Synthesis of Special Shaped Poly(methyl Methacrylate) via Halogenation of Growing Terminal in Stereospecific Living Anionic Polymerization

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Synthesis of Special Shaped Poly(methyl Methacrylate) via Halogenation of Growing Terminal in Stereospecific Living Anionic Polymerization

立体特異性リビングアニオン重合の生長末端ハロゲン化を用いたメタクリル酸メチルの特殊構造ポリマーの合成

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Contents

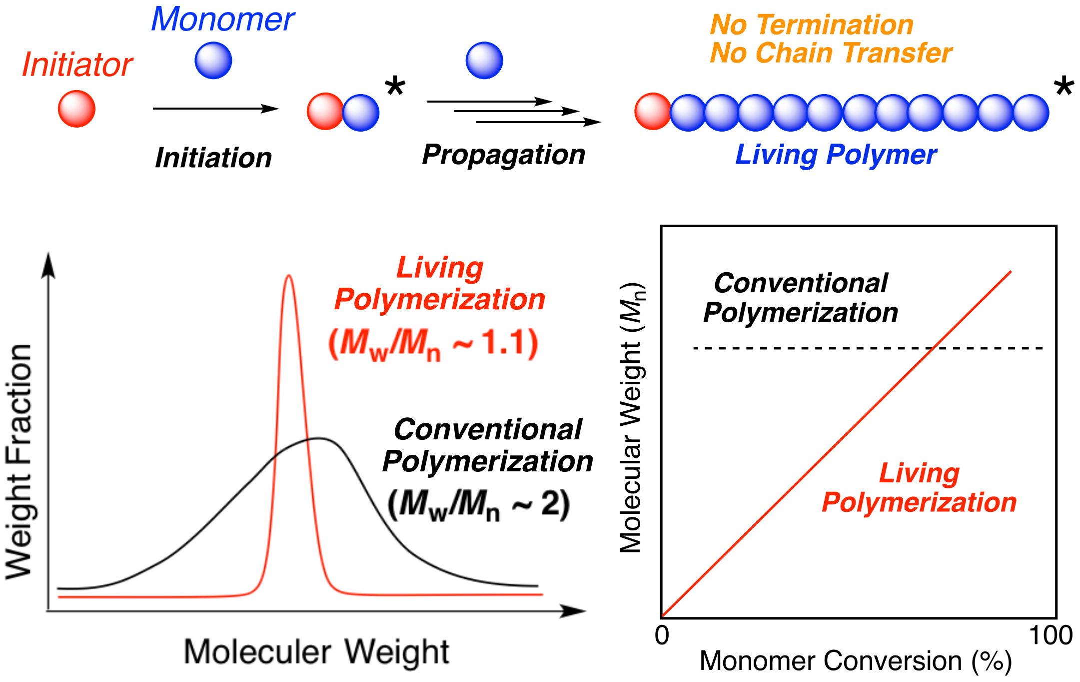
General Introduction

Background

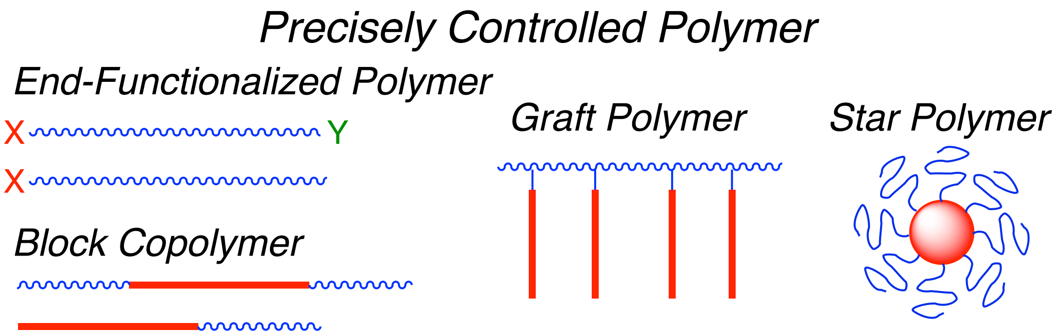
Living Polymerization

Since properties of polymers depend on their primary structures, such as molecular weights and stereostructures, methods for precision polymer synthesis are becoming important for development of new polymer materials.

In chain-growth polymerization such as addition polymerization of vinyl compounds, polymerization consisting of only initiation and propagation without side reactions such as termination and chain transfer reaction is called living polymerization (Scheme 1).[1] It is one of the most useful polymerizations for obtaining polymers with controlled molecular weights and terminal structures. Furthermore, living polymerization enables the synthesis of precisely controlled polymers, such as end-functionalized, block, graft, and star polymers, and is widely used for development of functional polymer materials based on special shaped polymers (Scheme 2).[2-28]



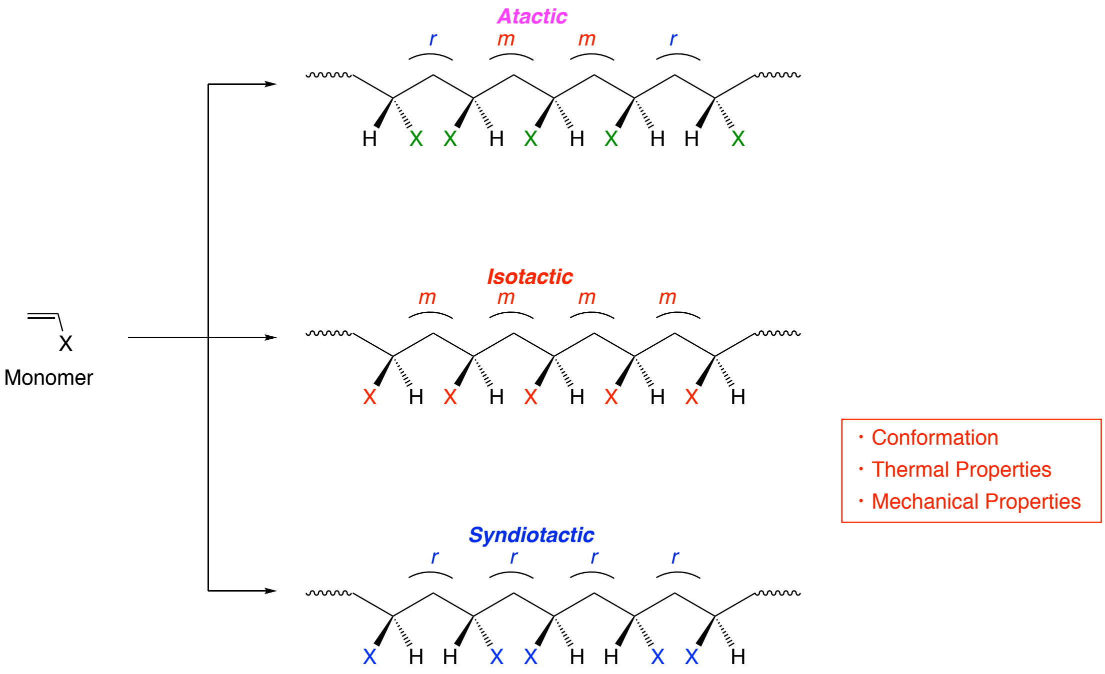
Scheme 1. Living Polymerization and Conventional Polymerization



Scheme 2. Precisely Controlled Polymer Synthesized by Living Polymerization

Stereospecific Polymerization

The configuration of adjacent monomer units in vinyl polymers, i.e., tacticity, is a very important factor, which determines the conformation of polymers and thus affects the thermal properties, such as glass transition temperature and melting point, and the mechanical properties. In conventional polymerizations of general vinyl monomers, atactic polymer with no stereoregularity is generally produced (Scheme 3).[29] However, it is possible to synthesize a stereoregular polymer, i.e., an isotactic polymer that consists of the same configuration between the adjacent monomer units or a syndiotactic polymer that consists of the opposite configuration, by designing the monomer structure as well as the initiator or catalyst.[30-35] Stereospecific polymerization thus improves the function and performance of the resulting polymers based on their controlled stereostructures.[36-37]



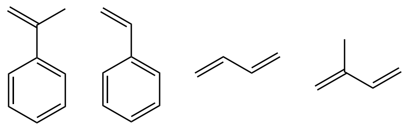
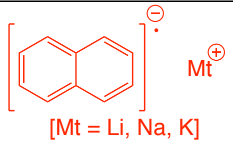
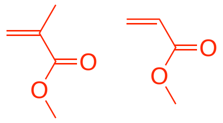
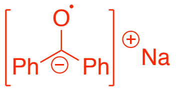
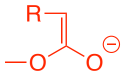
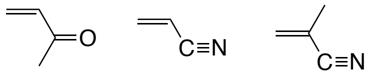
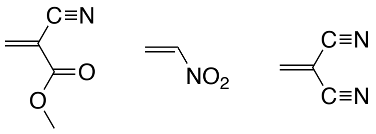
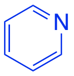
Scheme 3. Stereostructures in Vinyl Polymers

Living Anionic Polymerization

Among various living polymerizations, living anionic polymerization was first discovered in 1956 by Swarc et al. using sodium naphthalenide as the initiator for polymerization of styrene, which can generate a stable carbanion, in non-polar solvent under rigorously dried and vacuum conditions without water and oxygen.[38-39] A similar living anionic polymerization is achievable for conjugated monomers with no polar substituents including styrene and conjugated dienes, such as butadiene and isoprene, by organometallic reagents with high nucleophilicity such as butyllithium as the initiator.

In contrast, living anionic polymerization of polar vinyl monomers such as methacrylates and acrylates has been considered difficult due to side reactions associated with the carbonyl groups, though these monomers are polymerizable even with a weaker nucleophilic agent due to their higher reactivities originating from the stronger electron-withdrawing groups. However, since the discovery of group transfer polymerization in 1980s, various living anionic polymerizations of polar vinyl monomers have been developed. Table 1 summarizes the relationships between monomers with different reactivities and nucleophilic reagents with different nucleophilicities in anionic polymerization.[40] Living anionic polymerization of various vinyl monomers is now possible by designing the polymerizations.

Table 1. Relationships between Monomer and Initiator in Anionic Polymerization

	Monomer		Initiator
A		a	Li, Na, K RLi 
B		b	RMgX, R_2Mg tBuOK $LiAlH_4$  
C		c	RONa/ROH R_3Al R_2Zn NaOH $LiZnBuEt_2$, $LiAlBuEt_3$, $CaZnEt_4$
D		d	Et_3N Ph_3P  ROH H_2O

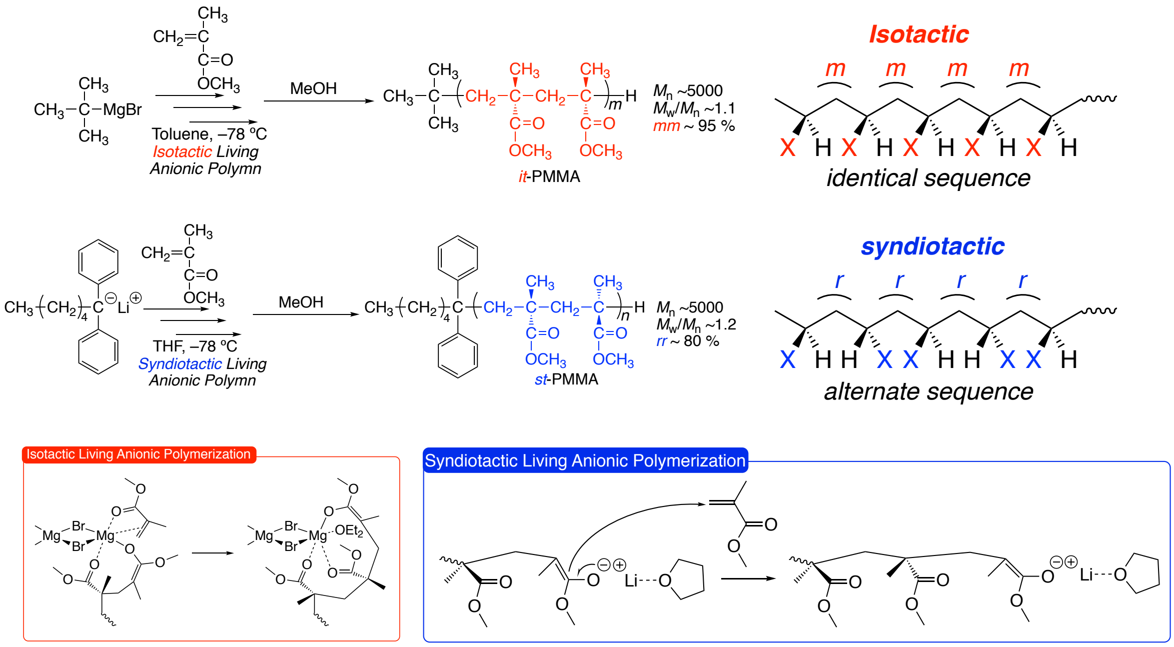
Stereospecific Living Anionic Polymerization

In living anionic polymerization, a counter-cation consisting of metal as the initiator component affects not only the reactivity of the growing anion but also the stereospecificity in the polymerization via interaction with the growing anion as well as the substituent in the side chain. Indeed, it is reported that stereospecificity in living anionic polymerizations can be changed by designing the initiators, solvents, and reaction conditions.[41-46]

For example, in living anionic polymerization of methyl methacrylate (MMA), isotactic poly(methyl methacrylate) (*it*-PMMA) is produced using *t*-BuMgBr as an initiator in toluene at –78 °C, where the molecular weight is well controlled and *mm* triad is as high as 95%. In this polymerization, the isotactic propagation is supposed to come from the unique coordination of the Mg counter-cation to not only the propagating enolate anion but also the carbonyl groups of the penultimate unit and the incoming monomer.

On the other hand, syndiotactic (*st*-) PMMA with *rr* of about 80% and controlled molecular weight can be obtained in living anionic polymerization of MMA with 1,1-diphenylhexyl lithium (DPHLi) as the initiator in tetrahydrofuran (THF) at –78 °C. In this polymerization, the bulky initiator 1,1-diphenylhexyl anion diminishes the side reaction in the initiation while THF coordinates to lithium cation and weakens interaction of with the enolate terminal to enable attack of the incoming monomer from the less sterically hindered side to the propagating anion and to enable the syndiotactic enchainment.

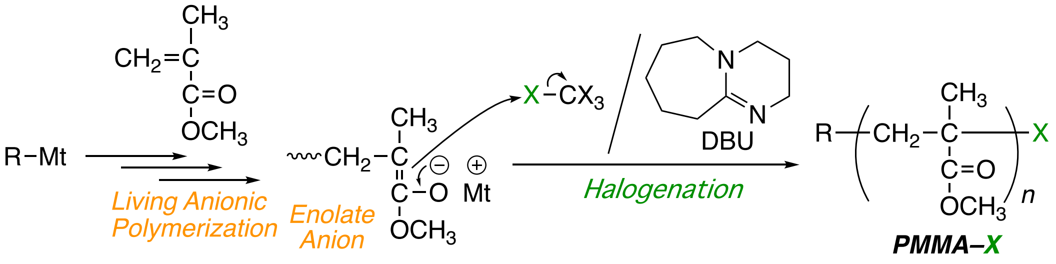
Thus, a designed living anionic polymerization is capable of simultaneous control of molecular weight and stereostructure of the resulting polymers. Such a stereospecific living anionic polymerization can be further utilized for the synthesis of special shaped polymers consisting of stereoregular polymer chains, however, the growing terminals in the stereospecific living anionic polymerizations are generally unstable to air, moisture, and temperature. Therefore, it is generally difficult to directly use the growing terminal for the precision synthesis of special shaped polymers (Scheme 4).

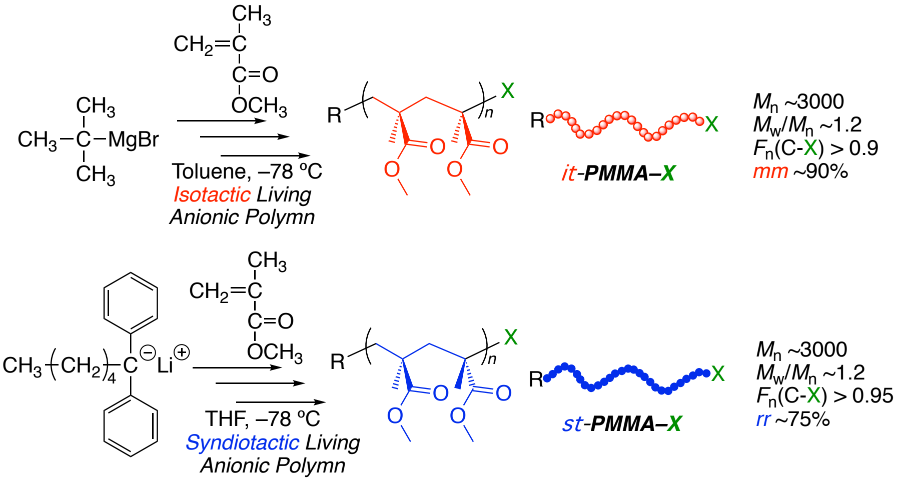


Scheme 4. Stereospecific Living Anionic Polymerization of MMA

Halogenation of Growing Anionic Terminal

Recently, the author's group reported that, in these stereospecific living anionic polymerizations of MMA, halogen compounds such as carbon tetrachloride and bromotrichloromethane were used as terminators in the presence of a strong base such as diazabicycloundecene (DBU) to generate the stereoregular PMMAs that possess carbon-halogen bond at the terminal almost quantitatively (Scheme 5).[47]





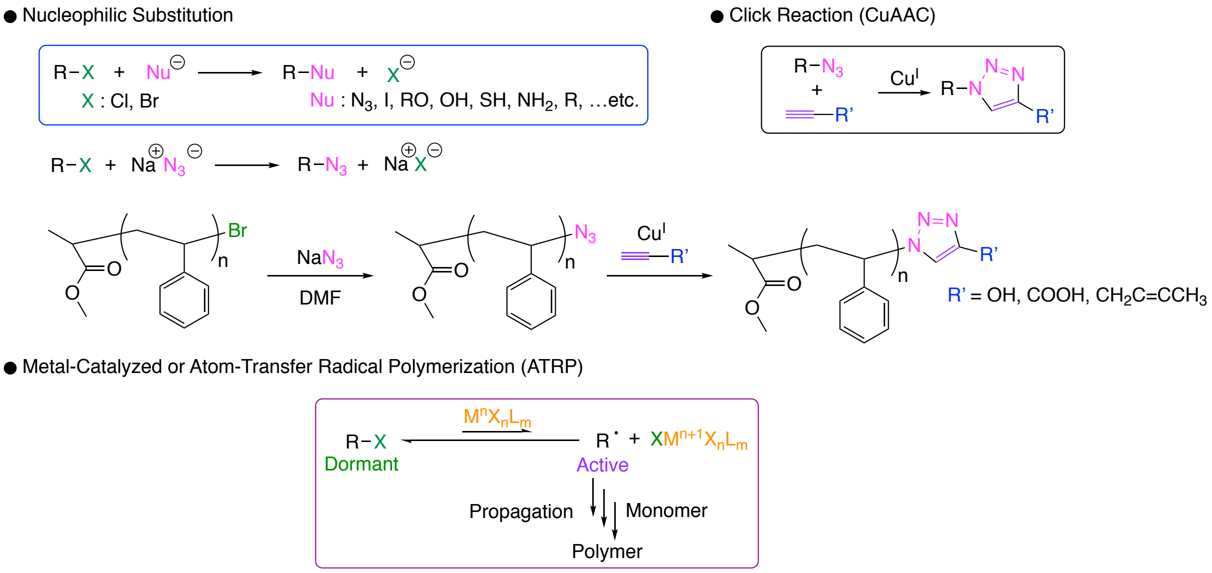
Scheme 5. Halogenation of Growing Terminal in Stereospecific Anionic Polymerization

Application of Halogenated Terminal

It is generally recognized that carbon–halogen bonds are stable but reactive and can be easily converted into various functional groups via nucleophilic substitution reactions (Scheme 6). In particular, recently, the nucleophilic substitution with azide anion using sodium azide is widely employed for the synthesis of not only organic compounds but also polymer molecules because the resulting azide group can be used for further functionalization through copper-catalyzed azide-alkyne cyclization addition reaction (CuAAC)[48-52], which is one of the highly efficient and highly selective click reactions.

In view of polymerization, the carbon–halogen bonds can be used as the starting site for the metal-catalyzed living radical polymerization or atom transfer radical polymerization (ATRP) via generation of the carbon radicals using appropriate transition metal catalysts.

