

**Supramolecular Self-Assembly of Well-Defined
Polymers: Positional Programming of
Complementary Hydrogen Bonds**

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2014

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GENERAL INTRODUCTION

Background

1. Hydrogen Bonds in Polymers

The more we know about natural polymers (peptides, genes, etc.), the more we realize that interactive “non-covalent bonds” are really essential for their behaviors and functions. These interactive sites are precisely placed at well-defined positions in natural macromolecules, which are constructed with covalent bonds, and thereby the programmed non-covalent bonds dictate and induce well-defined higher-order structures within natural polymers and, in turn, express remarkably precise, specific, and efficient functions. In addition to the structural control, the interactive sites are often essential in specific and selective recognition of other molecules or polymers for such functions as enzymatic catalysis.

The interactive non-covalent bonds in natural polymers include van der Waals, electrostatic, ionic, π - π , metal coordination, and hydrogen bonding forces and interactions. Among these, “hydrogen bond” has attracted attentions for scientists in the structural design, molecular-dynamics control, and developing unique functions in artificial molecules and synthetic polymers. The bond is an electrostatic interaction between a hydrogen atom (H) and a highly electronegative atom such as oxygen (O), nitrogen (N), and fluorine (F). Though weaker than a covalent bond (typical bond energy: ~ 20 kJ/mol versus ~ 350 kJ/mol), hydrogen-bond is unique in that it is highly directional, specific, dynamic, and sometimes cooperative.¹ For example, an array of precisely placed multiple hydrogen bonds allows a

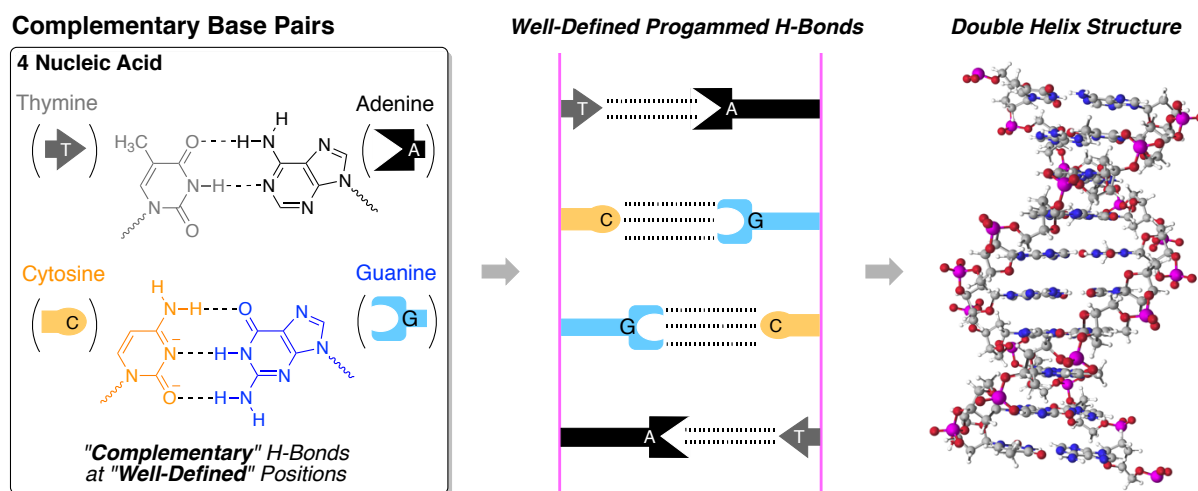


Figure 1. Complementary hydrogen bonds at well-defined positions in DNA.

stronger and specific interaction, as symbolized by the famous double helix via complementary base pairs (thymine/adenine and cytosine/guanine) in a deoxyribonucleic acid (DNA) (Figure 1). While structurally stable under normal conditions, upon special stimulus the DNA double strand can dissociate or associate by breaking or re-forming, respectively, the base-pair hydrogen-bond interactions, and this is a key to their functions in inheritance and peptide expression, among many others. Similarly, hydrogen-bonds play critical roles in the unique catalysis, molecular recognition and other functions by proteins.

