PR in the sliding time scale or sensitivity to temperature condition. This is planned to be further investigated as the properties of SRG prepared from PMMA based PR.

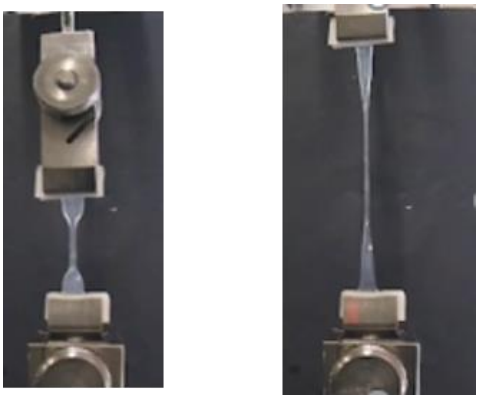


Fig 4.7 The extension of SRG (left) Origin shape (right) Extended

4.4 Summary

Using carbonyldiimidazole or diisocyante crosslinker to connect the hydroxy groups between PRs, the sliding-ring gel was successfully prepared from PMMA-based polyrotaxane. A block copolymer composed of poly(DMAPMA-HEMA+MMA-DMAPMA) was synthesized in order to prepare fixed crosslinked gel to compare with the slide-ring gel. In the compression test, SRG showed the resilience that the shape of the gel remained intact after 90% strain was applied and released. However, the fixed crosslinked gel was crashed at the applied strain over 50%. This suggests that PR prepared in this study showed the tough mechanical property originated from the sliding behavior. In the investigation for PR with various MW, it was found that SRG prepared from PR with higher MW showed more flexibility. This suggests that the extensibility of SRG is related to the sliding distance in PR as the force was dissipated through the movement of ring sliding along the main chain polymer.

Chapter 5 Conclusion and future work

A novel way to synthesize polyrotaxane has been proposed and investigated throughout many aspects of view. In a conventional way to synthesize polyrotaxane, it was hard to prepare polyrotaxane with a main chain polymer other than the polyethylene glycol. The reason can be considered that preferable combination of ring-linear molecules needed to be precipitated after complexation but water soluble for each component separately. Difficulties of finding proper combination has been an issue on the expansion for more application of polyrotaxane. Using the mechanism of rotaxanation, it became possible to synthesize polyrotaxane via a polymerizable monomer with a proper cyclodextrin. In this study, one of the combinations as MMA-γCD was shown as an exhibition for the possibility of this synthetic approach.

Using the combination of NMR and GPC analysis technics, the evidence of γCD existence was found. In the DOSY analysis, the resulting polymer was evaluated efficiently whether the γCD was threaded or not. In the three candidates of stoppers, DMAPMA was the most suitable stopper because there is no complexation with the γCD and a reasonable coverage ratio for the resulting polyrotaxane. Although PEGMA showed better efficiency to prevent γCD from dethreading, the inclusion complexes with side chains on PEGMA would be a bias for the evaluation of the coverage ratio.

Using DMAPMA as a stopper, a polyrotaxane was successfully synthesized as a PMMA based polyrotaxane. Main difference from a statistical polyrotaxane to a block polyrotaxane is that the linear segment was well defined as the sliding distance in a slide-ring material for the further investigation. The main parameters of MMA, CD, and macro CTA were investigated to illustrate the reaction scheme in the process. As increasing amount of the molar ratio of MMA to CD, excess MMA was forming monomer droplets that being stabilized by inclusion complexes as observed in the optical microscope. This result revealed that polymerization is possible to propagate in the channel structure as the secondary structure of inclusion complexes.

However, dethreading occurred during the polymer propagating because the hydrophobicity changes with the molecular weight, so is the stability of inclusion complex of polymer and γCD. Utilizing the special mechanism of RAFT polymerization, a PR with a molecular weight around 5k-100k with a coverage ratio around 1-10% was possible to be synthesized with desired value as performed in this study.

In the chapter 4, slide-ring gel was prepared from the polyrotaxane synthesized in chapter 3, which was composed of PMMA as a main chain polymer and γCD. To identify the resilience property from the sliding behavior, a polymer with fixed crosslinking point was synthesized using HEMA as alternative source of hydroxyl groups which were not slidable. As a result, the Slide-ring gel prepared from a polyrotaxane showed better extensibility and toughness than a fixed crosslinked gel in the compression tests. To investigate the relationship of the mechanical properties to the sliding distance, the slide-ring gel with various MW polyrotaxane were compared. In the tensile tests, the extensibility and the Young's modulus increased as higher Mw polyrotaxane was applied. This result suggests that the sliding distance between polystopper segment in the molecular structure of polyrotaxane is one of the important factors that effects the flexibility of a slide-ring material.

The polyrotaxane prepared in this study showed good thermal resistance and has potential to applied in other applications like ion exchange gel or self-healing painting. The mechanism of the polymerization involved with inclusion complex has not fully discovered as well. For the RAFT properties given in the polyrotaxane, possible modification via the special reaction or mechanism of RAFT would be one of the expectations to be further investigated.

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List of publications

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