A combination of halogenation of stereospecific living anionic polymerization and subsequent reactions based on the stable and reactive carbon–halogen bond is expected to enable the synthesis of special shaped polymers having stereoregular polymer chains with controlled chain lengths.[53-57]



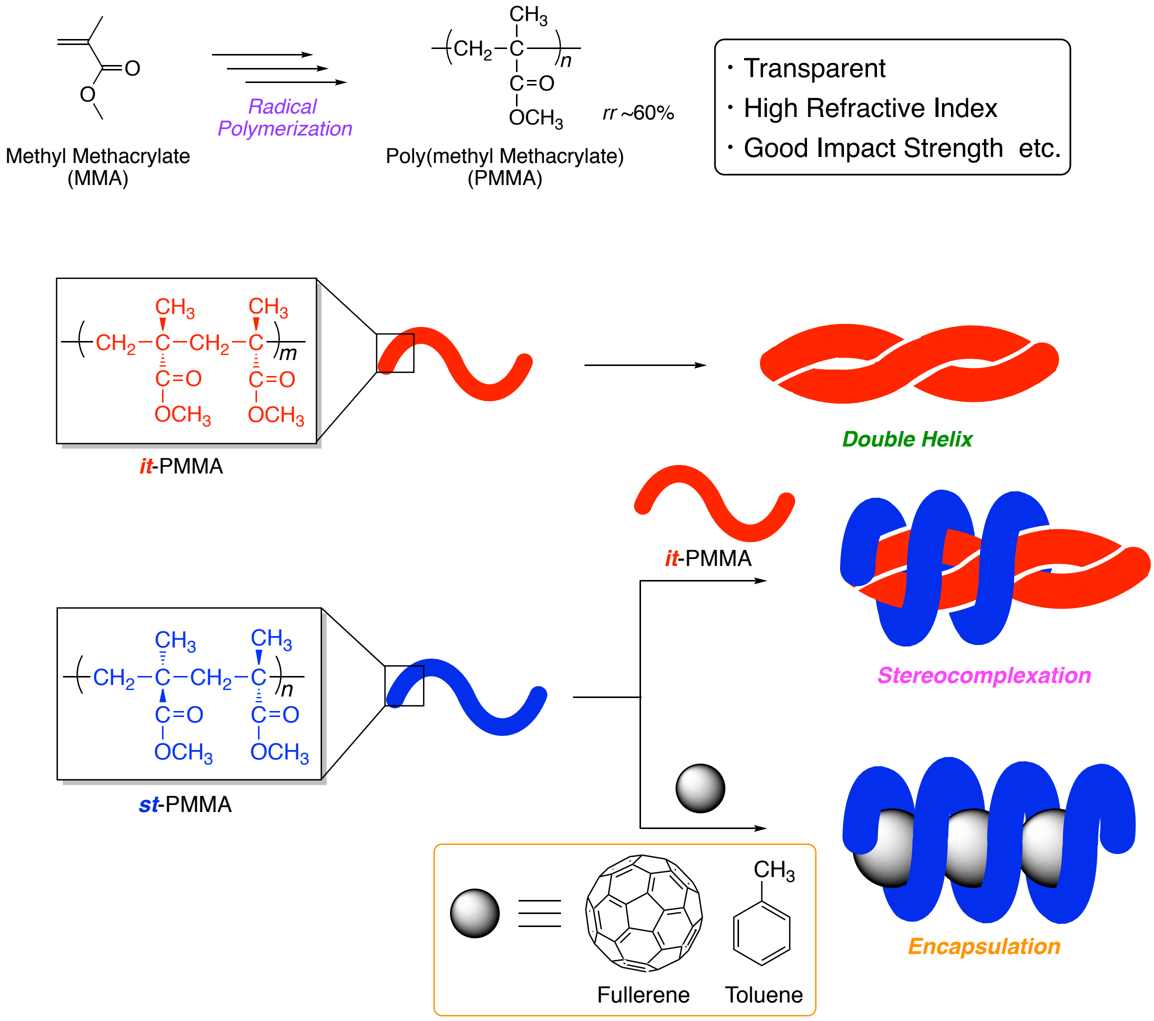
Scheme 6. Application of Halogenated Terminal

Poly(methyl Methacrylate) (PMMA)

Commercial PMMA is widely used as a transparent resin due to its excellent optical and mechanical properties and is generally produced by radical polymerization, which results in the atactic or somewhat syndiotactic rich (*rr* ~ 60%) polymer (Scheme 7).

As described above, stereoregular PMMA can be synthesized by stereospecific anionic polymerization. The *it*-PMMA and *st*-PMMA show different glass transition temperatures and furthermore crystallinity.[58-59] Additionally, it has been also reported that *it*-PMMA forms a double helical structure while *st*-PMMA forms stereocomplex with the *it*-PMMA double helical chains and encapsulates small molecules like fullerene and toluene.[60-78]

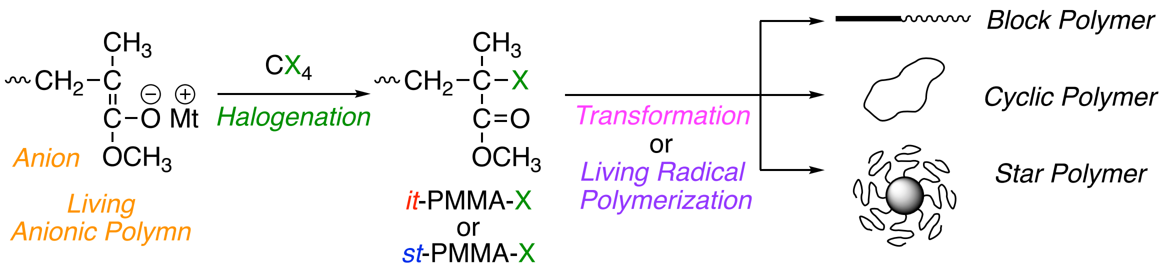
The incorporation of these well-controlled stereoregular structures, which can be achieved by the stereospecific living anionic polymerization, into various special shaped polymers is expected to contribute to developments of novel functional polymer materials based on the characteristics of the stereoregular chains and special architectures.[79-83]



Scheme 7. Properties of PMMA and Supramolecular Structures of Stereoregular PMMA

Objectives

Against this background, the author's research theme is to quantitatively halogenate the growing terminal of the stereospecific living anionic polymerization of MMA and to subsequently convert the halogen into the azide group capable of click reaction or to initiate the living radical polymerization from the carbon–halogen bond using the appropriate transition metal catalysts for the precision synthesis of special shaped polymers, such as block, cyclic, and star polymers, having highly stereoregular chains and special shapes (Scheme 8).



Scheme 8. Synthesis of Special Shaped Stereoregular PMMA via Halogenation of Growing Terminal in Stereospecific Living Anionic Polymerization

Based on this objective, the author's aimed at the following three things:

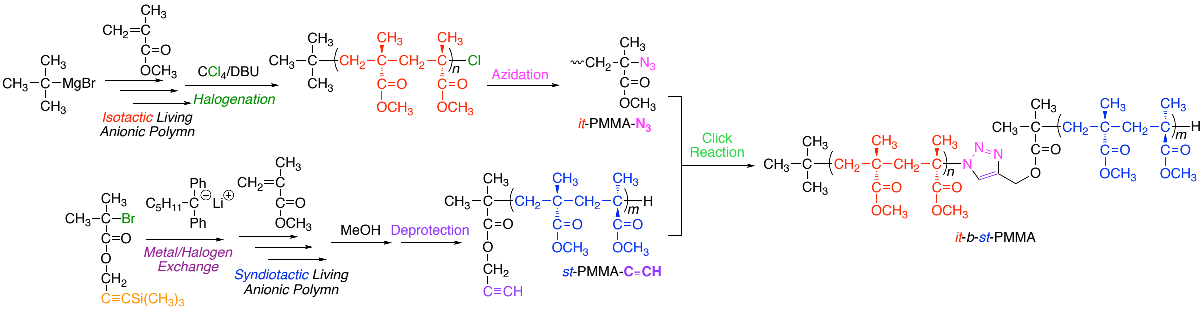
(1) Synthesis of stereoblock poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with metal-halogen exchange, halogenation, and intermolecular click reaction

(2) Synthesis of stereoregular macrocyclic poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with metal-halogen exchange, halogenation, and intramolecular click reaction

(3) Synthesis of stereoregular star poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with halogenation and crosslinking living radical polymerization

(1) Synthesis of stereoblock poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with metal-halogen exchange, halogenation, and intermolecular click reaction

The first objective of this thesis is the synthesis of stereoblock polymer consisting of *it*-PMMA and *st*-PMMA via combination of halogenation of the growing terminal, transformation of the terminal halogen into azide group capable of click reaction, and introduction of alkyne by end-functionalized initiator method using metal-halogen exchange reaction. The stereoblock PMMA can be obtained by intermolecular click reaction between the azide-capped *it*-PMMA obtained via halogenation of growing terminal in isotactic living anionic polymerization and alkyne-capped *st*-PMMA obtained via syndiotactic living anionic polymerization using an initiator with protected alkyne. The obtained stereoblock PMMA was evaluated by stereocomplex formation (Scheme 9).



Scheme 9. Synthesis of Stereoblock PMMA via Combination with Halogenation of Growing Terminal, Click Reaction, and Metal-Halogen Exchange Reaction

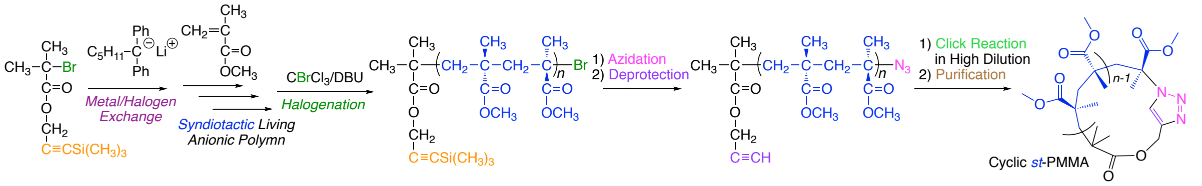
(2) Synthesis of stereoregular macrocyclic poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with metal-halogen exchange, halogenation, and intramolecular click reaction

The second objective of this thesis is the synthesis of syndiotactic cyclic polymers by combining halogenation of growing terminal in syndiotactic living anionic polymerization, transformation of terminal halogen into azide group capable of click reaction, and intramolecular click reaction between alkyne and azide groups at the chain ends of the heterotelechelic stereoregular polymer.

Since cyclic polymers have no terminals, they show specific features, such as small hydrodynamic radius, high glass transition temperature, and low viscosity, in comparison to the linear polymers with the their terminals. Recently, relatively high-yield synthesis of cyclic polymers has been reported via click reaction of heterotelechelic polymers under high dilution. In particular, combinations of living radical polymerization and highly efficient click reaction have enabled the synthesis of various cyclic polymers in relatively high yield.

Therefore, in this study, the author synthesized heterotelechelic syndiotactic PMMA capable of click reaction by controlling initiation and termination in syndiotactic living anionic polymerization of MMA, and then conducted cyclization to obtain the cyclic syndiotactic PMMA (Scheme 10).

Specifically, the precise synthesis of cyclic syndiotactic PMMA was examined as below: an α-haloester having a protected alkyne was enolated by metal-halogen exchange reaction, from which syndiotactic living anionic polymerization of MMA was started, after the polymerization, the growing terminal was halogenated and subsequently converted into the azide group, then deprotection of the alkyne at the initiating terminal was conducted, and then the synthesis was completed by intramolecular click reaction under high dilution.



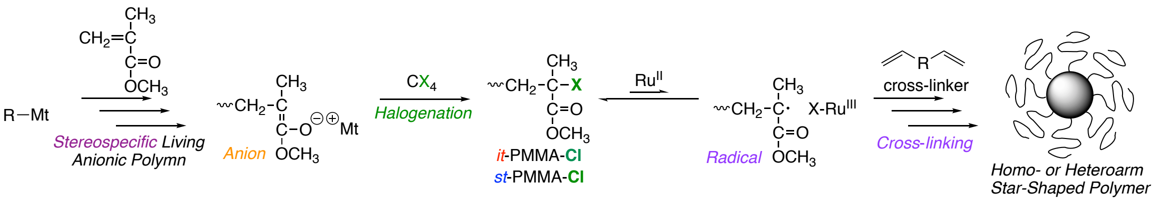
Scheme 10. Synthesis of Cyclic Syndiotactic PMMA via Combination with Halogenation of Growing Terminal and Transformation from Terminal Halogen into Azide

(3) Synthesis of stereoregular star poly(methyl methacrylate) via stereospecific living anionic polymerization in combination with halogenation and crosslinking living radical polymerization

The third objective of this thesis is the synthesis of star polymer by combining halogenation of growing terminal in stereospecific living anionic polymerization and metal-catalyzed living radical cross-linking polymerization initiated from the obtained terminal carbon–halogen bond (Scheme 11).

A star polymer composed of a core crosslinked with a large number of arm chains differs from a linear polymer. It shows low viscosity as compared to the linear polymer with the same molecular weight due to the low entanglement. A number of syntheses of star polymers have been reported so far by metal-catalyzed crosslinking of linear polymer chains with a stable carbon–halogen bond at the terminal, which can be also synthesized by living radical polymerization, in the presence of a small amount of divinyl compound as the cross-linking agent.

In this study, the author aimed at the synthesis of star polymer with various stereoregular PMMAs as the arm polymers, which was conducted by introducing a stable carbon–halogen bond at the terminal of *st*-PMMA and *it*-PMMA via halogenation of growing terminal in stereospecific living anionic polymerizations and crosslinking living radical polymerization of a divinyl compound initiated from the obtained terminal carbon–halogen bond using a transition metal catalyst.



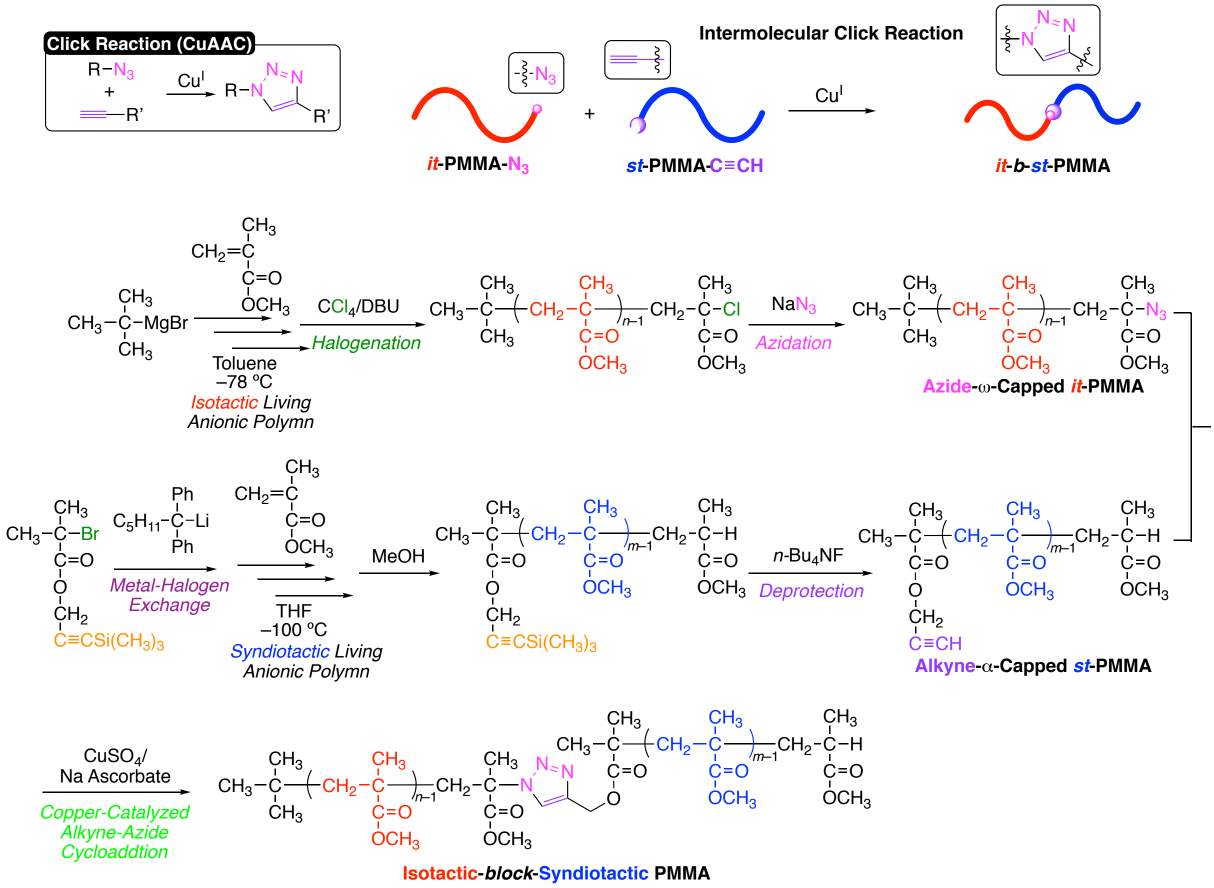
Scheme 11. Synthesis of Various Star Polymer Based on Stereoregular PMMA

Outline of This Study

This paper is composed of three chapters. The contents are in common based on stereospecific living anionic polymerization of methyl methacrylate and halogenation of the growing terminal. Then, the obtained stereoregular PMMAs with the carbon–halogen terminal were used for the synthesis of special shaped polymers, such as block, cyclic, and star polymers, via post-polymerization reactions associated with the carbon–halogen terminal bonds.

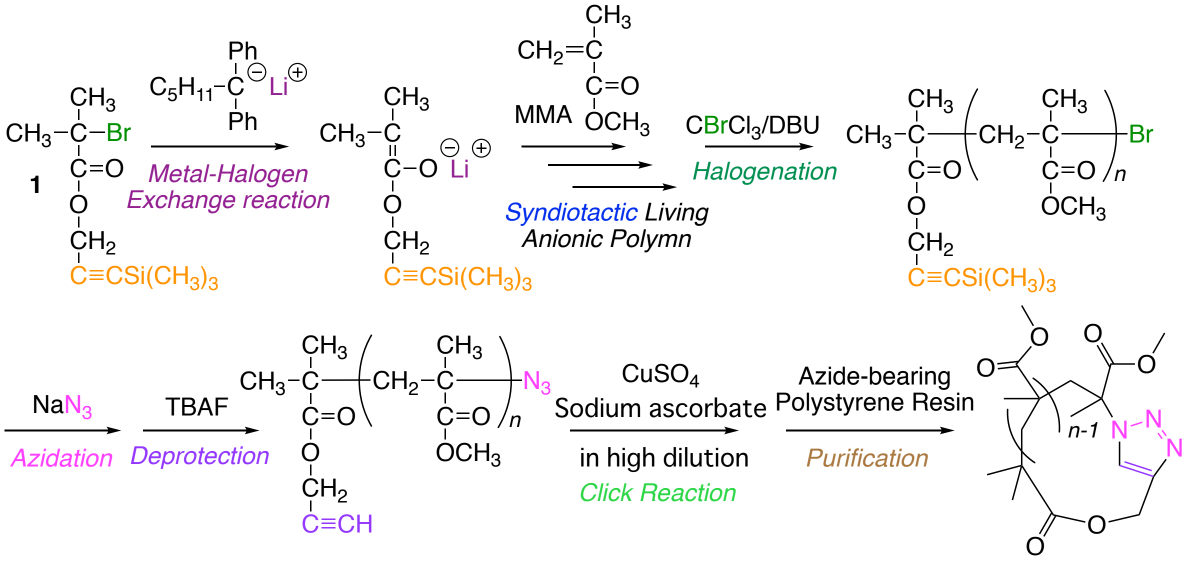
In chapter 1, stereoblock PMMA was prepared by an intermolecular click reaction between the azide group converted by substitution reaction of the terminal halogen, which was introduced by halogenation of growing terminal in stereospecific living anionic polymerization, and alkyne, which was introduced at the initiating terminal. In chapter 2, the author synthesized a stereoregular cyclic polymer by intramolecular click reaction. In chapter 3, the author synthesized various star polymers with stereoregular PMMAs as the arm polymers, which were prepared by halogenation of growing terminal in stereospecific living anionic polymerization, by crosslinking reaction with a divinyl compound by metal-catalyzed living radical polymerization.

Chapter 1 focuses on efficient synthetic method of a well-defined stereoblock PMMA composed of *it*-PMMA and *st*-PMMA, which was achieved by combining stereospecific living anionic polymerization and intermolecular click reaction (Scheme 12). The *it*-PMMA with an azide group at the terminal was prepared by isotactic living anionic polymerization of MMA via combination of halogenation of growing terminal and transformation into azide group. Particularly, the isotactic living anionic polymerization was initiated by *t*-BuMgBr in toluene at –78 ºC and terminated by using CCl_4 as halogenation agent in the presence of DBU. The terminal chlorine was then azidated with NaN_3. In contrast, *st*-PMMA with an alkyne initiating terminal was synthesized by syndiotactic living anionic polymerization of MMA, which was initiated via an *in-situ* metal-halogen exchange reaction between α-bromoester bearing a protected-alkyne and DPHLi, and following deprotection of the silyl-group with tetrabutylammonium fluoride (TBAF). Stereoblock PMMA with controlled molecular weight and narrow polydispersity was synthesized in a high yield by intermolecular CuAAC between these complimentary pairs of polymers. It was demonstrated that block lengths and *it*-/*st*- ratios affect the stereocomplexation.