Even this brief overview demonstrates the importance of *programmed complementary hydrogen bonds at well-defined positions* in the structures, functions, and biological phenomena in natural macromolecules and polymers.

Hydrogen bonds are also ubiquitously found in synthetic polymers and critical to determine the structures and the mechanical properties. Polyamides and polyurethanes are the typical examples where intermolecular hydrogen bonds induce crystalline structures and thus lead to superior thermal and mechanical properties (Figure 2).^{2,3}

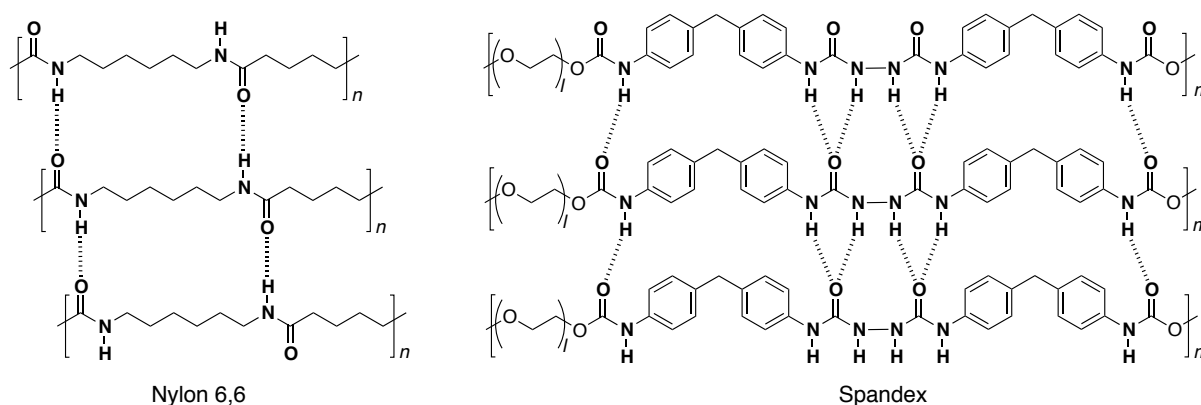


Figure 2. Hydrogen bond interactions in synthetic polymers.

2. Hydrogen Bonded Supramolecular Polymers

In a recent review, Meijer et al. define “supramolecular polymers” as polymeric arrays of monomeric units that are brought together by reversible and highly directional secondary interactions.^{4,5} In contrast to classical polymers consisting of covalent bonds, supramolecular polymers generally form from small molecules or oligomers carrying interactive sites that connect these monomeric units through non-covalent bonds. If the interactive associative force is strong enough, supramolecular polymers in fact show physical properties, such as high solution viscosity and elasticity, reminiscent to covalently built

polymers.^{6,7}

Hydrogen bond-based interaction has been widely utilized for such supramolecular polymers due to the high design diversity.⁸⁻¹⁴ A typical example shown in Figure 3 involves a highly self-associative 2-ureido-4[1H]-pyrimidinone (UPy) unit at both ends of an oligomeric "monomer".¹⁵ The terminal units intermolecularly associate to connect a large number of the monomers, to give supramolecular polymers that behave as an elastic solid similar to covalent polymers of a high molecular weight. Without terminal UPy but with simple hydroxyl groups, in contrast, the oligomeric molecule itself is a viscous liquid, demonstrating that the extremely strong intramolecular and complementary interaction between the two DDAA arrays (D: hydrogen donor; A: hydrogen acceptor) in the UPy terminals allows tough connections, though they can dissociate. Uniquely strong, directive, and selective, such complementary hydrogen bonds are often employed for supramolecular polymers.