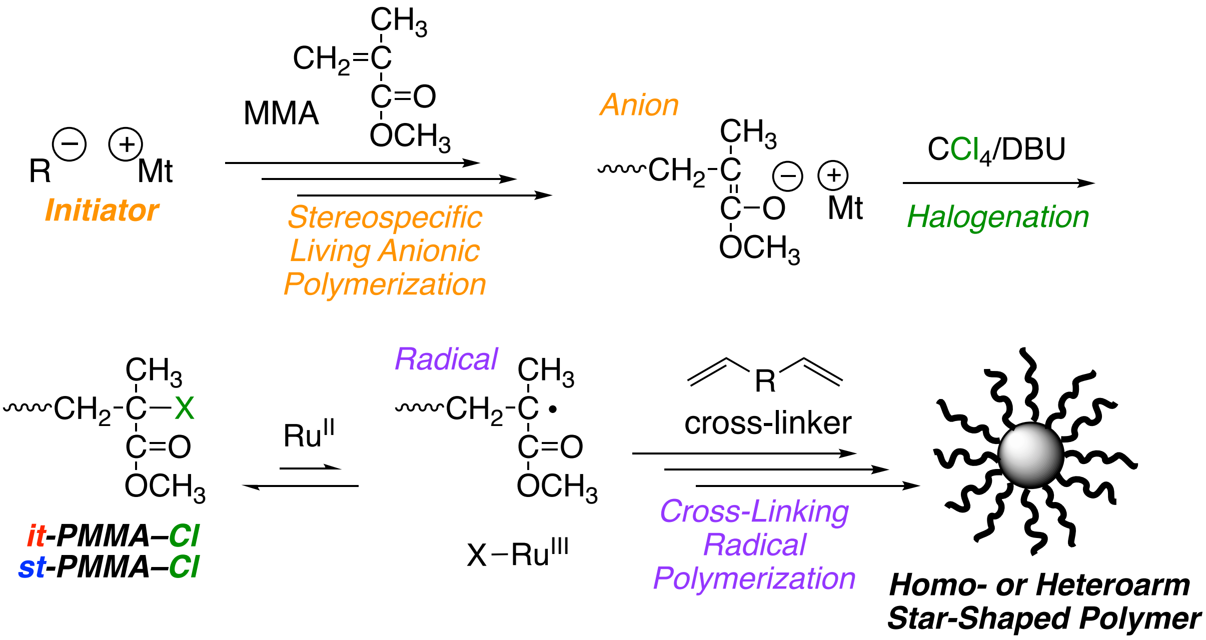
Scheme 12. Synthesis of Stereoblock PMMA via Intermolecular Click Reaction

Chapter 2 presents the novel synthetic method of a well-defined cyclic *st*-PMMA with high levels of syndiotacticity that it is synthesized by combining stereospecific living anionic polymerization and intramolecular click reaction (Scheme 13). A heterotelechelic *st*-PMMA with alkyne and azide groups at the chain ends was prepared by transformation of the end-functional groups, which was introduced by the living anionic polymerization as the precursor for the cyclic polymer. First, MMA was polymerized by syndiotactic living anionic polymerization in THF at –100 ºC, which was started with a protected-alkyne initiator (**1**; Scheme 13) prepared *in-situ* by metal-halogen exchange reaction between α-bromoester with a pendent protected-alkyne and DPHLi. The growing enolate terminal in the syndiotactic living anionic polymerization was quenched by $CBrCl_3$ as a halogenation agent and DBU as a strong base. The terminal halogen of the obtained *st*-PMMA was further converted into the azide group, which was subsequently employed for the intramolecular click reaction with the alkyne-initiating terminal by CuBr/PMDETA in high dilution to form the cyclic polymer, after deprotection of protected alkyne. The intramolecular click cyclization was confirmed by ^{1}H NMR, SEC and MALDI-TOF MS analysis.



Scheme 13. Synthesis of Cyclic *st*-PMMA via Intramolecular Click Reaction

Chapter 3 is directed to the synthesis of well-defined star PMMA via mechanistic transformation of an active species through the halogenation from living anionic polymerization to living radical polymerization (Scheme 14). The *it*-PMMA and *st*-PMMA as arm polymers were synthesized by halogenation of growing terminal in stereospecific living anionic polymerizations of MMA. The *it*-PMMA was initiated by *t*-BuMgBr in toluene at –78 ºC, and terminated by using CCl_4 as halogenation agent in the presence of a strong base. The *st*-PMMA was initiated by DPHLi in THF at –78 ºC, and also terminated by using CCl_4 as halogenation agent in the presence of a strong base. The homo-arm star polymer consists of only *it*-PMMA or *st*-PMMA was synthesized by ruthenium-catalyzed crosslinking living radical polymerization of divinyl monomer in toluene at 80 ºC, which was initiated by *it*-PMMA or *st*-PMMA as the macroinitiator. In the same way, hetero-arm star polymer consisting of both *it*-PMMA and *st*-PMMA was synthesized by simultaneously using *it*-PMMA and *st*-PMMA as the macroinitiators. It was demonstrated that molecular weight of arm polymer in each *it*-/*st*- star polymer affects the stereocomplexation.



Scheme 14. Synthesis of Star Polymer of Stereoregular via Living Radical Linking Reaction

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Chapter 1

Synthesis of Isotactic-*block*-Syndiotactic Poly(methyl Methacrylate) via Stereospecific Living Anionic Polymerizations in Combination with Metal-Halogen Exchange, Halogenation, and Click Reactions

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Abstract

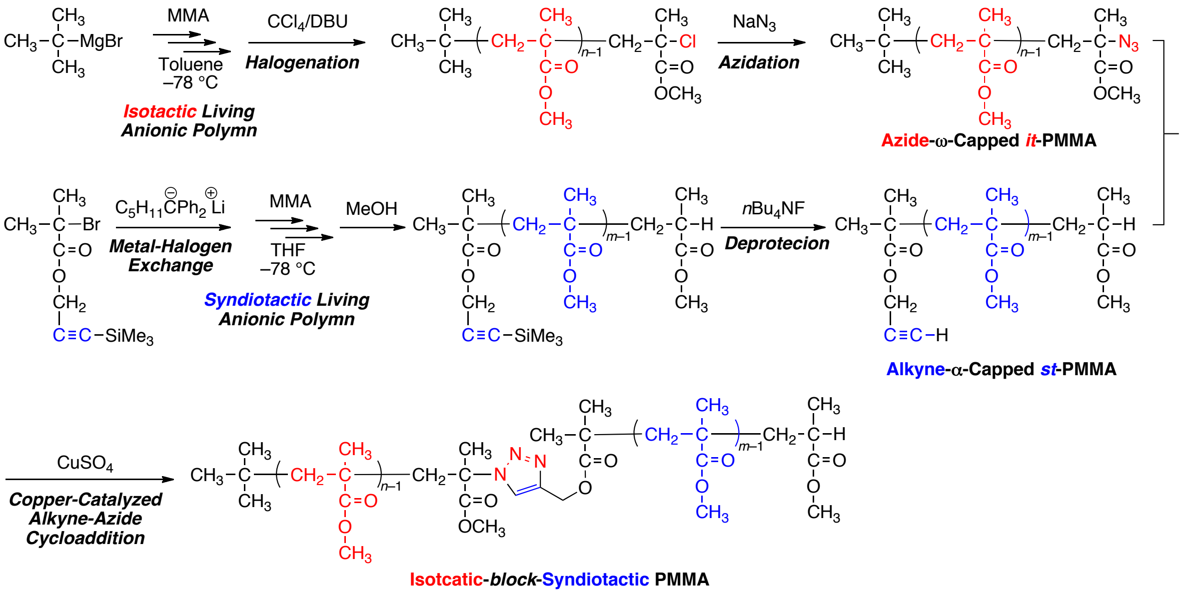
Isotactic (*it*-) and syndiotactic (*st*-) poly(methyl methacrylate)s (PMMAs) form unique crystalline stereocomplexes, which are attractive from both fundamental and application viewpoints. This study is directed at the efficient synthesis of *it*- and *st*-stereoblock (*it*-*b*-*st*-) PMMAs via stereospecific living anionic polymerizations in combination with metal-halogen exchange, halogenation, and click reactions. The azide-capped *it*-PMMA was prepared by living anionic polymerization of MMA, which was initiated with *t*-BuMgBr in toluene at -78 ºC, and was followed by termination using CCl_4 as the halogenating agent in the presence of a strong Lewis base and subsequent azidation with NaN_3. The alkyne-capped *st*-PMMA was obtained by living anionic polymerization of MMA, which was initiated via an *in situ* metal-halogen exchange reaction between 1,1-diphenylhexyl lithium and an α-bromoester bearing a pendent silyl-protected alkyne group. Finally, copper-catalyzed alkyne-azide cycloaddition (CuAAC) between these complimentary pairs of polymers resulted in a high yield of *it*-*b*-*st*-PMMAs, with controlled molecular weights and narrow molecular weight distributions. The stereocomplexation was evaluated in CH_3CN and was affected by the block lengths and ratios.

Introduction

Recent advances in controlled polymerizations, including living and stereospecific polymerizations, as well as highly efficient reactions, such as click reactions, enable the synthesis of various architecturally controlled polymers.[1] In addition, an alternative and more efficient synthetic route for polymer structures can be created by these developments, which is the case in the synthesis of organic molecules, such as medicines and natural products due to the development of new reactions.

Typical stereoregular poly(methyl methacrylate)s (PMMAs), *i.e.*, isotactic (*it*-) and syndiotactic (*st*-) PMMAs, are known to associate in the solid state and specific solutions to form a crystalline polymer complex, *i.e.*, a stereocomplex, in which inner single or double helixes of the *it*-PMMA chain are surrounded by an outer *st*-PMMA helical chain with a larger radius.[2-10] The unique structures and properties of synthetic polymers have attracted attention from both fundamental and application viewpoints.[11-19] Furthermore, these stereoregular polymer chains have been incorporated into various well-defined polymers, such as block, star, graft, and end-functionalized polymers, to create novel properties and functions.[20-39]

Stereoblock PMMAs that consist of *it*- and *st*-PMMA blocks connected in one linear chain have been prepared via various approaches. Although there have been several reports on the formation of *it*-*b*-*st*-stereoblock PMMAs via anionic polymerization under certain conditions since the 1950s, they are mostly mixtures of *it*- and *st*-PMMAs or are randomly segmented *it*- and *st*-PMMA blocks with uncontrolled block lengths and broad molecular weight distributions (MWDs).[3,40-49] The well-defined *it*-*b*-*st*-stereoblock PMMA was first synthesized in 1986 via a sequential living anionic block copolymerization of two monomers, diphenylmethyl and triphenylmethyl methacrylates, which resulted in syndiotactic (*rr* = 84%) and isotactic (*mm* = 91%) sequences, respectively, followed by hydrolysis and methylation of their ester moieties.[22] Later, the direct synthesis of an *it*-*b*-*st*-stereoblock PMMA was achieved via the transformation of the isotactic living anionic polymerization of MMA, initiated with *t*-BuMgBr in toluene at -60 ºC (*mm* = 96%) into a syndiotactic polymerization via the addition of Me_3Al at a ratio of Al/Mg $\geq$ 6 at -78 ºC (*rr* $\leq$ 75%).[23] Another synthetic route to synthesize *it*-*b*-*st*-stereoblock PMMA was reported via a coupling reaction between the alcohol-capped *it*- (*mm* = 97%) and *st*-PMMAs (*rr* = 89%) by sebacoyl dichloride, where the two prepolymers were prepared by living anionic polymerizations of MMA with *t*-BuMgBr and *t*-BuLi/*n*-Bu_3Al, respectively, in toluene at -78 ºC followed by termination with allyliodide and a subsequent hydroboration-oxidation.[24-27] This approach was further used for the synthesis of uniform *it*-*b*-*st*-stereoblock PMMA with a single molecular weight via fractionation using preparative size-exclusion chromatography (SEC) and supercritical fluid chromatography (SFC). The stereocomplexation behavior was analyzed in detail. However, this coupling reaction statistically results in 50% homo-coupling products (*it*-*b*-*it* and *st*-*b*-*st*), which should be separated from the desired hetero-coupling products by chromatography. A more efficient synthetic approach can be developed by designing polymerization and coupling reactions.



Scheme 1. Synthesis of Isotactic-*block*-Syndiotactic Poly(methyl Methacrylate) via Stereospecific Living Anionic Polymerizations in Combination with Halogen-Metal Exchange, Halogenation, and Click Reactions

We have recently determined that the halogenation of the growing enolate terminal in the isotactic and syndiotactic living anionic polymerization of MMA is efficient and feasible upon the addition of CCl_4 or CCl_3Br in the presence of a strong Lewis base, such as 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU).[50] Furthermore, the halogen terminal of PMMA can be almost quantitatively transformed into an azide terminal via a reaction with sodium azide.[33,36] In addition, an alkyne-capped PMMA can be synthesized by a living anionic polymerization of MMA that is initiated via an *in situ* metal-halogen exchange reaction between 1,1-diphenylhexyl lithium, *i.e.*, the sacrificial anion source, and an α-haloester bearing a pendent silyl-protected alkyne group, *i.e.*, a precursor of the functionalized initiator.[36] In our previous report, both α-alkyne and ω-azide chain-end functionalizations were used in a single polymer chain of *st*-PMMA to enable the synthesis of cyclic *st*-PMMA. Here, we report a more efficient synthesis of *it*-*b*-*st*-stereoblock PMMA via a copper-catalyzed azide-alkyne cycloaddition (CuAAC) between azide-ω-capped *it*-PMMA and alkyne-α-capped *st*-PMMA prepared via a stereospecific anionic polymerization (Scheme 1.)

Materials and Methods

Materials

Methyl methacrylate (MMA; TCI, Tokyo, Japan, >99.8%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; TCI, Tokyo, Japan, >98.0%), and CCl_4 (Kanto, Tokyo, Japan, >99.9%) were distilled from calcium hydride before use. *t*-BuMgBr, diphenylhexyllithium (DPHLi), and 3-(trimethylsilyl)propargyl α-bromoisobutyrate (**1**) were prepared according to the literature.[36, 50-53] Toluene (Kanto, Tokyo, Japan, >99.5%; H_2O <0.001%) and tetrahydrofuran (THF; Kanto, >99.5%; H_2O <0.001%) were dried and deoxygenized by passage through columns of Glass Contour Solvent Systems (Glass Contour, Nashua, NH, USA) before use. Tetrabutylammonium fluoride (*n*-Bu_4NF; TCI, Tokyo, Japan, ca. 1 mol/L in THF), sodium azide (NaN_3; TCI, Tokyo, Japan, >99.0%), $CuSO_4$ (Kanto, Tokyo, Japan, >97.5%), ascorbic acid (TCI, Tokyo, Japan, >99.0%), sodium ascorbate (Kanto, Tokyo, Japan, >98.0%), CH_3CN (Kanto, Tokyo, Japan, 99.5%), and DMSO (Kanto, Tokyo, Japan, 99.5%) were used as received. CuCl (Aldrich, St. Louis, MO, USA, 99.99%), $CuCl_2$ (Aldrich, St. Louis, MO, USA, 99.99%) and 2,2'-bipyridyl (bpy; Aldrich, St. Louis, MO, USA, >99.0%) was used as received and handled in a glove box (MBRAUN LABmaster sp, Garching, Germany) under a moisture and oxygen-free argon atmosphere (O_2, <1 ppm).

Synthesis of Azide-ω-Capped *it*-PMMA via Isotactic Living Anionic Polymerization of MMA Followed by Termination with Halogenation and Subsequent Azidation

The reactions were carried out by syringe techniques under dry argon in a 100 mL baked glass tube equipped with a three-way stopcock. The following is a typical example for *it*-50-PMMA. The polymerization was initiated by adding MMA (5.2 mL, 49 mmol) slowly via a dry syringe into the prechilled initiator solution (31 mL), containing *t*-BuMgBr (0.97 mmol, 3.5 mL, 276 mM in Et_2O) and toluene (27 mL), at -78 ºC. The total volume of the reaction mixture was thus 36 mL. After stirring for 26 h, the THF solution (56 mL) of CCl_4 (44 mmol, 4.3 mL) and DPHLi (3.4 mmol, 8.4 mL, 400 mM in THF) was added to the reaction mixture. After 1 h, into the reaction mixture was then added DBU (9.7 mmol, 1.5 mL) and the reaction temperature was gradually raised to 0 ºC. After additional 24 h, the reaction was quenched by 6.8 mL of argon-bubbled methanol. The quenched solution was diluted with 100 mL of toluene and washed with diluted hydrochloric acid and water, evaporated to dryness under reduced pressure, and then vacuum-dried to give the product (M_n = 5000, M_w/M_n = 1.50) containing low molecular weight residues. The obtained product was dissolved with toluene and reprecipitated into hexane three times to result in the chlorine-capped *it*-PMMA (M_n = 5100, M_w/M_n = 1.61, *mm* / *mr* / *rr* = 92 / 7 / 1)

The obtained chlorine-capped *it*-PMMA (1.0 g, 0.20 mmol), sodium azide (130 mg, 2.0 mmol), and ascorbic acid (5.3 mg, 0.030 mmol) were dissolved in 20 mL of CH_3CN/H_2O (9:1). A catalyst solution of CuCl/$CuCl_2$/bpy (0.10/0.067/0.33 M in CH_3CN/H_2O (9:1), 1.19 mL) was then added. The flask was immersed in thermostatic oil bath at 40 ºC and kept stirred for 18 h. The solution was diluted with 50 mL of toluene, and washed with diluted hydrochloric acid and water. The solution was concentrated and dried to give the azide-ω-ended *it*-PMMA (M_n = 4800, M_w/M_n = 1.59).

Synthesis of Alkyne-α-Capped *st*-PMMA via Syndiotactic Living Anionic Polymerization of MMA Initiated via a Metal-Halogen Exchange Reaction

The reactions were carried out by syringe techniques under dry argon in a 100 mL baked glass tube equipped with a three-way stopcock. The following is a typical example for *st*-50-PMMA. Prior to the polymerization, the functionalized enolate initiator was *in situ* prepared by adding 6.4 mL of **1** (1.7 mmol, 272 mM in THF) into the THF solution (40 mL) of DPHLi (2.6 mmol) at -100 ºC. Into the mixture, MMA (48 mmol, 5.1 mL) was added dropwise, and the total volume of the reaction mixture was thus 52 mL. After stirring for 30 min, the polymerization was terminated with acidic methanol (4.5 mL). The solution was diluted with 100 mL toluene, and was washed with diluted hydrochloric acid and water, evaporated to dryness under reduced pressure, and then vacuum-dried to give the product (M_n = 6300, M_w/M_n = 1.11, *mm* / *mr* / *rr* = 1 / 22 / 77).

The obtained *st*-PMMA with a protected alkyne (3.4 g, 0.63 mmol) was dissolved in 58 mL of THF. To the solution, 1.3 mL of the THF solution of *n*-Bu_4NF (1.0 M, 1.3 mmol) was added at 0 ºC. After 1 h, the solution was diluted with 30 mL of toluene, washed with diluted hydrochloric acid and water, and evaporated to dryness to the alkyne-α-ended *st*-PMMA (M_n = 6100, M_w/M_n = 1.11).

Synthesis of *it*-*b*-*st*-Stereoblock PMMA via Copper-Catalyzed Alkyne-Azide Cycloaddition

The CuAAc reaction was carried out with $CuSO_4$ in the presence of sodium ascorbate as the reducing agent in DMSO/H_2O (98/2) in a baked glass tube equipped with a three-way stopcock. The following is a typical example for *it*-50-*b*-*st*-100-PMMA. The azide-ω-ended *it*-PMMA (M_n = 4800, M_w/M_n = 1.59, $F_n(N_3)$ = 0.74, 247 mg, 0.051 mmol) and alkyne-α-ended *st*-PMMA (M_n = 12000, M_w/M_n = 1.11, F_n(C≡C–H) = 1.04, 462 mg, 0.039 mmol) were dissolved in DMSO (1.9 mL). To this solution, 0.04 mL of H_2O, $CuSO_4$ (2.1 mg, 0.013 mmol), and sodium ascorbate (10 mg, 0.051 mmol) were added. The flask was immersed in thermostatic oil bath at 70 ºC, and the reaction mixture was allowed to stir for 24 h. The reaction was quenched by dilution with toluene (50 mL). The mixture was washed with diluted hydrochloric acid and water. The solution was evaporated to drynesss under reduced pressure in order to give the crude stereoblock PMMA (M_n = 12400, M_w/M_n = 1.20). The obtained product was dissolved in toluene and reprecipitated into hexane three times to result in the *it*-50-*b*-*st*-100-PMMA (M_n = 14000, M_w/M_n = 1.20).

Measurements

The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of the polymers were measured by size-exclusion chromatography (SEC) using THF at a flow rate 1.0 mL/min at 40 °C on two polystyrene gel columns [Shodex KF-805L (Showa Denko K.K., Tokyo, Japan, pore size: 20–1000 Å; 8.0 mm i.d. × 30 cm)] that were connected to a JASCO PU-2080 precision pump and a JASCO RI-2031 detector (JASCO, Toky, Japan). The columns were calibrated against seven standard PMMA samples (Agilent Technologies, Santa Clara, CA, USA; M_p = 202–1677000, M_w/M_n = 1.02–1.23). ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ESC-400 spectrometer (JEOL, Tokyo, Japan) operating at 400 and 100 MHz, respectively. The triad tacticity of the polymer was determined by the peak intensity of carbonyl C=O carbons observed at 175–180 ppm in the ^{13}C NMR spectrum. The transmittance of polymer solutions was recorded in CH_3CN using a JASCO V-550 spectrophotometer (JASCO, Tokyo, Japan) (cooling rate = 1 ºC/min; wavelength 500 nm). The glass transition (T_g) and melting (T_m) temperatures were recorded on Q200 differential scanning calorimeter (DSC) (TA Instruments Inc., New Castle, DE, USA). T_g was obtaines from the second scan, where the samples were heated to 180 ºC at 10 ºC/ min, equilibrated at 180 ºC for 5 min, cooled to 0 ºC at 5 ºC/ min, held at 0 ºC for 5 min, and then reheated to 200 ºC at 10 ºC/ min. T_m was obtained from the first scan, where the samples were heated from 40 ºC to 250 ºC at 10 ºC/ min. The samples for T_m were obtained by evaporating CH_3CN from the solution of stereoblock PMMA (50 mg/ mL) and dried under vacuo overnight.

Results and Discussion

Synthesis of Azide-ω-Capped *it*-PMMA via Isotactic Living Anionic Polymerization of MMA Followed by Termination with Halogenation and Subsequent Azidation

Isotactic living anionic polymerization of MMA was conducted with *t*-BuMgBr in toluene at -78 ºC[51,52] at different molar ratios ($[M]_0/[t\text{-BuMgBr}]_0 = 25$ and 50) to synthesize *it*-PMMA with different molecular weights. The polymers obtained after quenching the reaction with acidic methanol had controlled molecular weights and narrow MWDs, as shown in the SEC curves (Figures 1A,E). The ^{13}C NMR showed isotactic-rich enchainments (*mm*/*mr*/*rr* = 91/7/2 or 92/7/1), as reported.[51,52] The termination with CCl_4 as the chlorinating agent in the presence of DBU, a strong Lewis base, also resulted in polymers with similar molecular weights and narrow MWDs.[50] Although higher and lower molecular weight fractions were slightly observed, probably being due to high viscosity upon quenching (Figures 1B,F), the SEC curves were nearly unimodal after the reprecipitations (Figures 1C,G).

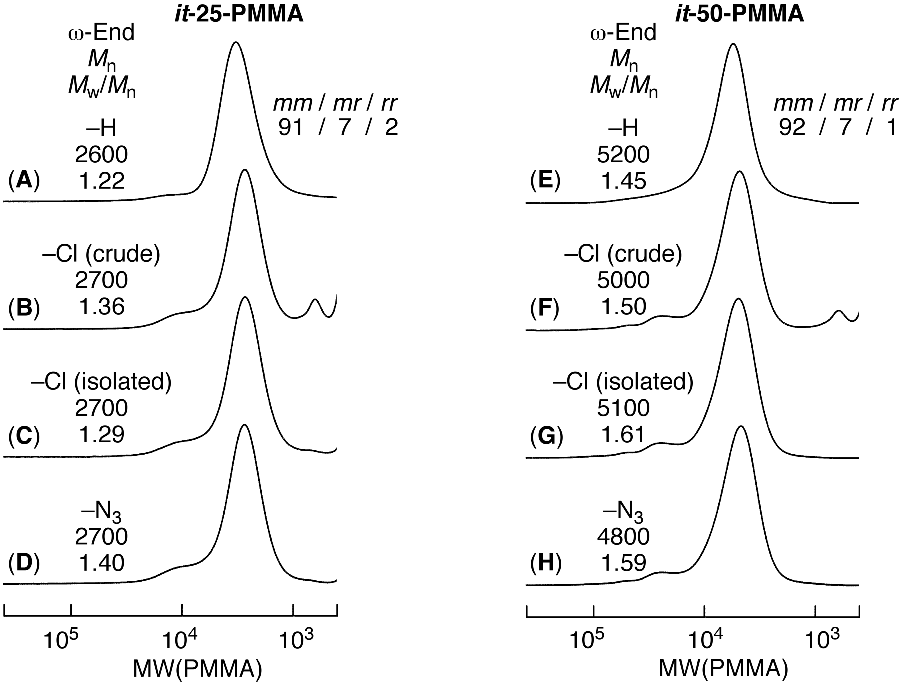


Figure 1. Size-exclusion chromatography (SEC) curves of a series of *it*- poly(methyl methacrylate)s (PMMAs) ((**A**-**D**): *it*-25, (**E**-**H**): *it*-50) obtained in isotactic anionic polymerization of Methyl methacrylate (MMA) with *t*-BuMgBr in toluene at -78 ºC and subsequent procedures: (**A**,**E**) Quenching the polymerization ($[M]_0/[t\text{-BuMgBr}]_0$ = 1350/54 or 1350/27 mM) with acidic methanol; (**B**,**F**) Quenching the polymerization with CCl_4/DBU ($[M]_0/[t\text{-BuMgBr}]_0/[CCl_4]_{add}/[DBU]_{add}$ = 1350/54/2160/540 or 1350/27/1080/270 mM); (**C**,**G**) Reprecipitations; (**D**,**H**) Azidation with $NaN_3/CuCl/CuCl_2$/bpy in CH_3CN/H_2O = 9/1 at 40 ºC ($[\text{-Cl}]_0/[NaN_3]_0/[CuCl]_0/[CuCl_2]_0/[bpy]_0$ = 10/100/6.5/4.3/22 mM)

The ^{1}H NMR spectrum of the polymers obtained by termination with CCl_4 shows new peaks, a_2 and c_2, which are assignable to the terminal methyl ester and methylene protons that are adjacent to the chloride chain end, respectively (Figure 2B). The terminal chloride functionality (F_n(Cl)) was determined by the ratio of M_n(SEC), as measured by SEC based on the PMMA calibration to M_n(NMR), which was obtained from the peak intensity ratio of c_2 to the methyl ester protons (c) of the repeating MMA units. The obtained F_n(Cl) values were

1.00 and 0.81 for M_n = 2700 and 5100, respectively. In addition, the F_n(Cl) values that were calculated from the peak area ratio of the ω-end methyl ester (c_2) to the α-end *t*-butyl (*d*) protons were 1.00 and 0.78, respectively. These results indicate that most of the isotactic living chain ends of the PMMAs were capped with chlorine.

The chlorine ω-chain-end polymers were then reacted with NaN_3 in the presence of copper catalysts in CH_3CN/H_2O = 9/1 at 40 ºC. The SEC curve of the polymers that were obtained after azidation showed similarly narrow MWDs (Figures 1D,H). The terminal methylene peak (a_2) clearly shifted upfield (a_3) via the transformation from a chloride into an azide terminal (Figure 2C). The chain-end functionality of the azide group ($F_n(N_3)$) was similarly calculated by the ratio of M_n(SEC) to M_n(NMR), which was obtained from the peak intensity ratio of the methyl ester protons, c_3 and *c*. The $F_n(N_3)$ values were 1.00 and 0.74 for M_n = 2700 and 4800, respectively. In addition, similar values were obtained from the peak area ratio of the ω-end methyl ester (c_3) to the α-end *t*-butyl (*d*) protons were 0.96 and 0.75, respectively. They were close to those for F_n(Cl) and indicated that the chloride terminal was almost quantitatively converted into the azide terminal. These results indicate that the *it*-PMMA with an azide group at the ω-chain end was successfully obtained by isotactic living anionic polymerization of MMA, followed by chlorination for quenching and subsequent azidation.

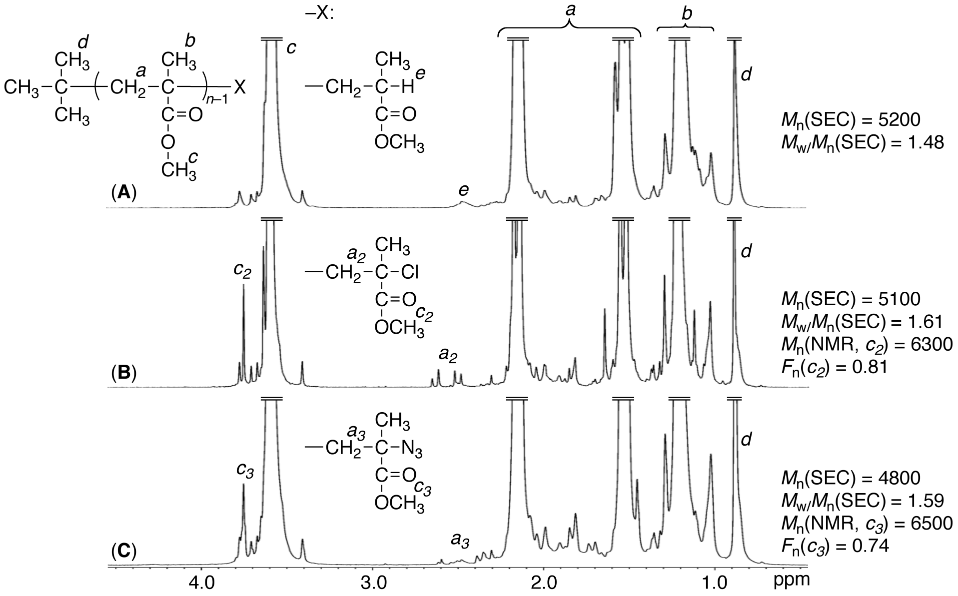


Figure 2. ^{1}H NMR spectra (in $CDCl_3$ at 55 ºC) of *it*-50-PMMAs obtained in anionic polymerization of MMA with *t*-BuMgBr in toluene at -78 ºC and subsequent procedures: (**A**) Quenching the polymerization ($[M]_0/[t\text{-BuMgBr}]_0$ = 1350/27) with acidic methanol; (**B**) Quenching the polymerization with CCl_4/DBU ($[M]_0/[t\text{-BuMgBr}]_0/[CCl_4]_{add}/[DBU]_{add}$ = 1350/27/1080/270) followed by reprecipitations; (**C**) Azidation with $NaN_3/CuCl/CuCl_2$/bpy in CH_3CN/H_2O = 9/1 at 40 ºC ($[\text{-Cl}]_0/[NaN_3]_0/[CuCl]_0/[CuCl_2]_0/[bpy]_0$ = 10/100/6.5/4.3/22 mM).

Synthesis of Alkyne-α-Capped *st*-PMMA via Syndiotactic Living Anionic Polymerization of MMA Initiated via a Metal-Halogen Exchange Reaction

To synthesize the alkyne-capped functionalized *st*-PMMA, syndiotactic living anionic polymerization of MMA was initiated via a metal-halogen exchange reaction between 1,1-diphenylhexyl lithium (DPHLi) and an α-bromoisobutyric acid ester bearing a Me_3Si-protected alkyne (**1**) in THF at -100 ºC.[36] The 50- and 100-mer alkyne-end-functionalized *st*-PMMAs were synthesized by changing the feed ratios of the monomer to the initiator. The polymers that were obtained after quenching the reaction with acidic methanol showed controlled molecular weights, narrow MWDs (Figures 3A,C), and syndiotactic-rich enchainments (*mm*/*mr*/*rr* = 1/22/77).

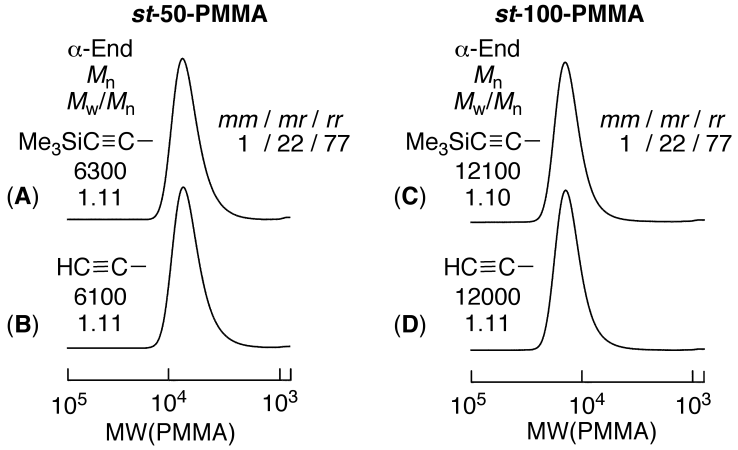


Figure 3. SEC curves of a series of *st*-PMMAs ((**A**,**B**): *st*-50, (**C**,**D**): *st*-100) obtained in DPHLi/**1** in THF at -100 ºC and subsequent procedures: (**A**,**B**) Quenching the polymerization ($[M]_0/[DPHLi]_0/[\mathbf{1}]_0$ = 924/34/51 or 1870/34/51 mM) with acidic methanol; (**C**,**D**) Deprotection of Me_3Si-group by *n*-Bu_4NF in THF at 0 ºC ($[Me_3Si\text{-}]_0/[n\text{-}Bu_4NF]_0$ = 10/20 mM).

The ^{1}H NMR showed the presence of protected Me_3Si- (*h*) and methylene protons (g_1) adjacent to the alkyne function. The chain-end functionality of the protected alkyne group (F_n(C≡C–$SiMe_3$)) was calculated from the ratio of M_n(SEC) to M_n(NMR), which was calculated from the peak intensity ratio of g_1 to the methyl ester protons (*c*) of the repeating MMA units (Figure 4A). They were close to unity for both of the polymers with different molecular weights (F_n = 0.98 and 1.12 for M_n(SEC) = 6300 and 12100, respectively), indicating that the alkyne-functionalized α-bromoisobutyric acid ester quantitatively initiates the syndiotactic living anionic polymerization via a metal-halogen exchange reaction in the presence of DPHLi to result in the well-defined alkyne-functionalized *st*-PMMA.

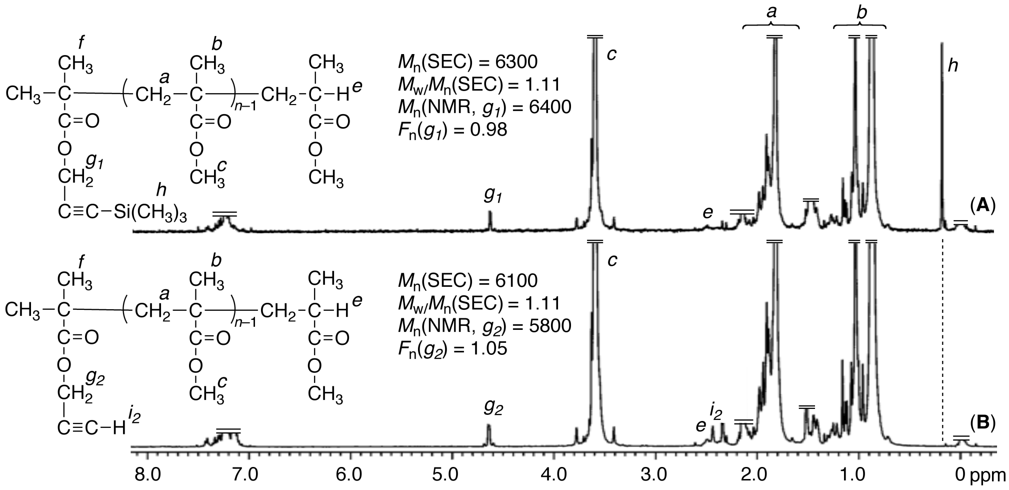


Figure 4. ^{1}H NMR spectra (in $CDCl_3$ at 55 ºC) of *st*-50-PMMAs obtained in anionic polymerization of MMA with DPHLi/**1** in THF at -100 ºC and subsequent procedures: (**A**) Quenching the polymerization ($[M]_0/[DPHLi]_0/[\mathbf{1}]_0$ = 924/34/51) with acidic methanol; (**B**) Deprotection of Me_3Si-group by *n*-Bu_4NF in THF at 0 ºC ($[Me_3Si\text{-}]_0/[n\text{-}Bu_4NF]_0$ = 10/20 mM).

The deprotection of the Me_3Si-group at the α-end was conducted using tetrabutylammonium fluoride (*n*-Bu_4NF) in THF at 0 ºC. There were almost no changes in the SEC curves with narrow MWDs after the deprotection (Figures 3B,D). The complete and successful deprotection was confirmed by the disappearance of the characteristic Me_3Si-protons (*h*), and the appearance of a new peak that was assignable to the ethynyl proton (i_2). The chain-end functionalities of the deprotected alkyne group (F_n(C≡C–H)) were similarly calculated from the methylene protons (g_2) and were close to unity (F_n = 1.05 and 1.04 for M_n(SEC) = 6100 and 12000, respectively). These results show that *st*-PMMA with an alkyne group at the α-chain end was successfully obtained by syndiotactic living anionic polymerization of MMA initiated via a metal-halogen exchange reaction between the protected alkyne-functionalized α-bromoester and DPHLi followed by deprotection.

Synthesis of *it-b-st*-Stereoblock PMMA via Copper-Catalyzed Azide-Alkyne Cycloaddition and Stereocomplexation

Using two series of polymers with different molecular weights, *i.e.*, *it*-PMMA-N_3 (DP_n~ 25 and 50) and *st*-PMMA-C≡CH (DP_n~ 50 and 100), CuAAC was conducted with four pairs of the polymers to produce *it-b-st*-stereoblock PMMAs with different block lengths (*it*-25-*b*-*st*-50, *it*-25-*b*-*st*-100, *it*-50-*b*-*st*-50, and *it*-50-*b*-*st*-100). The click reactions between *it*-PMMA-N_3 and *st*-PMMA-C≡CH were carried out in the presence of $CuSO_4$/sodium ascorbate in DMSO/H_2O (98/2) at 70 ºC, and the two polymers were mixed at the same molar ratio of the two functional groups using each F_n value. After the reaction, the SEC curves shifted to higher molecular weights (Figures 5A-D) although lower molecular weight peaks slightly remained, most probably due to the presence of a small amount of unfunctionalized prepolymers. The coupling products were further purified by reprecipitation in *n*-hexane to result in narrow SEC curves with higher molecular weights than the starting prepolymers.

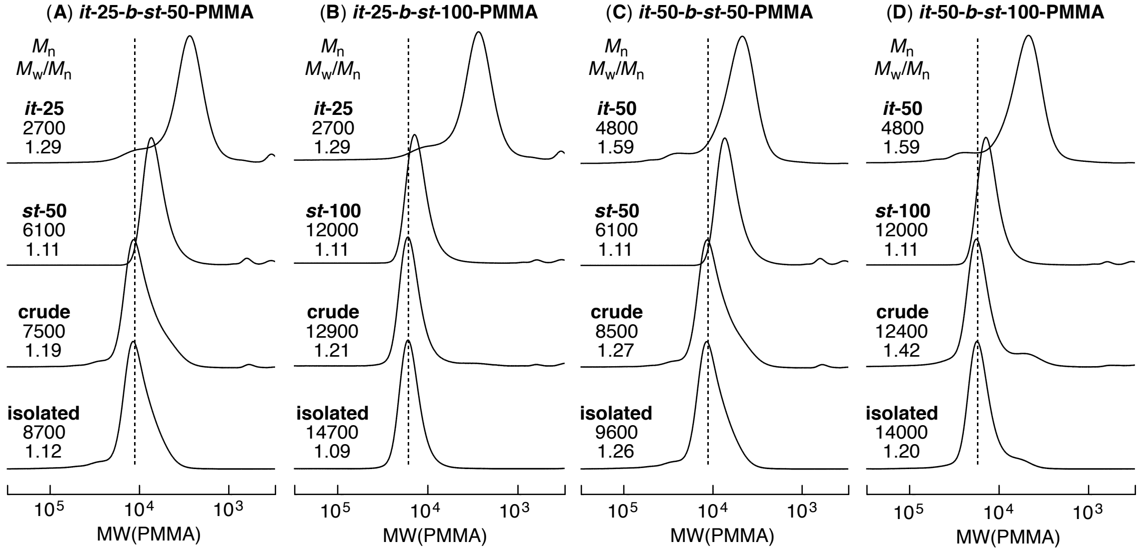


Figure 5. SEC curves of a series of *it*-PMMA-N_3, *st*-PMMA-C≡CH, and *it-b-st*-stereoblock PMMAs obtained via CuAAC in the presence of $CuSO_4$/sodium ascorbate in DMSO/H_2O (98/2) at 70 ºC ($[-N_3]_0/[-C{\equiv}CH]_0/[CuSO_4]_0/[\text{sodium ascorbate}]_0$ = 15/15/5/20 mM) as

prepared and after reprecipitations. (**A**) *it*-25-*b*-*st*-50; (**B**) *it*-25-*b*-*st*-100; (**C**) *it*-50-*b*-*st*-50; (**D**) *it*-50-*b*-*st*-100.

In the ^{1}H NMR spectrum of the obtained polymers, new peaks for the triazole-ring methine (j) at 7.8 ppm and the adjacent methylene (g_4) protons at 5.2 ppm appeared due to the reaction of the alkyne group at the α-end of *st*-PMMA with the azide ω-terminal of *it*-PMMA (Figure 6C). Although a small peak for methylene protons (g_2) was observed due to the unreacted remaining *st*-PMMA prepolymers, the purity of the block polymers was relatively high (90%). The purity was calculated from the peak intensity ratio, $g_4/(g_2 + g_4)$. The ^{13}C NMR spectrum of the carbonyl groups of the obtained coupling products (Figure 6F) was a weighed superimposition of the two spectra of *it*-PMMA (Figure 6D) and *st*-PMMA (Figure 6E). The block length ratio was calculated from the tacticities of both the *it*-PMMA and *st*-PMMA prepolymers ($mm_{\mathrm{total}} = x_{it}\times mm_{it} + x_{st}\times mm_{st}$, $rr_{\mathrm{total}} = x_{it}\times rr_{it} + x_{st}\times rr_{st}$) and was x_{it}: x_{st} = 0.28: 0.72, which was close to the theoretical value, x_{it}: x_{st} = 0.31: 0.69, assuming the formation of *it*-*b*-*st*-stereoblock PMMA with the expected block length. These results indicate that *it*-*b*-*st*-stereoblock PMMAs with various block lengths were efficiently synthesized via CuAAC between the azide-capped *it*-PMMA and alkyne-capped *st*-PMMA (Table 1).