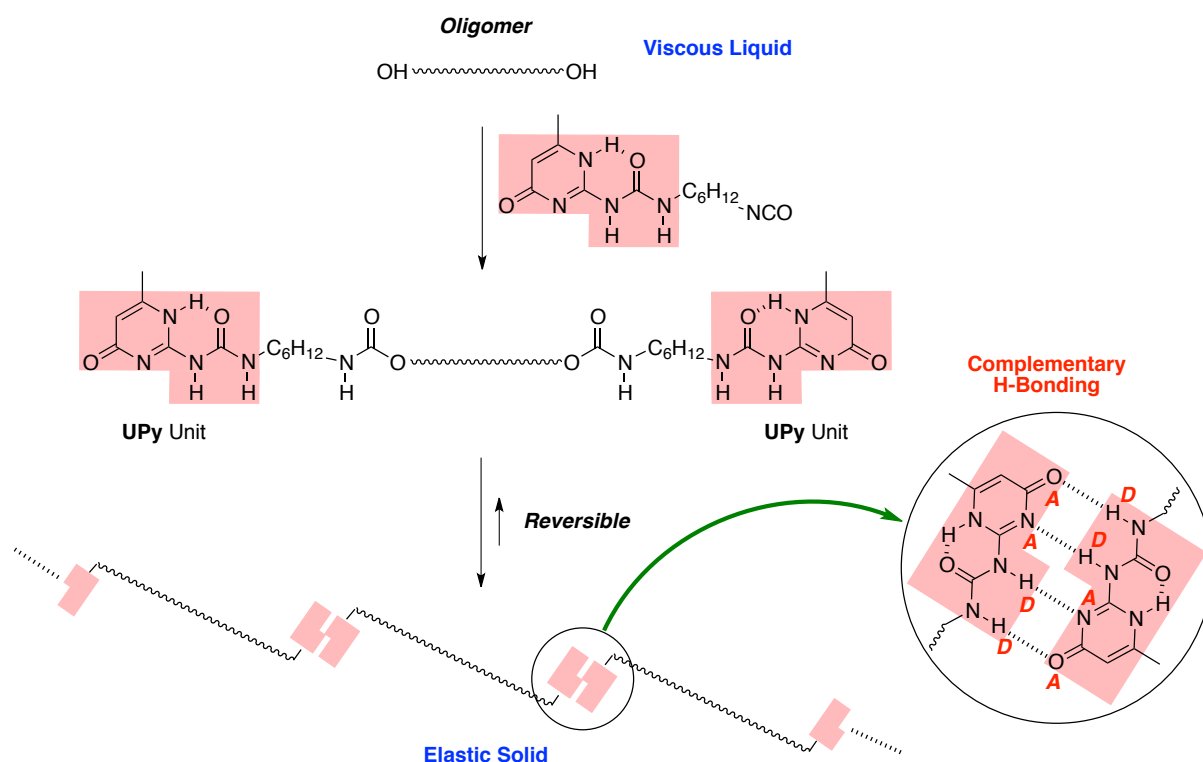


Figure 3. Supramolecular polymer with oligomers carrying Upy units at the both terminals.

3. Complementary Hydrogen Bonds

Like the Upy unit, arrays of a set of hydrogen donors and acceptors have been designed for stronger and complementary interaction. The interaction power, or the

association constant (K_a), is dependent on the number and the order (sequence) of D and A components per interactive unit. In achieving strong and specific associative interaction, the number is obviously important, but the D–A sequence is sometimes more serious and delicate; in the latter one should consider such a factor as dipole–dipole interaction among the in-unit D and A components, which often disturb directive interaction among D–A pairs. For example, 2,6-diaminopyridine derivatives can interact with thymine via triple hydrogen bonding sites for an ADA-DAD style with K_a about $10^2 \sim 10^3 \text{ M}^{-1}$ (Figure 4A).^{16,17} In general, an increase in the number of hydrogen bonds allows stronger interaction. Indeed, a larger K_a ($\sim 4.0 \times 10^4 \text{ M}^{-1}$) is found for the so-called Hamilton receptor, consisting of two 2,6-diamidepyridine units in a DADDAD array, which can interact with an ADADA-type unit (a cyanuric acid derivative) (Figure 4B).¹⁸ However, the DDAA–AADD interaction in Upy units (Figure 4C; also see above) is less in number than the Hamilton receptor but is one of the strongest ($K_a \sim 6.0 \times 10^7 \text{ M}^{-1}$) among multipoint hydrogen bonded couples, because the array is designed to avoid neighboring interactions.¹⁹ This implies that innovative design will help constructing interesting supramolecular polymers.