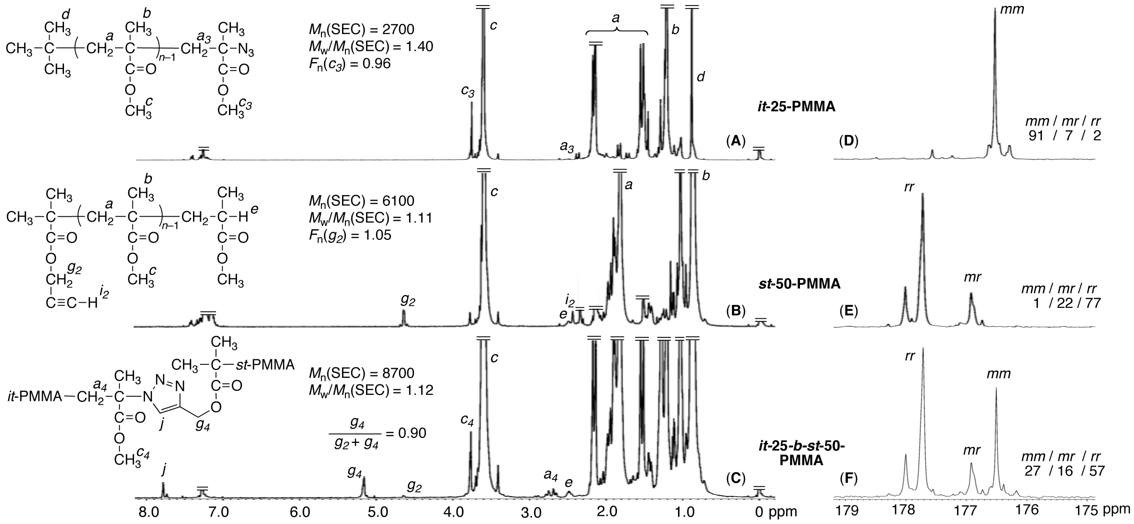


Figure 6. ^{1}H and ^{13}C NMR spectra (in $CDCl_3$ at 55 ºC) of *it*-25-, *st*-50-, and *it*-25-*b*-*st*-50-PMMAs: (**A**,**D**) *it*-25-PMMA-N_3 obtained in isotactic anionic polymerization of MMA followed by chlorination and azidation; (**B**,**E**) *st*-50-PMMA-C≡CH obtained in syndiotactic anionic polymerization of MMA followed by deprotection of Me_3Si-group; (**C**,**F**) *it*-25-*b*-*st*-50-PMMA obtained via CuAAC between *it*-25-PMMA-N_3 and *st*-50-PMMA-C≡CH in the presence of $CuSO_4$/sodium ascorbate in DMSO/H_2O (98/2) at 70 ºC ($[-N_3]_0/[-C{\equiv}CH]_0/[CuSO_4]_0$/[sodium ascorbate]$_0$ = 15/15/5/20 mM).

Table 1. Molecular weight and tacticity of prepolymers and *it*-*b*-*st* PMMAs.

Code	M_n (*it*)	*mm*/*mr*/*rr* (*it*)	M_n (*st*)	*mm*/*mr*/*rr* (*st*)	M_n (*it*-*b*-*st*)	M_w/M_n (*it*-*b*-*st*)	*mm*/*mr*/*rr* (*it*-*b*-*st*)	*it*-/*st*- Calcd	*it*-/*st*- NMR
it-25-*b*-*st*-50	2700	91/7/2	6100	1/2/77	8700	1.12	27/16/57	31/69	28/72
it-25-*b*-*st*-100	2700	91/7/2	12000	1/2/77	14700	1.09	18/20/62	18/82	19/81
it-50-*b*-*st*-50	4800	92/7/1	6100	1/2/77	9600	1.26	43/13/44	44/56	45/55
it-50-*b*-*st*-100	4800	92/7/1	12000	1/2/77	14000	1.20	31/16/53	29/71	32/68

The stereocomplexation of these stereoblock polymers was evaluated in CH_3CN by measuring the transmittance of the solutions (100 mg/mL). Figure 7 plots the relative values as compared to the transmittance at 70 ºC. The solution gradually became turbid as the temperature decreased, and the transmittance of the samples approached 0%, except for *it*-25-*b*-*st*-100. Furthermore, the solution of *it*-50-*b*-*st*-100 formed a gel, whereas no gelation occurred in the other solutions.

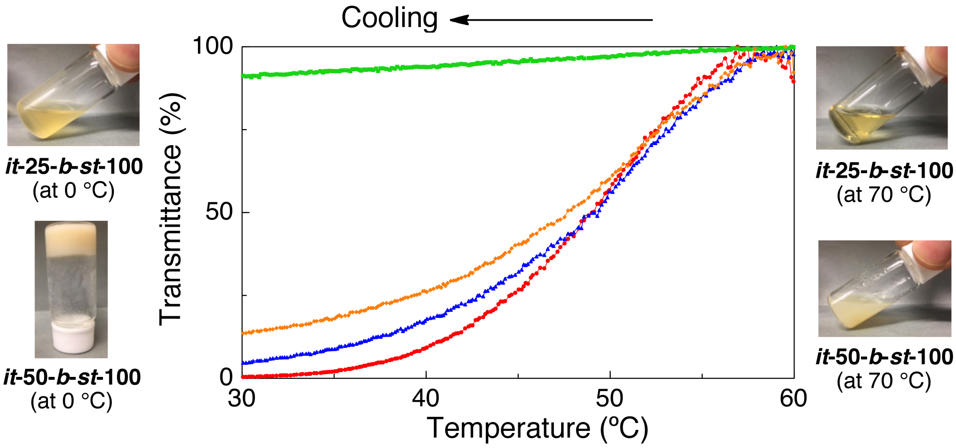


***Figure** 7.* Relative transmittance (wavelength = 500 nm) of a series of SEC curves of solutions of *it*-*b*-*st*-stereoblock PMMAs in CH_3CN (100 mg/mL) with varying temperatures at cooling rate of 1 ºC/min: Orange, *it*-25-*b*-*st*-50; Green, *it*-25-*b*-*st*-100; Blue, *it*-50-*b*-*st*-50; Red, *it*-50-*b*-*st*-100.

According to the most recent studies on stereocomplexation, two *it*-PMMA chains intermolecularly aggregate to form a double helix, which is surrounded by a single helix of *st*-PMMA to form a unique triple helix-like structure.[2,7] In this model, the degree of polymerization of the outer *st*-PMMA chain is double that of the inner *it*-PMMA chain (*it*: *st* = 1:2), while the MMA unit ratio of the total *it*-PMMA chains and *st*-PMMA chain is 1:1 because of the two *it*-chains per *st*-chain in the stereocomplex.

If this model is applied to *it*-*b*-*st*-stereoblock PMMA, the *it*-segments in two block polymer chains can form a double helix to result in a supramolecular structure, *e.g.*, a Y-shape containing two independent single helixes of *st*-segments that are connected to each *it*-segment in the double helix of the *it*-segments. The *it*-double helix segment in the Y-shape supramolecule can be incorporated into a single *st*-helix of another Y-shape molecule to induce further intermolecular associations and finally result in a gel. Among the four *it*-*b*-*st*-streoblock PMMAs with different block lengths, the *it*-50-*b*-*st*-100 PMMA has the most suitable ratio (*it*:*st* = 1:2) of block lengths for this stereocomplexation model, and can easily result in a gel, whereas the total chain length of *it*-25-*b*-*st*-50 PMMA is shorter and less efficient for gel formation, in spite of the suitable ratio (*it*:*st* = 1:2). Irrespective of the longer *st*-segment in *it*-25-*b*-*st*-100 PMMA, the solution was nearly transparent even at low temperatures, suggesting a low degree of association or intramolecular association due to the long *st*-segment in comparison to that with the short *it*-segment (*it*:*st* = 1:4).

To investigate the effects of the block structure on the stereocomplexation, the four precursor non-block polymers, *i.e.*, *it*-25- or *it*-50-PMMA and *st*-50- or *st*-100-PMMA, were mixed together at the same molar ratio in CH_3CN. All of the solutions became turbid upon decreasing the temperature. However, no gelation occurred for any of the *it*- and *st*-mixtures at 100 mg/mL. Only the mixture of *it*-50- and *st*-100-PMMAs formed a gel at a higher concentration, *i.e.*, 200 mg/mL. These results indicate that connecting the *it*- and *st*-PMMA segments via a covalent linkage in *it*-*b*-*st*-PMMA enhances gelation via stereocomplexation.

To further confirm the stereocomplexation, the polymers were analyzed by DSC. The precursor linear *it*-50- and *st*-100-PMMA showed T_g around 25 and 110 ºC, respectively. The sample of *it*-50-*b*-*st*-100 PMMA, which was obtained by evaporating CH_3CN from the solution and dried in vacuo, showed melting temperatures at 166 and 185 ºC, which were slightly higher than those that were reported to the stereocomplexes of linear *it*- and *st*-PMMAs[33]. These results also support that the *it*-*b*-*st*-stereoblock PMMA forms the stereocomplex.

Conclusions

The isotactic-syndiotactic stereoblock PMMAs were efficiently prepared via CuAAC between end-functionalized isotactic and syndiotactic PMMAs that were obtained by streospecific living anionic polymeraization of MMA in combination with a metal-halogen exchange reaction for initiation and a halogenation reaction for termination. The reversible transformation between the halide and living anionic chain end, which was used for initiation or termination, enables efficient end-functionalization of stereoregular polymethacrylates, which can be further utilized for construction of structurally controlled polymers and supramolecular architectures.

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Chapter 2

Synthesis of Syndiotactic Macrocyclic Poly(methyl Methacrylate) via Transformation of the Growing Terminal in Stereospecific Anionic Polymerization

Chapter 2

Synthesis of Syndiotactic Macrocyclic Poly(methyl Methacrylate) via Transformation of the Growing Terminal in Stereospecific Anionic Polymerization

Abstract

In this study, the synthesis of well-defined cyclic syndiotactic poly(methyl methacrylate) (*st*-PMMA) was investigated by transformation of the growing terminal in stereospecific anionic polymerization. *st*-PMMA was first synthesized by living syndiospecific anionic polymerization in THF at a low temperature, which was started with a protected-alkyne initiator prepared *in-situ* by metal-halogen exchange reaction of an α-haloester bearing a pendent protected-alkyne with 1,1-diphenylhexyl lithium. The anionic polymerization was terminated with halogenation of the growing enolate terminal by $CBrCl_3$. The terminal halogen of the obtained *st*-PMMA was further converted into azide group, which was subsequently employed in the intramolecular copper-catalyzed click reaction in high dilution with the alkyne-initiating terminal after deprotection. The macrocyclic *st*-PMMA was confirmed by ^{1}H NMR, SEC, and MALDI-TOF MS analyses.

Introduction

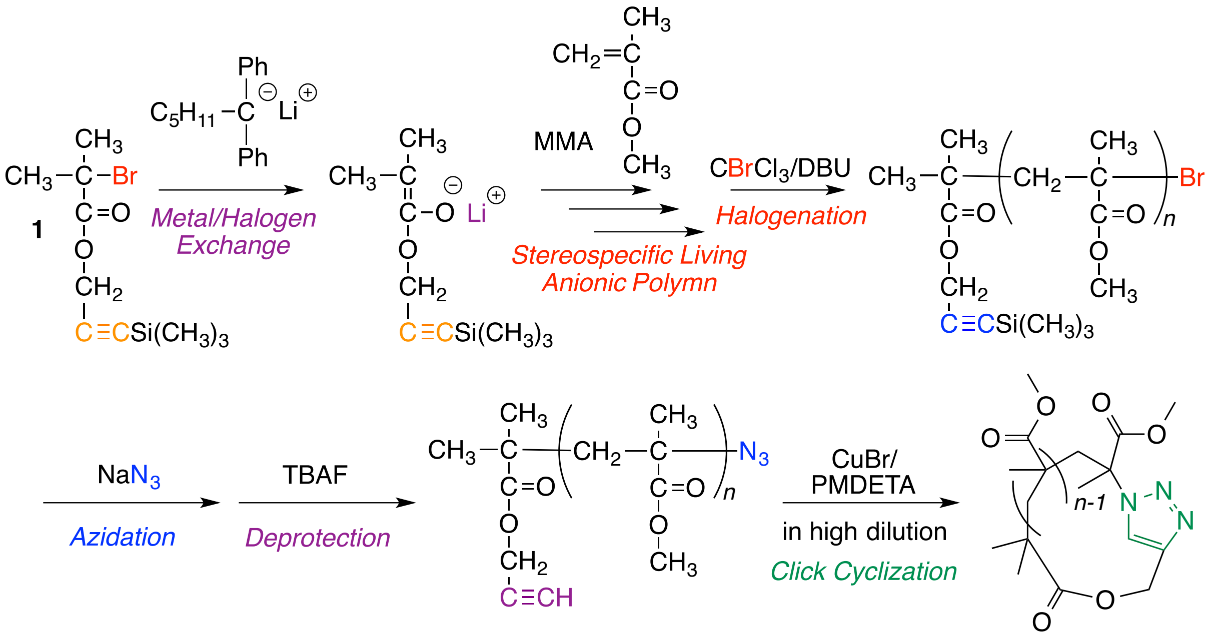
Poly(methyl methacrylate) (PMMA) is one of the commodity polymeric materials with high transparency and moderate thermal properties. Though the commodity PMMA is industrially produced by radical polymerization, MMA has also been polymerized by anionic polymerizations to provide well-defined PMMAs with controlled molecular weights and distributions as well as a wide range of tacticity depending on the initiating systems.[1-4]

Especially, syndiotactic PMMA (*st*-PMMA) has been reported to form stereocomplex with isotactic PMMA or to encapsulate small molecules, such as solvent and fullerenes, forming semicrystalline composite.[5,6] By using PMMA with controlled topology such as branching, star, and ring using precision polymerization, it should lead to creating new functional materials owing to the inclusion and stereo complexation behavior.[7,8]

Among many topologies, macrocyclic ring is a simple but attractive structure, because the cyclic polymer exhibits various characteristic properties, which are different from their linear counterparts, including smaller hydrodynamic volumes, higher glass transition temperatures, and lower viscosities due to the absence of end groups.[9-11] Recently, remarkable progress in click chemistry, such as copper-catalyzed alkyne-azide cycloaddition (CuAAc) and metathesis reaction, has enabled controlled synthesis of various well-defined cyclic polymers with high purity, in which intramolecular ring-closure reaction was conducted in high dilution between the both chain ends of telechelic polymers.[10,11] Especially, the combination of CuAAc with controlled/living polymerization is an efficient method to produce the cyclic polymers since CuAAc offers high activity and selectivity without side reaction even in extremely high dilution,[12-20] which was first reported by Grayson et al. using a heterotelechelic polymer with an alkyne and azide at the a- and w-end, respectively, prepared by the copper-catalyzed atom transfer radical polymerization.[12] To synthesize such a heterotelechelic polymer, it is generally required to combine two methods of introducing a functional group at the end of living polymer chain: initiator and terminator methods. Whereas the former conducts a protected or inert functional group introduced into the initiator that should be intact during the propagation, the latter requires a highly efficient terminating agent bearing a functional group as well as high fidelity of the chain-end structure during the living polymerization.

Recently, we have also reported the synthesis of moderately syndiotactic PMMA using stereospecific living radical polymerization,[21] which was further employed for macrocyclization.[22] Although anionic polymerization provides a wide range of tacticity during MMA polymerization, however, synthetic strategy for the macrocyclic polymers with anionic polymerization has been limited to the combination of hydrocarbon monomers, such as styrenes and dienes, even with click reactions, probably due to the lack of the variety in easily available functional initiators and/or highly efficient reaction for end-functionality for the polymerization of polar monomers like MMA.[9,23,24]

This study is directed to the synthesis of cyclic *st*-PMMA, of which the main chain is formed with stereospecific living anionic polymerization. For that, we investigated the synthesis of clickable heterotelechelic *st*-PMMA using both novel initiator and terminator methodologies. The functional initiator for the anionic polymerization of methacrylate has been rather limited because the pendent carbonyl groups sometimes cause a 1,2-addition by highly reactive nucleophiles.[4] Herein, we first examined a protected alkyne-bearing initiator, which was *in-situ* prepared from a haloester by metal-halogen exchange reaction,[25] for the syndiospecific living anionic polymerization of MMA, which was combined with the direct terminal halogenation[26] and conversion to an azide group. The obtained heterotelechelic polymer with alkyne and azide groups was consequently amenable to the intramolecular click reaction leading to a macrocyclic *st*-PMMA (Scheme 1).



Scheme 1. Synthesis of Syndiotactic Macrocyclic Poly(methyl Methacrylate) via Stereospecific Anionic Polymerization

Experimental Section

Materials

Methyl methacrylate (MMA; TCI, >99.8%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; TCI, >98.0%), *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA; TCI, >98%), and CCl_3Br (TCI, >98%) were distilled from calcium hydride before use. CuBr (Wako, >99.9%) was used as received and handled in a glove box (MBRAUN LABmaster sp) under a moisture- and oxygen-free argon atmosphere (O_2, <1 ppm). Diphenylhexyllithium (DPHLi) was prepared according to the literature.[27] Toluene (Kanto, >99.5%; H_2O <10 ppm), dimethylformamide (DMF; Kanto, >99.5%; H_2O <0.001%), and tetrahydrofuran (THF; Kanto, >99.5%; H_2O <0.001%) were dried and deoxygenized by passage through columns of Glass Contour Solvent Systems before use. Tetrabutylammonium fluoride (TCI, ca. 1 mol/L in THF) and sodium azide (Kanto, >97.0%) were used as received.

Heterotelechelic Polymer by Anionic Polymerization

Polymerization was carried out under dry argon or nitrogen in baked glass tubes equipped with a three-way stopcock using the syringe technique. The following is a typical example for the MMA polymerization by **1**/DPHLi. Prior to the polymerization, the enolate initiator was *in-situ* prepared by adding 1.12 mL of α-bromoisobutyric acid ester (0.307 mmol, 272 mM in THF) bearing a pendent protected-alkyne [**1**: 3-(trimethylsilyl)propargyl α-bromoisobutyrate], which was prepared by the esterification reaction between 3-(trimethylsilyl)propargyl alcohol (Aldrich, 99%) and 2-bromoisobutyryl bromide (TCI, >98.0%), into the THF solution of DPHLi (0.46 mmol) at –78 °C. Into the mixture, MMA (7.67 mmol, 0.82 mL) was added dropwise, and the total volume of the reaction mixture was thus 9 mL. After stirring for 10 min, the polymerization was terminated with CCl_3Br (13.2 mmol, 1.30 mL). After 2 h, DBU (1.60 mmol, 0.24 mL) was added. After additional 23 h, methanol (4.9 mL) containing 1 *N* HCl was added into the reaction mixture. The solution was diluted with toluene, washed with 1 *N* HCl and water to remove initiator residues, evaporated to dryness under reduced pressure to give the heterotelechelic *st*-PMMA (1.04 g, $M_n = 4700$, $M_w/M_n = 1.08$).

Post-polymerization Modification Procedures

The obtained *st*-PMMA with a protected alkyne and bromine termini (0.69 g, 0.14 mmol) was dissolved in 13.8 mL of DMF along with sodium azide (47 mg, 0.72 mmol). The flask was immersed in thermostatic oil bath at 40 °C and kept stirred for 17 h. The solution was diluted with 30 mL of toluene, and washed with H_2O. The solution was concentrated and dried to give PMMA carrying a protected alkyne and azide terminal groups (0.66 g, 96 % yield). Then, for the deprotection of trimethylsilyl group, the polymer (0.63 g, 0.13 mmol) was dissolved in 12.2 mL of THF. To the solution, 0.26 mL of the THF solution of tetrabutylammonium fluoride (1.0 M, 0.26 mmol) was added at 0 °C. After 1 h, the solution was diluted with 30 mL of toluene, washed with 1 *N* HCl and H_2O, and evaporated to dryness to give the clickable PMMA carrying an alkyne and azide terminal groups (0.60 g, 91 % yield).

Intramolecular CuAAc

The intramolecular CuAAc reaction was carried out with $CuSO_4$ in the presence of sodium ascorbate as the reducing agent in DMSO/H_2O (98/2) in high dilution using a 2L glass flask equipped with a stopcock. The heterotelechelic *st*-PMMA (236 mg, 0.050 mmol) and $CuSO_4$ (1.34 g, 8.37 mmol) were dissolved in DMSO (1.64 L). To this solution, 33.5 mL (1.0 M) of the aqueous solution of sodium ascorbate (9.13 g, 46 mmol) was added under a N_2 atmosphere. The flask was immersed in thermostatic oil bath at 70 °C, and the reaction mixture was allowed to stir for 60 h. The reaction was quenched by dilution with toluene (3 L). The mixture was washed with 5 % of EDTA aqueous solution, of which the organic layer was filtered and washed again with water three times. The solution was evaporated to dryness under reduced pressure to give the crude cyclic *st*-PMMA (132 mg, 56 % yield).

For further purification to remove the linear polymers with alkyne terminal, the product was allowed to CuAAc again by the CuBr/PMDETA system with azide-bearing polystyrene resin, which was prepared by reacting ca. 10% chloromethyl-pendent polystyrene resin (TCI, crosslinked with 1% divinylbenzene) with sodium azide. The crude cyclic polymer (22 mg) was redissolved in 154 mL of toluene, and into the solution 0.33 g of the azidemethyl resin was added as well as CuBr (22 mg, 0.156 mmol) and PMDETA (0.03 mL, 0.156 mmol) as the catalyst. The heterogeneous mixture was allowed to stir at 60 °C for 48 h. The product was purified with the same procedure as for the first CuAAc, and pure cyclic *st*-PMMA (14 mg) was obtained in 64 % yield.

Measurements

The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of the polymers were measured by size exclusion chromatography (SEC) using THF at a flow rate 1.0 mL/min at 40 °C on two polystyrene gel columns [Shodex KF-805L (pore size: 20–1000 Å; 8.0 mm i.d. × 30 cm)] that were connected to a JASCO PU-2080 precision pump and a JASCO RI-2031 detector. The columns were calibrated against 7 standard PMMA samples (Varian; M_p = 202–1677000, M_w/M_n = 1.02–1.23). ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ESC-400 spectrometer operating at 400 and 100 MHz, respectively. The triad tacticity of the polymer was determined by the peak intensity of carbonyl C=O carbons observed at 175–180 ppm in the ^{13}C NMR spectrum. MALDI-TOF-MS spectra were measured on a Shimazu AXIMA-CFR Plus mass spectrometer (linear mode) using 1,8-Dihydroxy-9[10H]-anthracenone (Dithranol) as the ionizing matrix and sodium trifluoroacetate as the ion source.

Results and Discussion

Synthesis of Hetero-Telechelic *st*-PMMA by Anionic Polymerization

It is known that the syndiospecific anionic polymerization of MMA proceeds with lithium cation as the counterion in polar solvents like THF at a lower temperature, in which a lithium-based nucleophile like 1,1-diphenylhexyl lithium prepared by the 1:1 addition of butyl lithium to 1,1-dipehnylethylene has been employed as the initiator.[1,28] Herein, we first examined the synthesis of syndiotactic PMMA with an alkyne terminal using a lithium enolate initiator bearing a protected-alkyne. The initiator was *in-situ* prepared from of α-bromoisobutyric acid ester bearing a pendent protected-alkyne (**1**) by the metal-halogen exchange reaction with 1,1-diphenylhexyl lithium (DPHLi) in THF at –78 °C: $[\mathbf{1}]_0$ = 34 mM and $[\text{DPHLi}]_0$ = 51 mM. By adding MMA monomer into the initiator solution

([MMA]$_{add}$/[DPHLi]$_0$ = 16.7), the MMA polymerization was conducted in THF to afford a living polymer with narrow molecular weight distributions (M_w/M_n = 1.08), although the number-average molecular weight (M_n) of the polymer (M_n = 4900) was much higher than that obtained in the absence of the α-bromoester (**1**) (M_n = 2100) and the theoretical value calculated by the [MMA]/[Li] ratio [M_n(calcd) = 1870], which suggests low initiating efficiency as also discussed later. As the result of anionic polymerization in THF, the syndiotacticity was relatively high, of which the triad tacticity was *rr*/*mr*/*mm* = 75/23/2 by ^{13}C NMR analysis.

Figure 1 shows the ^{1}H NMR spectra of the PMMA obtained in the absence or presence of **1** after quenching with acidic methanol. The characteristic aromatic protons (*h*) and methyl protons (*g*) originated from DPHLi as the initiator were observed in the ^{1}H NMR spectrum without **1**. On the other hand, the polymer obtained with **1** did not show those peaks (*g* and *h*) at all but exhibited the peaks ascribed to the ester group bearing protected-alkyne at the α-end (*d* and *e*) at 4.7 and 0.2 ppm, respectively, besides the large absorptions (*a*–*c*) attributed to the repeat units of MMA at 1.0, 2.0, and 3.7 ppm. The molecular weight determined from the peak intensity ratio of the ester-protons (*d*) at the α-terminal to the main-chain methoxy protons (*c*) of the MMA units was in a good agreement with that by SEC indicating that all the polymer chains were initiated with the alkyne-bearing lithium enolate initiator (F_n = 0.99).

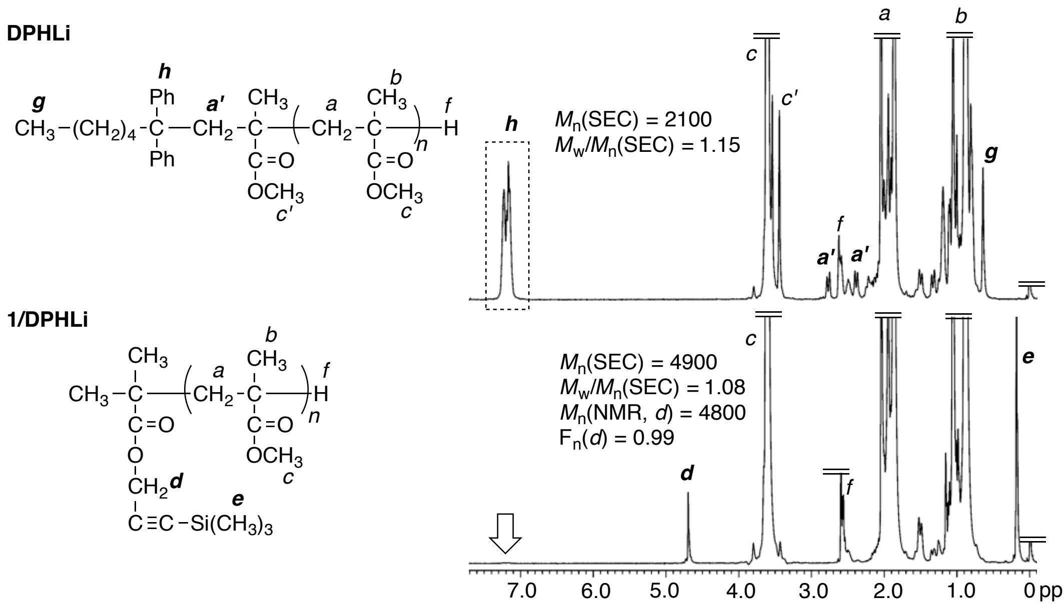


Figure 1. ^{1}H NMR spectra (acetone-d_6, 55 °C) of PMMA obtained with diphenylhexyllithium or **1**/diphenylhexyllithium using methanol as the quenching agent: [MMA] = 850 mM, $[1]_0$ = 0 or 34 mM, $[\text{DPHLi}]_0$ = 51 mM in THF at –78 °C.

The chain-end structure of the polymers obtained with and without **1** was also confirmed by MALDI-TOF MS (Figure 2). Both of the spectra consist of the sharp peaks separated by a 100 Da interval, which corresponds to the molecular weight of MMA monomer. The absolute molecular weights of each peak carrying sodium cation as the ionizer agreed with the calculated values for those initiated by DPHLi and the alkyne-bearing lithium enolate, respectively, which are the exact chain structure expected from the reaction mechanism. Especially, the spectrum with the **1**/DPHLi initiating system displayed only a single series of the peaks and was free from the peaks observed in the spectrum without **1**. Thus, facile functionalization at the α-end in the anionic polymerization of MMA was achieved by the metal-halogen exchange reaction, specifically in this case, to give polymers with a protected alkyne group at the initiating site.

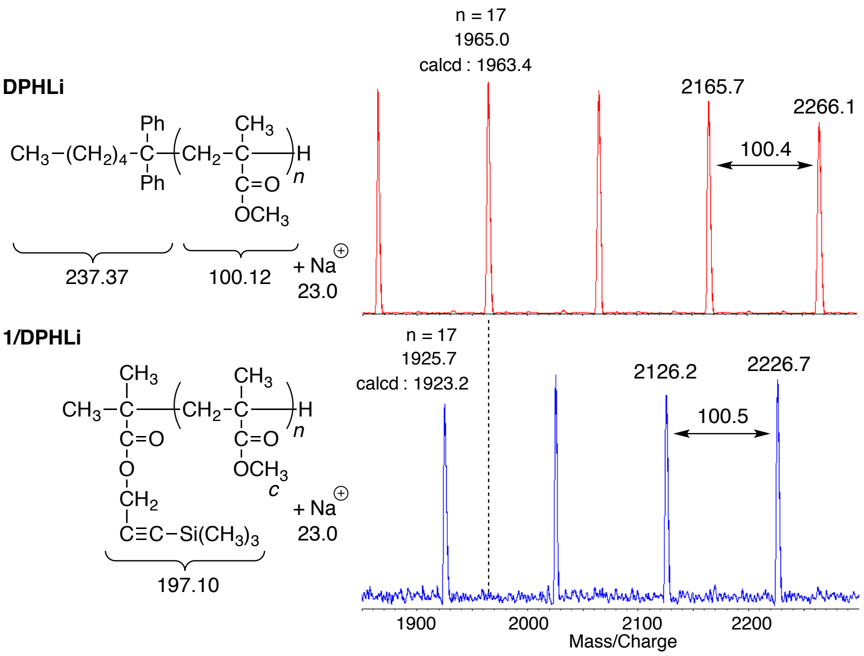


Figure 2. MALDI-TOF mass spectra of PMMA analyzed by ^{1}H NMR in Figure 1.

To introduce another functionality at the growing ω-terminal, the MMA polymerization was then terminated by CCl_3Br as the halogenating agents in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the Lewis base additive.[26] As shown in Figure 3, halogenation of the growing anionic species by CCl_3Br was confirmed by ^{1}H NMR spectoroscopy. In addition to the peaks (*d* and *e*) of the protected alkyne derived from **1**, the spectrum gave the peaks (*a′* and *c′*) derived from the unit adjacent to bromine terminal at the growing end. The quantitative functionality was calculated from the peak intensity ratio of *c′* and *d* [F_n(C–Br) = 1.00]. Thus, heterotelechelic *st*-PMMA with quantitative an alkyne and a halogen at chain ends, which is exactly the same structure as in the previous work by stereospecific living radical polymerization,[22] was obtained by the combination of the metal-halogen exchange reaction and terminal halogenation in anionic polymerization.

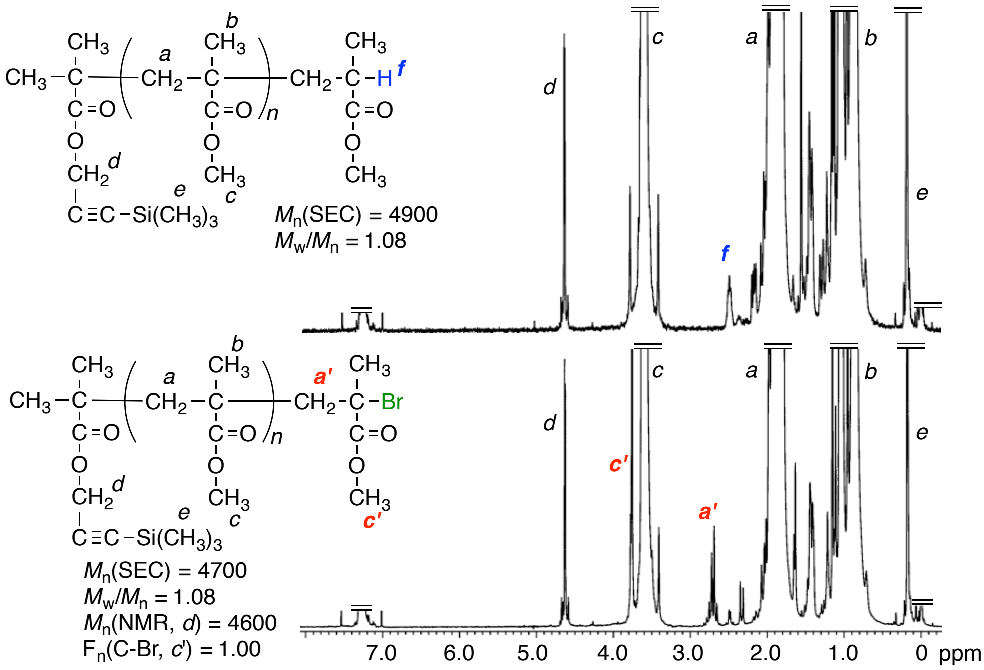


Figure 3. ^{1}H NMR spectra (CDCl$_3$, 55 °C) of PMMA-X (X = H and Br) obtained with **1**/diphenylhexyllithium in THF at –78 °C ([MMA]$_0$/[**1**]$_0$/[DPHLi]$_0$ = 850/34/51 mM) using methanol (**A**) or CCl$_3$Br (**B**) as the quenching agent: [**1**]$_0$/[CBrCl$_3$]$_{add}$/[DBU]$_{add}$ = 1/40/5 at –78 °C for 2 h and then gradually raising temperature to r.t. for 23 h.

To improve the syndiotacticity of PMMA, the anionic polymerization was further examined at a lower temperature as well as changing initial feed ratio of the initiator and monomers. MMA was polymerized at –100 °C in THF by the protected alkyne-containing initiator *in-situ* prepared from α-bromoester (**1**) and DPHLi, in which the initial concentration of MMA was varied from 442 to 850 mM and those of **1** and DPHLi were constant at 34 and 51 mM, respectively. The polymerization was also terminated by CCl$_3$Br as the halogenation agent. Figure 4 shows the M_n of the polymers obtained in –78 °C and –100 °C as a function of [MMA]$_0$/[DPHLi]$_0$ ratio. At both temperatures, the M_n was higher than the calculated values but increased in proportion to the [MMA]$_0$/[DPHLi]$_0$ ratio to give polymers with narrow molecular weight distributions. These indicate that the polymerization proceeded in a living manner though the conversion efficiency from the halide into enolate was low, probably due to the consumption of DPHLi in the elimination with 1,1-diphenylhexylbromide that is a by-product of the metal-halogen exchange reaction. As a result of analyzing the produced polymer by ^{13}C NMR, the syndiospecific polymerization was carried out similarly to the conventional alkyllithium-initiated polymerization without **1**, in which the heterotelechelic *st*-PMMA with 81% of *rr* triad was obtained at a lower temperature of –100 °C.

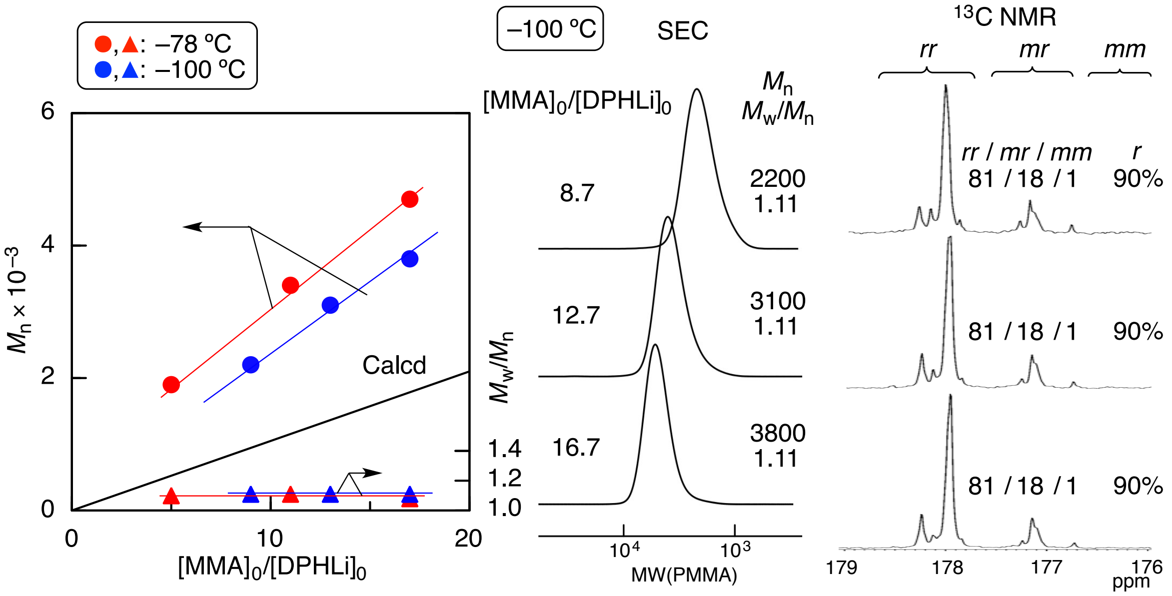


Figure 4. M_n, M_w/M_n, and SEC curves and ^{13}C NMR spectra (CDCl$_3$, 55 °C) of PMMA obtained in the anionic polymerization with **1**/diphenylhexyllithium in THF at –78 or –100 °C: [MMA]$_0$ = 272, 544, 850 (for –78 °C) or 442, 646, 850 mM (for –100 °C), [**1**]$_0$ = 34 mM, [DPHLi]$_0$ = 51 mM in THF. The polymerization was quenched by halogenation with CCl$_3$Br under the same condition as for Figure 3.

Synthesis of Macrocyclic *st*-PMMA by Intramolecular Click Cyclization

In order to carry out the intramolecular CuAAc reaction, the obtained heterotelechelic polymer was further subject to the post-polymerization modification of the terminal groups, as in the case with the polymers obtained by stereospecific living radical polymerization. The polymers through the post-reactions with sodium azide at the ω-end followed by the deprotection of silyl group at the α-end were also monitored by ^{1}H NMR spectroscopy (Figure 5). The terminal bromine at the ω-end of *st*-PMMA was converted to an azide group by S_N2 reaction with NaN_3 in DMF at 40 °C. Upon the substitution of bromine to the azide group, the characteristic methylene proton of the terminal MMA unit (*a′*) disappeared, whereas the peaks attributed to the α-end (*d* and *e*) were intact (Figure 5B). The functionality of the azide group at the ω-end, however, was estimated to be slightly decreased because E2 reaction occurred during the nucleophilic substitution to form C=C bond observed at 6.7 ppm in the NMR spectrum [$F_n(C–N_3) = 0.85$]. Then, the deprotection of the silyl group at the α-end was carried out using tetrabutylammonium fluoride in THF at 0 °C. After the deprotection, the spectrum showed the complete disappearance of trimethylsilyl group (*e*) and a new peak attributed to ethynyl group (*e′*) was observed (Figure 5C). Thus, the heterotelechelic *st*-PMMA with terminal alkyne and azide was now prepared by the post-polymerization modification.

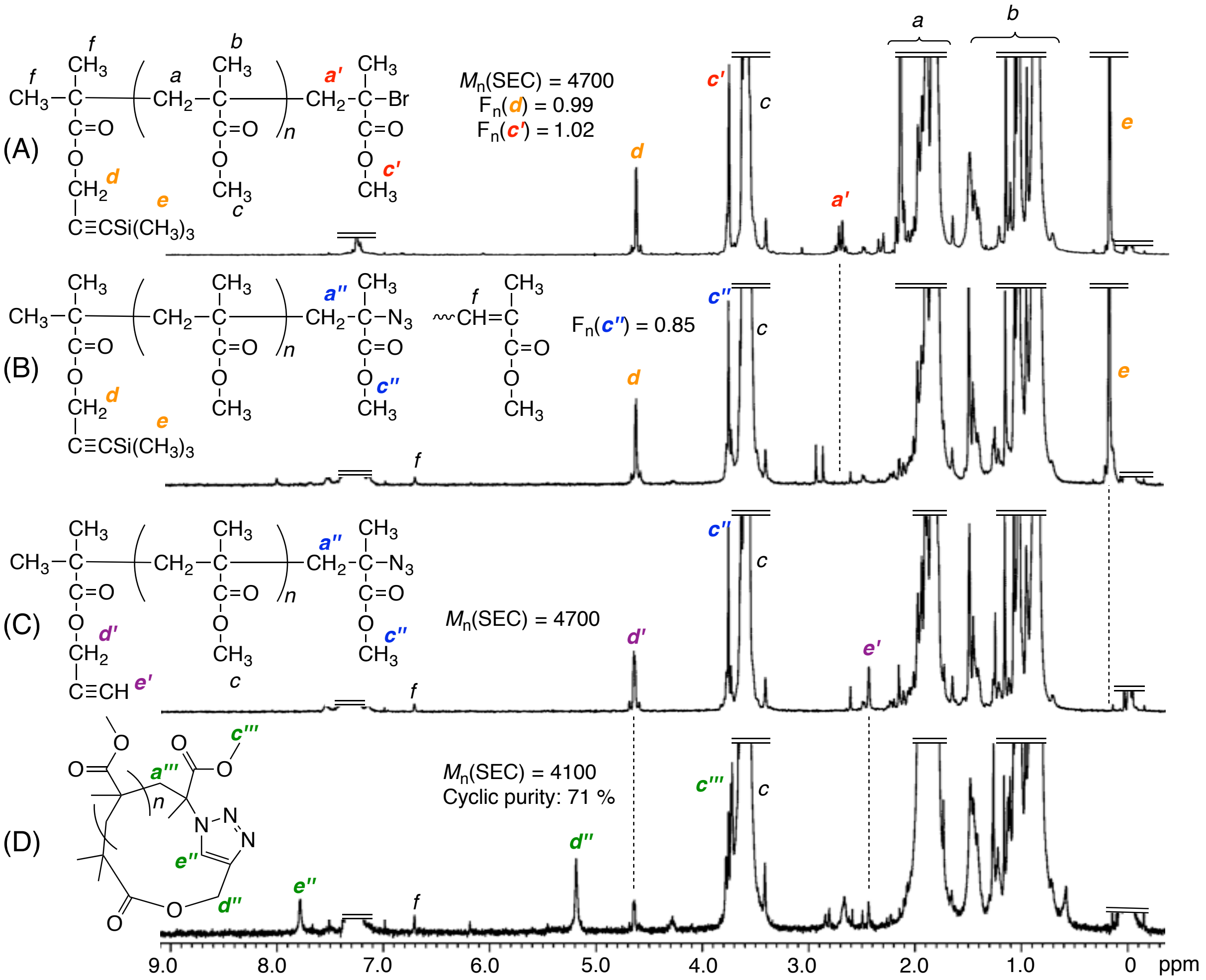


Figure 5. ^{1}H NMR spectra of *st*-PMMA obtained by anionic polymerization from **1** and termination with $CBrCl_3$ (**A**), azidation with NaN_3 (**B**), deprotection of trimethylsilyl group (**C**), and click intramolecular cyclization (**D**).

Finally, macrocyclic *st*-PMMA was synthesized by reacting the terminal azide and alkyne using CuAAc with $CuSO_4$ using sodium ascorbate as the reducing agent in DMSO/H_2O (98/2) under highly dilution conditions. As shown in the ^{1}H NMR spectrum in Figure 5D, the peak of the ethynyl group (*e′*) decreased and new peaks of triazole ring (*e″*) and the adjacent peak (*d″*) appeared as the CuAAc reaction proceeded. These results clearly indicate that well-defined macrocyclic *st*-PMMA formed by intramolecular click cyclization, though it was slightly contaminated by linear polymers with alkyne at the α-end and C=C bond at the ω-end (cyclic purity > 70 %).

The macrocyclization by CuAAc was also performed to the heterotelechelic *st*-PMMAs with various molecular weights using the CuBr/PMDETA system in toluene at 60 °C. Figure 6 shows the SEC curves for the various molecular weight *st*-PMMA before and after the click reaction under similar diluted conditions using CuBr/PMDETA (A) or $CuSO_4$/sodium ascorbate (B). In all cases, the peak top of the SEC curves shifted to the lower molecular weight region retaining unimodal and narrow molecular weight distributions, which differentiates cyclic polymers from their linear precursors. These also strongly support the formation of cyclic *st*-PMMA by intramolecular cyclization.