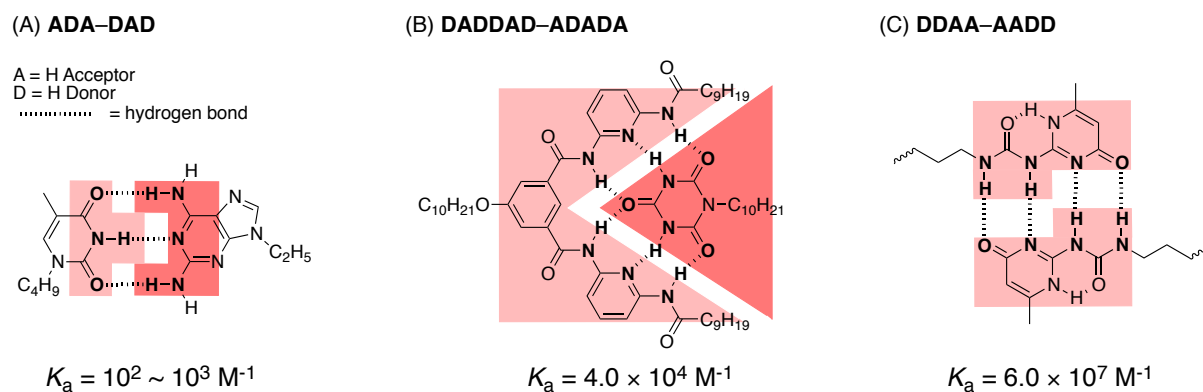


Figure 4. Examples of complementary hydrogen bonding pairs with association constant (K_a).

4. Living Radical Polymerization

Apart from the multiple hydrogen-bond interaction for supramolecular polymers as discussed above, living polymerization is an important tool for the precision synthesis of polymeric architectures (*e.g.*, block, graft, and star polymers) as well as for the precision control of molecular weight and terminal groups.²⁰ Especially, the development of living radical polymerization in the 1990s^{21–24} has opened the door to the construction of tailor-made

“functional” polymers without the protection/deprotection process often required in ionic living polymerization.²⁵⁻²⁸ Figure 5 shows the representative examples of living radical polymerization: metal-catalyzed living radical polymerization [Mt-LRP,²⁹⁻³² also called ATRP (atom transfer radical polymerization)^{33,34}], nitroxide-mediated radical polymerization (NMP),^{35,36} and reversible addition-fragmentation chain transfer (RAFT) polymerization.^{37,38}

As shown in Figure 5, crucial in living radical polymerization is that the growing radical (or the active species) is reversibly generated under chemical or physical stimulus from a “dormant” species, a covalently capped terminal that is per se incapable of propagation but an effective precursor and reservoir of the true active species. The equilibrium between active and dormant species allows a decrease in the instantaneous concentration of the former (radicals), while keeping propagation proceeding, and consequently irreversible side reactions such as irreversible coupling and disproportionation are suppressed. For example, in