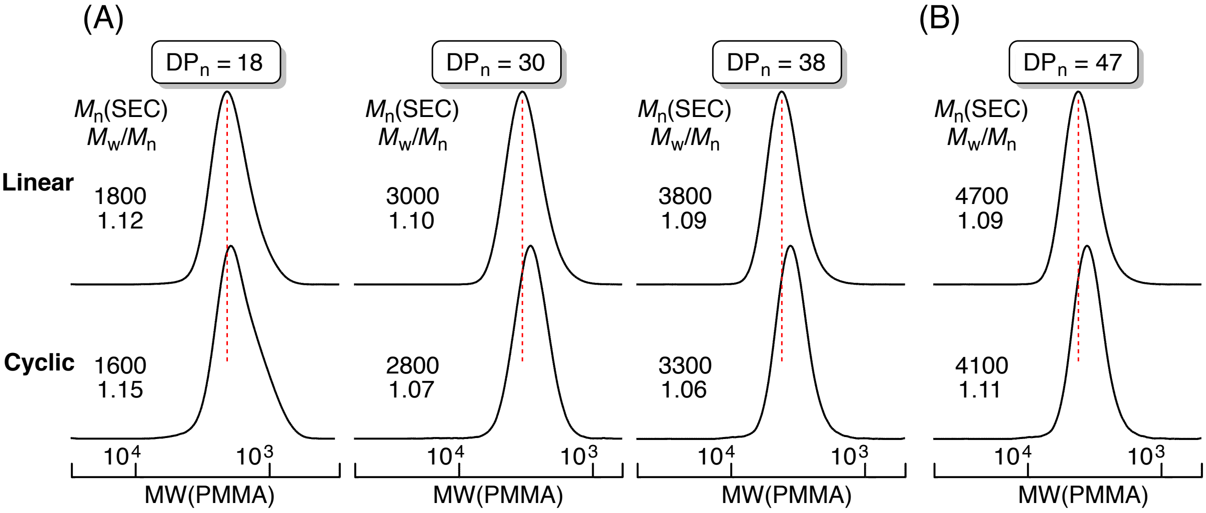


Figure 6. SEC curves for the click intramolecular cyclization of *st*-PMMA with CuBr/PMDETA in toluene (**A**) or $CuSO_4$/sodium ascorbate in DMSO/H_2O (98/2) (**B**) in high dilution: $[PMMA]_0 = 0.066$ (**A**) or 0.03 mM (**B**).

The formation of macrocyclic polymers was also confirmed by the MALDI-TOF-MS analysis (Figure 7). In the MALDI-TOF spectra, the main peaks were observed at 100 intervals before the reaction, and each peak well agreed with the calculated value assumed to bear alkyne and azide group at the termini (Figure 7A). Beside the main peak series, two minor series were observed, which were assignable to the polymers without azide group at the ω-end as well as those losing azide or nitrogen molecule upon the laser irradiation during the MS analysis. After the reaction, the shape of the entire peak hardly changed, in which the absolute value did not change from that before the reaction with the linear contaminant (Figure 7B). Thus, it was confirmed that the intramolecuar click addition reaction proceeded to produce cyclic *st*-PMMA. Furthermore, the purification of macrocyclic *st*-PMMA, i.e. removal of the linear polymers, was investigated using CuAAc with azide-bearing polystyrene resin.[29] Since the residual linear possessed an alkyne group at the α-end beside the less reactive C=C bond at the ω-end, the product mixture was treated with cross-linked polystyrene resin with azidomethylstyrene units (ca. 10%) in the presence of the Cu(I) catalyst to scavenge the excess of alkyne functionalized linear PMMA. After the reaction and filtration, the minor peaks disappeared in the MALDI-TOF spectra, indicating almost pure macrocyclic *st*-PMMA was obtained.

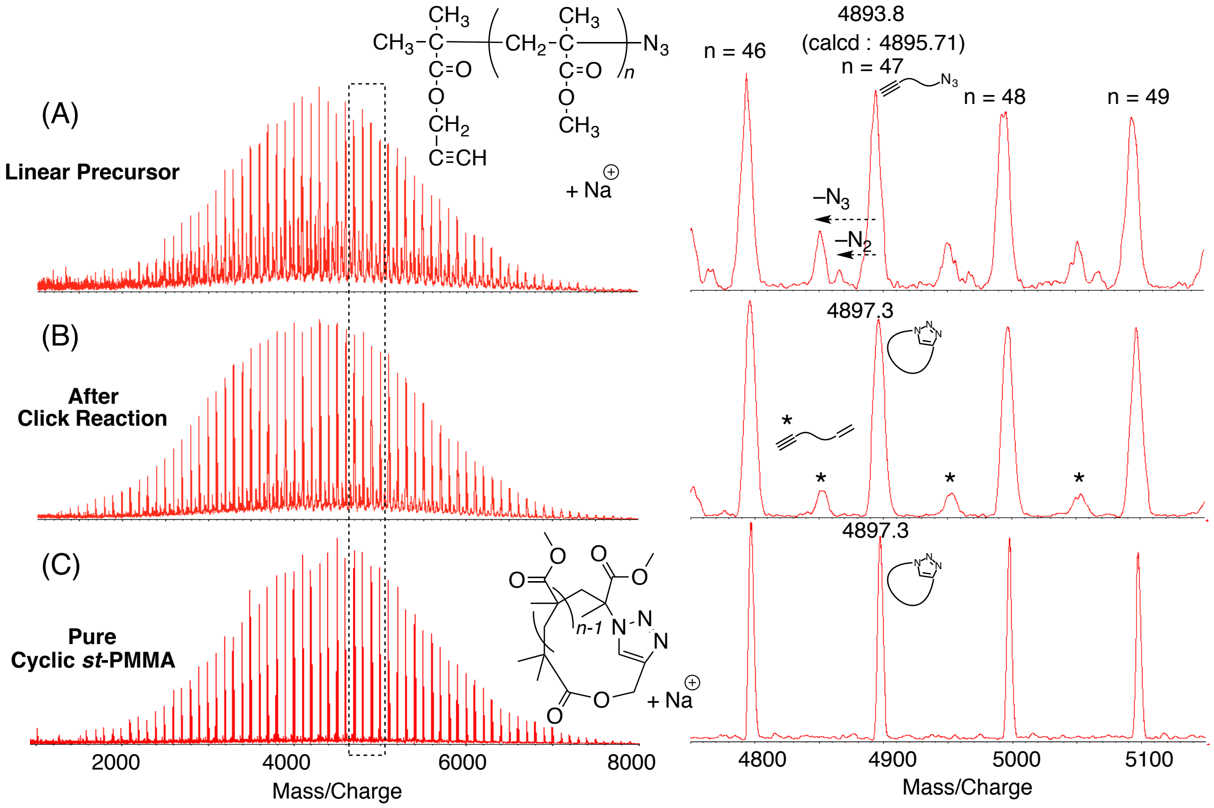


Figure 7. MALDI-TOF-MS spectra of *st*-PMMA (M_n = 4700 and M_w/M_n = 1.09) before (**A**) and after (**B**) cyclization, and pure macrocyclic *st*-PMMA after purification with azide-bearing polystyrene resin (**C**).

Conclusions

In conclusion, the well-defined cyclic *st*-PMMA could be prepared even via stereospecific living anionic polymerization of MMA by transformation of the growing terminal. By the facile metal-halogen exchange reaction of α-haloester with DPHLi, the living anionic polymerization was initiated to produce polymers with functional group at the α-end, which was combined with halogenation of the growing ω-end to form a heterotelechelic polymer in almost a quantitative yield. After the conversion of the end-functionalities into alkyne and azide group, the polymer was amenable to intramolecular

CuAAc to form macrocyclic *st*-PMMA, which was further purified using residual functional end-group.

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Chapter 3

Synthesis and Stereocomplexation of PMMA-Based Star Polymers Prepared by a Combination of Stereospecific Anionic Polymerization and Crosslinking Radical Polymerization

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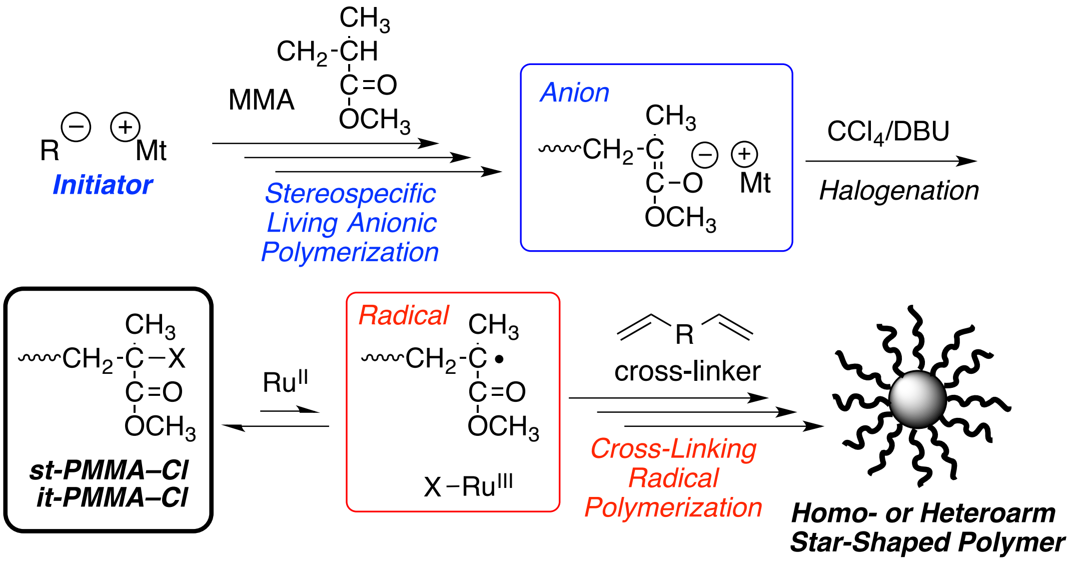
Introduction

Living polymerization facilitates the design of macromolecular architectures such as block, comb graft, and star polymers.[1] A core-linked star-shaped polymer consisting of a central crosslinked core and corona arm polymers is regarded as a unimolecular micelle, which shows characteristic features in terms of high end-group density and low viscosity compared to its linear analogues.[2-7] Core-crosslinked star polymers have been synthesized via various living polymerization, in which linear living polymer chains as the arms react with a small amount of divinyl compounds.[8-18] Transition metal-catalyzed atom transfer radical polymerization, which affords polymers with a stable carbon-halogen terminal, has also been utilized for the efficient formation of core-crosslinked star polymers with a low molecular weight dispersity.[15-18] Star polymers with syndiotactic poly(methyl methacrylate) (*st*-PMMA) arms, which were prepared by a stereospecific Ru-catalyzed living polymerization of MMA in fluoroalcohol solvents, induced stereocomplexation[19-24] with a linear isotacitic PMMA (*it*-PMMA).[17] According to the most recent studies on stereocomplexation, two *it*-PMMA chains intermolecularly aggregate to form a double helix, which is surrounded by a single helix of *st*-PMMA for form a unique triple helix-like structure.[22-24]

Recently, the author's group discovered that a carbon-halogen bond, which is a potential initiating moiety for transition metal-catalyzed radical polymerization, can be introduced into the growing end in the stereospecific living anionic polymerization of MMA.[25] Thus, the mechanistic transformation of an active species can be easily achieved through the halogenation from a living anionic polymerization to a living radical polymerization to form block copolymers. Therefore, a polymer with a higher stereoregularity due to anionic polymerization instead of radical polymerization could be used as a macroinitiator for a radical polymerization, resulting in the synthesis of novel stereoregular macromolecular architectures.[26,27] In this study, the synthesis of novel core-crosslinked star polymers with various stereoregular arm polymers was examined by introducing a halogen atom into the end of syndiotactic and isotactic PMMAs via an anionic polymerization and adapting the linking reaction via a radical polymerization of a divinyl compound using a transition metal catalyst (Scheme 1).



Scheme 1. Star Polymer Synthesis by Anionic and Radical Polymerization Through C-Cl Bond

Experimental

Materials

Methyl methacrylate (MMA; TCI, >99.8%), ethylene glycol dimethacrylate (EGDMA; TCI, >97.0%), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; TCI, >98.0%), CCl_4 (Kanto, >99.9%), and triethylamine (TCI, >99.0%) were distilled from calcium hydride before use. *t*-BuMgBr and Diphenylhexyllithium (DPHLi) were prepared according to the literature.[28,29] Toluene (Kanto, >99.5%; H_2O <0.001%), and tetrahydrofuran (THF; Kanto, >99.5%; H_2O <0.001%) were dried and deoxygenized by passage through columns of Glass Contour Solvent Systems before use. $Ru(Ind)Cl(PPh_3)_2$ (provided from Wako) was used as received and handled in a glove box (MBRAUN LABmaster sp) under a moisture and oxygen-free argon atmosphere (O_2, <1 ppm).

Synthesis of Star Polymers

The stereoregular PMMAs with C-Cl terminal were synthesized by stereospecific living anionic polymerization terminated with halogenation using CCl_4, as reported in the previous paper.[25] The crosslinking radical reaction of the PMMAs was conducted according to the literature.[18] A typical reaction procedure for the polymer with hetero-stereoregular arms is as follows: *it*-PMMA [M_n = 4500, F_n(C-Cl) = 0.78, 347 mg, 0.077 mmol)] and *st*-PMMA [M_n = 5500, F_n(C-Cl) = 1.01, 447 mg, 0.077 mmol], $Ru(Ind)Cl(PPh_3)_2$ (23.9 mg, 0.0308 mmol) were added to a dry round-bottom flask equipped with a three-way stopcock in a glove box. Into the flask, toluene (13.68 mL), EGDMA (0.29 mL, 1.54 mmol), and tryethylamine (0.76 mL of 812 mM toluene solution, 0.616 mmol) were added to make a solution at ambient temperature. Aliquots (1 mL) of the reaction mixture were extracted and flame-sealed in glass ampules under argon atmosphere. The amplules were immersed in a thermostatic oil bath at 80 ºC. At predetermined intervals, the reaction was terminated by cooling the ampule to –78 ºC. A sample was extracted for NMR spectroscopic analysis (EGDMA conversion = 98% for 121 h) and the remaining polymeric product was diluted with toluene and mixed with an absorbent [Kyowaad 2000G-7 ($Mg_{0.7}Al_{0.3}O_{1.15}$); Kyowa Chemical]. The absorbent was filtered off and the filtrate was washed with 1N HCl and water. The organic phase was concentrated in vacuo to afford the star polymer as a clear solid (M_n = 67,000, M_w/M_n = 1.30, star yield = 85%).

Measurements

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ESC-400 spectrometer, operating at 400 and 100 MHz for ^{1}H and ^{13}C, respectively. The number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of the polymers were measured by size exclusion chromatography (SEC) using THF at a flow rate 1.0 mL/min at 40 °C on two polystyrene gel columns [Shodex KF-805L (pore size: 20–1000 Å; 8.0 mm i.d. × 30 cm)] that were connected to a JASCO PU-2080 precision pump and a JASCO RI-2031 detector. The columns were calibrated against standard Poly(MMA) samples (Agilent Technologies; M_p = 202–1677000, M_w/M_n = 1.02–1.23). The MALS analysis was performed in THF on a Dawn HELEOS photometer (Wyatt Technology; 1-633 nm). The triad tacticity of PMMA was determined by the area of the side chain carbonyl C=O carbons between 175-180 ppm in the ^{13}C NMR spectrum. The transmittance of the solution (50 mg/mL in CH_3CN) was recorded at 500 nm of light using a JASCO V-550 spectrophotometer at a cooling rate 1.0 ºC/min from 70 ºC, which was the relative value compared to the transmittance at 55 or 70 ºC.

Results and Discussion

To synthesize stereoregular PMMAs with C-Cl terminals as the arm polymers, halogenation of the growing end was first examined during the streospecific living anionic polymerization of MMA, as reported in a previous paper.[25] MMA was polymerized using 1,1-diphenylhexyllithium (DPHLi) as the initiator in THF to obtain the syndiotactic polymer,[27] whereas polymerization with *t*-BuMgBr in toluene was conducted to obtain the isotactic polymer at -78 ºC.[28] Both of the anionic polymerizations were terminated by the addition of CCl_4 in the presence of diazabicycloundecene (DBU). Thus, living PMMAs were obtained in both cases, in which the number average molecular weights (M_n) of the produced polymers were close to the calculated value assuming that one molecule of the polymer was generated from one initiator molecule with relatively narrow molecular weight distributions (MWDs), as shown in Figure 1. The obtained polymers were further analyzed by NMR spectroscopy (Figure 2). The triad stereoregularities of the obtained PMMAs, which were calculated based on the splitting of the carbonyl group in the ^{13}C NMR spectra, were estimated to be predominantly syndiotactic and isotactic (*rr*/*mr*/*mm* = 77/22/1 and 5/4/91, respectively). In the ^{1}H NMR spectra, a methyl ester peak adjacent to the chlorine terminal was observed in both cases, and the functionalities of the chlorine terminal were estimated by comparing the peak intensity to the molecular weights based on SEC of 1.01 for *st*-PMMA and 0.78 for *it*-PMMA.

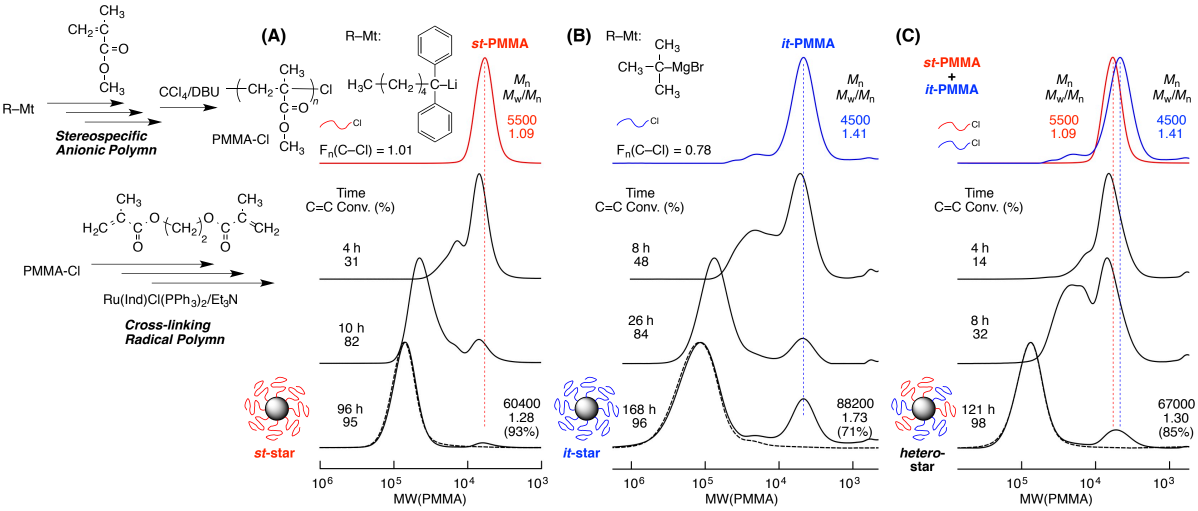


Figure 1. SEC chromatographs for PMMA-Cl macroinitiators by anionic polymerization terminated by CCl$_4$/DBU (upper trace) and the products during the core cross-linking reaction (lower trace) for (A) *st*-PMMA, (B) *it*-PMMA, and (C) 1:1 mixture of *st*- and *it*-PMMA, where the dotted lines are the star polymers after precipitation from hexanes. Anionic polymerization: $[MMA]_0/[DPHLi]_0$ = 1000/20 mM in THF (for syndiotactic) or $[MMA]_0/[t\text{-}BuMgBr]_0$ = 1350/27 mM in toluene (for isotactic) at -78 ºC, terminated with 40 equiv. of CCl$_4$ in the presence of DBU (CCl$_4$/DBU = 4/1). Linking radical polymerization: $[EGDMA]_0/[C\text{-}Cl]_0/[Ru(Ind)Cl(PPh_3)_2]_0/[Et_3N]_0$ = 100/10/2/40 mM in toluene at 80 ºC.

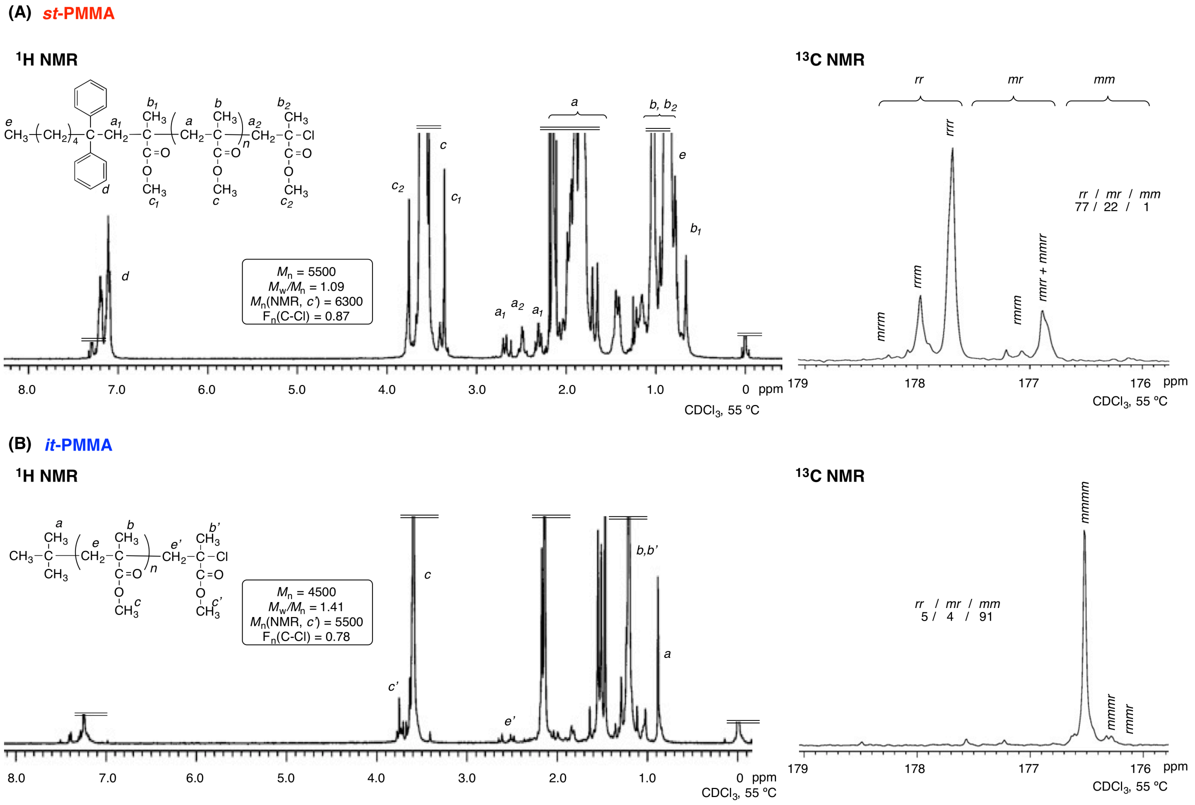


Figure 2. ^{1}H and ^{13}C NMR spectra of syndiotactic and isotactic PMMA obtained via living anionic polymerization of MMA terminated with CCl_4/DBU (the same experiments as for the upper part of Figure 1).

After a typical purification procedure, the resulting stereoregular PMMAs with the C-Cl terminal were used as the arm polymers in the synthesis of core-crosslinked star polymers via a Ru-catalyzed radical polymerization. The radical crosslinking reaction was carried out in toluene at 80 °C by polymerizing ethylene glycol dimethacrylate (EGDMA) (10 equivalents to **1** equivalent of C-Cl), i.e., the crosslinking agent, with the stereoregular PMMAs with chlorine terminals, i.e., the macroinitiator, using an indenyl-type ruthenium catalyst, $[Ru(Ind)Cl(PPh_3)_2]$, in the presence of triethylamine as the accelerator.[18] As shown in the lower part of Figure 1, the crosslinking reaction proceeded well in both cases until almost all of EGDMA was included in the microgel nuclei, but gelation did not occur. In both SEC curves, the peak of the macroinitiator, i.e., the arm precursor, decreased, and new peaks were observed in the higher molecular weight region as the reaction proceeded, which indicated the efficient formation of the core crosslinked star polymers with the *st*-PMMA and *it*-PMMA arm polymers (A and B, respectively). In particular, the *st*-PMMA macroinitiator, which has a higher functionality of the chlorine end, was almost quantitatively consumed to form a star polymer (>90%) having with a narrow MWD ($M_w/M_n = 1.28$).

Furthermore, the synthesis of heterostereoregular arm star polymer was also examined by mixing the *st*-PMMA and *it*-PMMA arm precursors (C in Figure 1). The stoichiometrically equimolar amounts of the *st*-PMMA and *it*-PMMA were dissolved in the reaction mixture and treated with the Ru catalyst in the presence of 10 equivalents of EGDMA. As in the case of homo-arm precursors, the reaction also progressed via co-crosslinking of the hetero-stereoregular macroinitiators to form unimodal star polymers with a relatively narrow MWD ($M_w/M_n = 1.30$) in a moderate yield (85%). Figure 3 shows the expanded ^{13}C NMR spectra in the carbonyl carbon region of the arm polymer precursors and the produced star polymer, and the spectra clearly showed that the obtained core crosslinked star polymer was composed of *st*-PMMA and *it*-PMMA as the corona arms; however, detailed values could not be calculated because the peaks overlapped with those of EGDMA. Thus, the combination of the stereospecific anionic polymerization and crosslinking radical polymerization also led to core-crosslinked star polymers with hetero stereoregular arms, which cannot be efficiency prepared via stereospecific anionic polymerizations.[11]

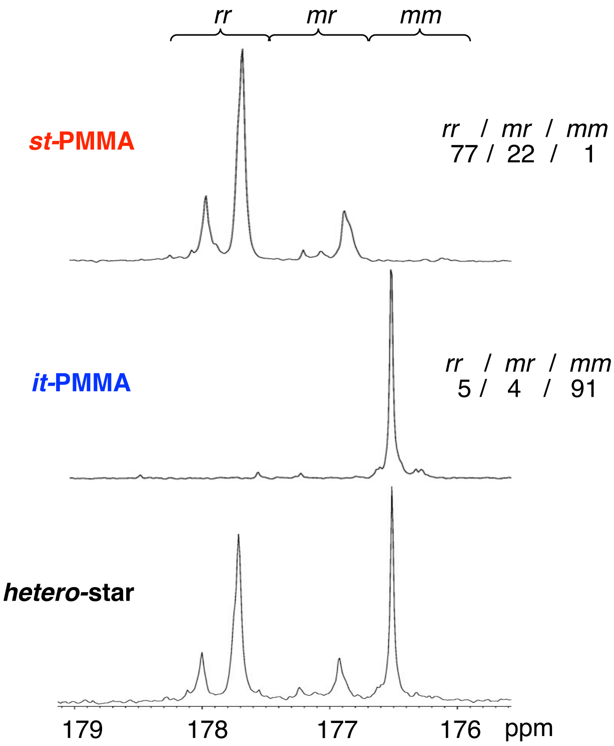


Figure 3. ^{13}C NMR spectra ($CDCl_3$, 55 ºC) of *st*-PMMA and *it*-PMMA by anionic polymerization, and *st*-PMMA and *it*-PMMA hetero arm-star polymers by radical linking reaction.

By changing the initial molecular weights of the arm precursor, various star polymers can also be prepared with different corona arm lengths (Table 1). Using the same methodology, *st*-PMMA, which has a higher M_n and *it*-PMMA, which has a lower M_n, were employed for the synthesis of star polymers. Although the MWDs were broader with the arm polymer with a lower M_n, core crosslinked star polymers were produced in all cases, as shown in Figure 4 and 5. In general, there is a large difference between the absolute molecular weights and those determined by the SEC for non-linear star-shaped polymers because the star shape is more compact with a smaller hydrodynamic volume than the corresponding linear counterpart.[10] Using a multi-angle light scattering detector (MALS), the absolute molecular weights of each star polymer were calculated to be between 20,000 to 1,130,000, which are much higher than those calculated by the SEC measurement using PMMA standards. In addition, the average number of arms on the star polymers could be estimated to be between 15 and 200. Thus, by a mechanistic transformation from an anionic polymerization to a radical polymerization, star polymers with various stereoregular PMMAs in the arm polymers were facilely synthesized, even using a mixture of arm precursors.

TABLE 1 Characterization of Arm Precursor and Resultant Core Crosslinked Star Polymers.

Code	M_n (arm)[b]	M_w/M_n (arm)[b]	F_n(C–Cl) (arm)[c]	M_n(RI) (star)[b]	M_w/M_n(RI) (star)[b]	M_w(MALS) (star)[d]	Star yield, %[b]	N_{arm} (star)[e]
st50	5,500	1.09	1.01	60,400	1.28	201,100	93	26
st100	11,800	1.08	1.00	95,500	1.11	233,700	95	16
it25	2,700	1.29	1.00	87,200	1.83	1,127,000	88	198
it50	4,500	1.41	0.78	88,200	1.73	943,300	71	101
hetero50[a]	—[a]	—[a]	—[a]	67,000	1.30	491,800	85	39

[a] Equimolar mixture of *st*-PMMA (st50) and *it*-PMMA (it50) was used as the arm. [b] Determined by RI detector during SEC measurement against PMMA standard samples. [c] Determined by ^{1}H NMR. [d] Determined by multi-angle light scattering detector (MALS). [e] Calculated by using M_n(arm), M_w(MALS), M_w/M_n, and actual weight fraction of the arm in the star polymers.

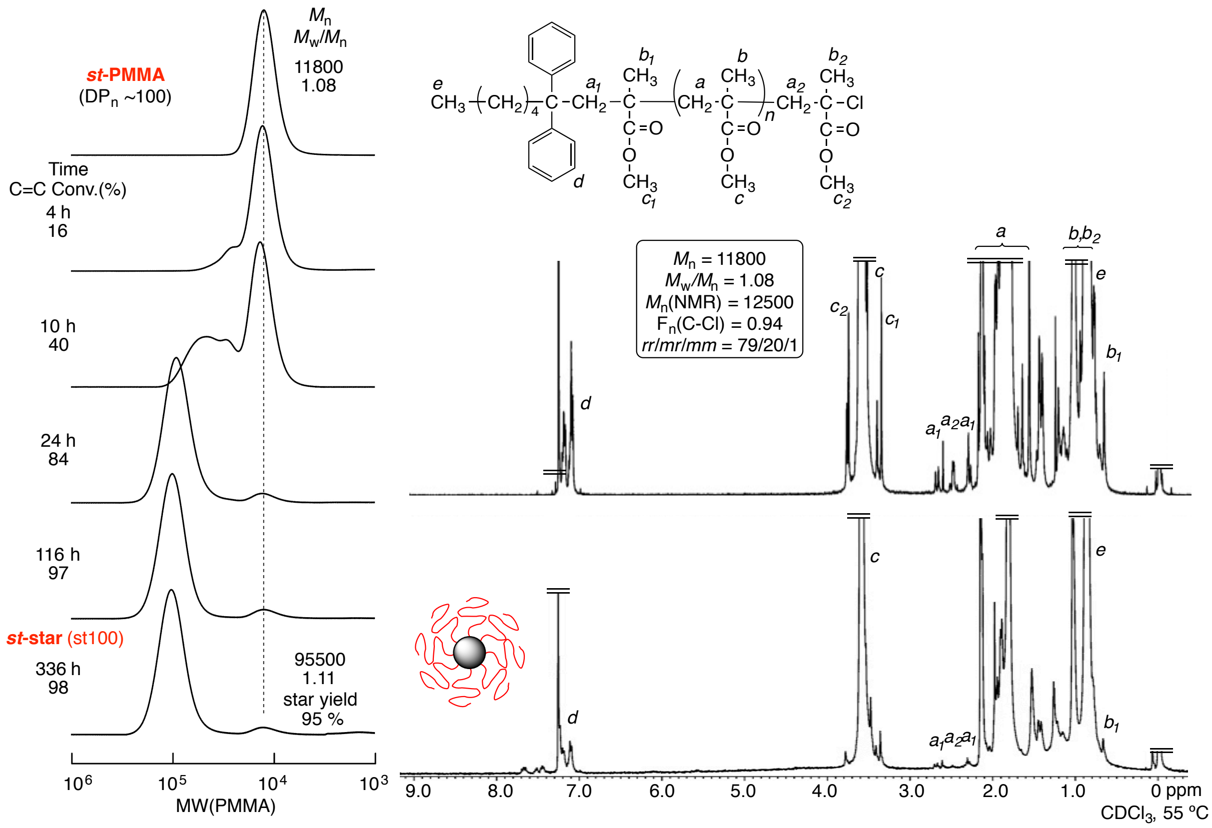


Figure 4. SEC curves and ^{1}H NMR spectra for the synthesis syndiotactic PMMA star polymer using a higher M_n arm polymer. See st100 in Table 1 in the main text.

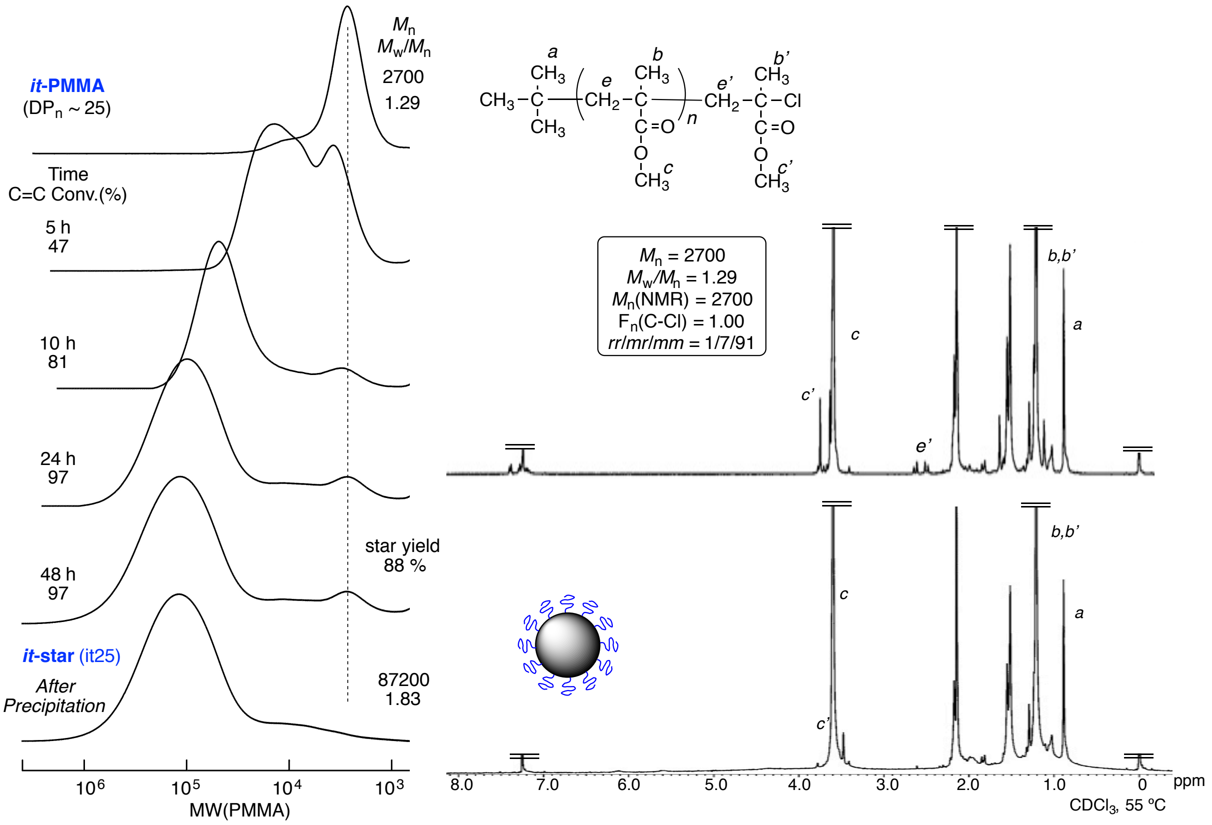


Figure 5. SEC curves and ^{1}H NMR spectra for the synthesis isotactic PMMA star polymer using a lower M_n arm polymer. See it25 in Table 1 in the main text.

The formation of stereocomplexes of the star polymers was evaluated in a 50 mg/mL CH_3CN solution. As in the case of the *st*-PMMA star polymers formed via a stereospecific living radical polymerization with a linear *it*-PMMA in the previous paper,[17] the *st*-PMMA stars obtained by the combination of an anionic polymerization and a radical linking reaction formed thermally reversible gels with the linear *it*-PMMA, and these gels solidified at low temperatures. Similarly, the *st*-PMMA star polymers formed complexes with the star polymer with *it*-PMMA arms, but the solutions of each star polymer did not show any thermally responsive features (Figure 6A). Meanwhile, the solution of the hetero-stereoregular arm star polymer containing both *st*-PMA and *it*-PMMA became a thermally responsive gel. Since the formation of the stereocomplex caused the solution to become turbid, the complexation behavior was further analyzed by measuring the light transmittance of solutions at 500 nm. The results clearly showed that the solutions became turbid as the function of temperature due to the formation of the stereocomplex. All of the solutions were clear with a high transmittance at temperatures higher than 65 ºC, but the solutions gradually became turbid with cooling (Figure 6B). The chain length of the arm polymers affected this behavior, and the stars with longer arm chains became turbid at higher temperatures than those with shorter arm chains.

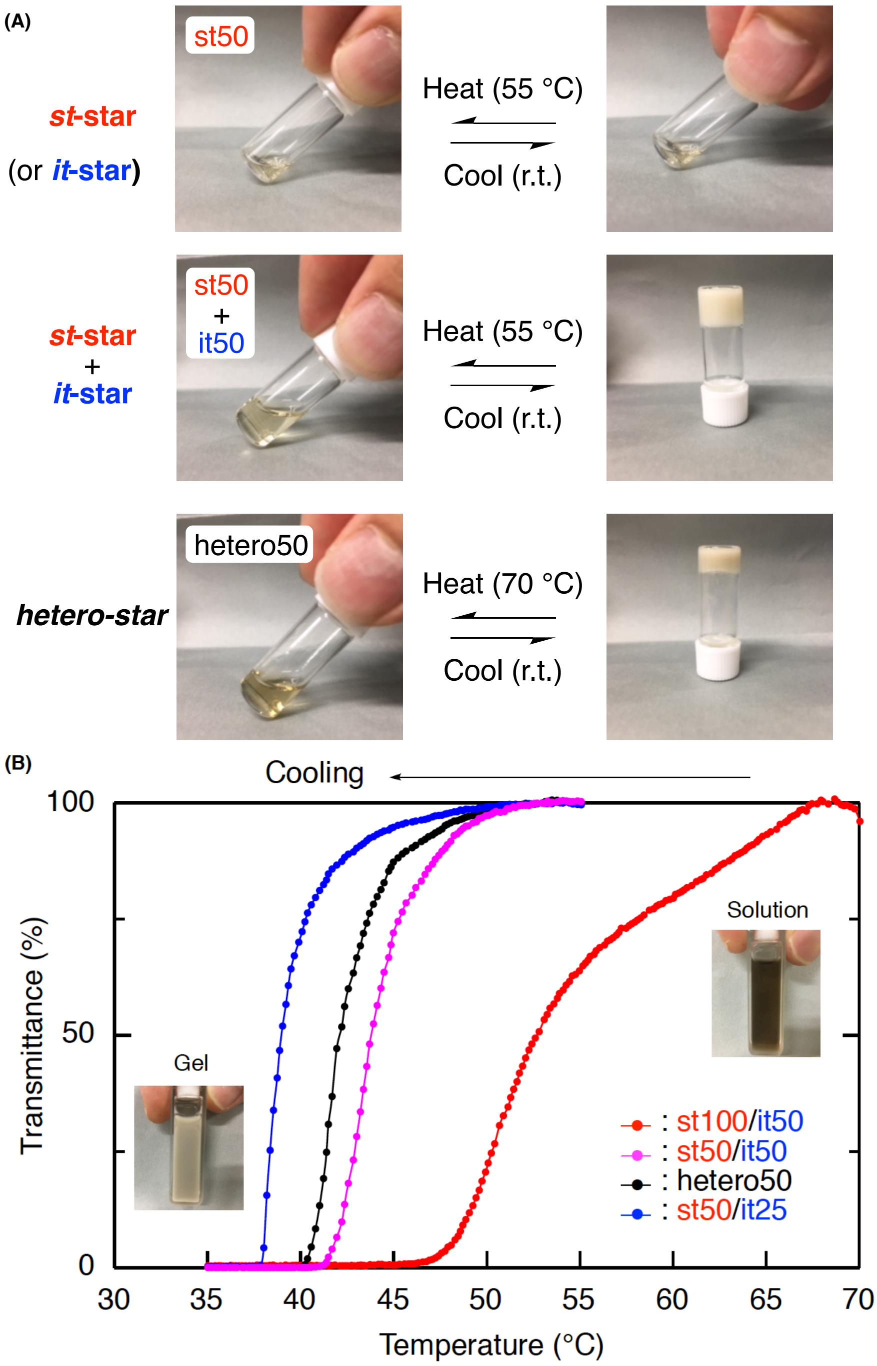


Figure 6. Stereocomplex formation of star polymers in CH_3CN (50 mg/mL): **(A)** photographs for *st*50/*it*50 mixture or only hetero50, and **(B)** the relative transmittance of solutions for *st*100/*it*50, *st*50/*it*50, *st*50/*it*25 mixtures or hetero50 (the codes correspond to those in Table 1).

Conclusions

In summary, novel star-shaped polymers with various stereo-regular arm polymers were successfully synthesized by a combination of seterospecific living anionic polymerization and transition metal-catalyzed radical linking polymerization, in which the terminal halogen mediated the transformation of the growing active species from a carbanion into a carbon radical. Using this technique, a series of star polymers with *it*- and *st*-PMMA arms were prepared with various stereocomplexation behaviors. This technique utilizes both merits of living anionic and radical polymerization, i.e., highly precise control for the former and versatility and robustness for the latter. These results indicate that mechanistic transformation is powerful for novel polymer synthesis.[30]

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List of Publication

Papers

Chapter 1

‘’Synthesis of Isotactic-block-Syndiotacitc Poly(methyl Methacrylate) via Stereospecific Living Anionic Polymerizations in Combination with Metal-Halogen Exchange, Halogenation, and Click Reactions’’
Naoya Usuki, Kotaro Satoh, Masami Kamigato
Polymers, **2017**, *9*, 723.

Chapter 2

‘’Synthesis of Syndiotactic Macrocyclic Poly(methyl Methacrylate) via Transformation of the Growing Terminal in Stereospecific Anionic Polymerization’’
Naoya Usuki, Kotaro Satoh, Masami Kamigaito
Macromol. Chem. Phys., **2017**, *218*, 1700041.

Chapter 3

‘’Synthesis and Stereocomplexation of PMMA-Based Star Polymers Prepared by a Combination of Stereospecific Anionic Polymerization and Crosslinking Radical Polymerization’’
Naoya Usuki, Hisakazu Okura, Kotaro Satoh, Masami, Kamigaito
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