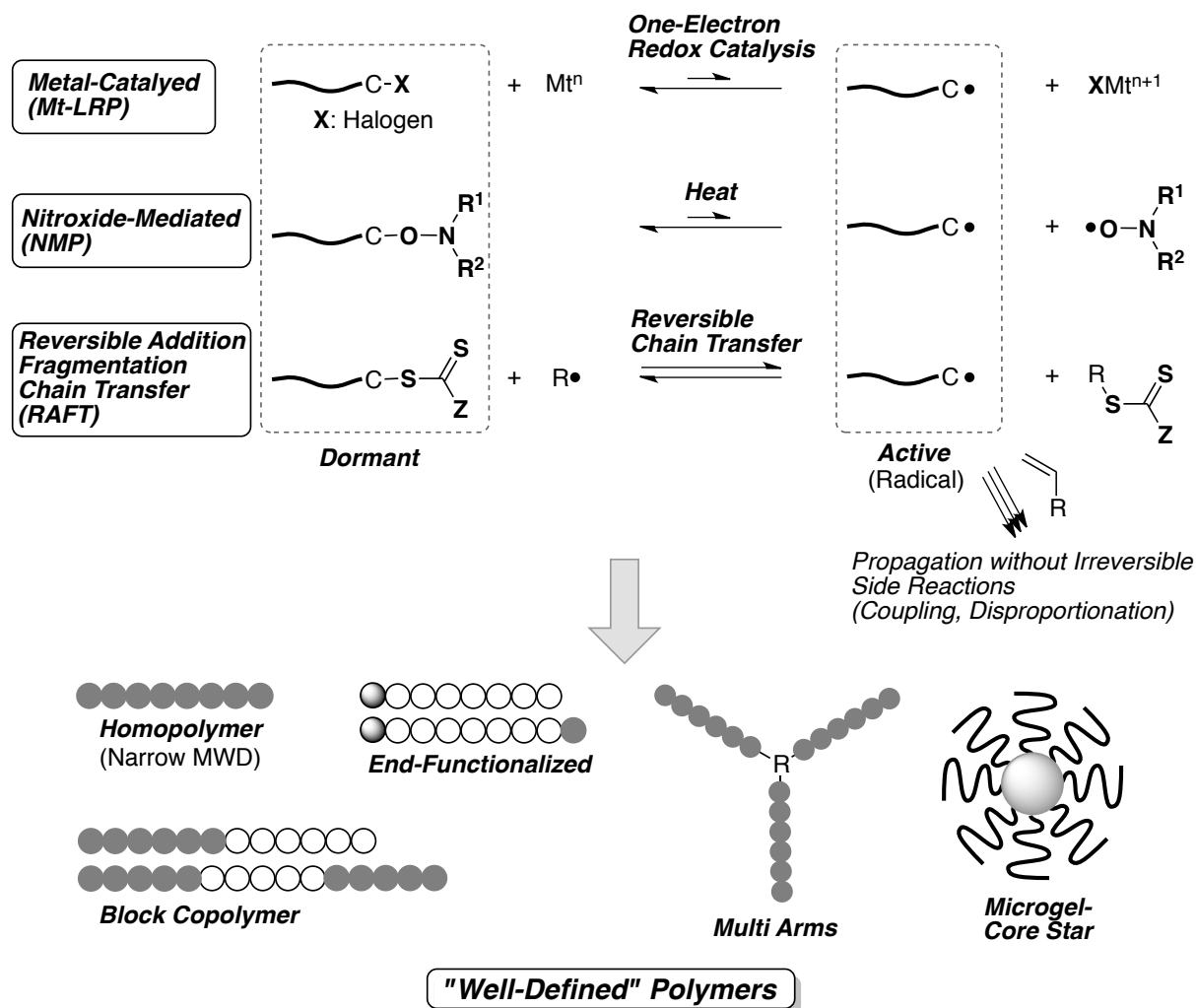


Figure 5. Examples of living radical polymerization and well-defined polymer architectures.

Mt-LRP, a halogen (X) is the leaving group for the dormant species, and the carbon–halogen (C–X) bond therein is reversibly activated by a transition metal complex as a catalyst via one-electron redox ($Mt^n \leftrightarrow XMt^{n+1}$). In NMP and RAFT, a nitroxide radical and a thiocarbonylthio group, respectively, are leaving groups susceptible to heat and radical species upon reversible activation. In these living radical polymerizations, polymer chains quantitatively carry a terminal group derived from the initiator or the chain transfer agent, leading to end-functionalized polymers and block copolymers.

5. Introduction of Multiple Hydrogen Bonds at Polymer Terminals

The brief discussion in the preceding sections implies that the design of initiators or chain transfer agents with multiple hydrogen bonds in living polymerization would allow the quantitative introduction of interactive sites at polymer terminals.³⁹ Indeed, studies have been conducted on this research line. Figure 6 shows typical examples in Mt-LRP, NMP, and RAFT.⁴⁰

Among these three approaches, Mt-LRP is more versatile in initiator design: an ester or an amide is easily introduced into an initiator simply through esterification or amidation. For example, Hawker and co-workers incorporated a Upy group into an initiator for Mt-LRP to obtain supramolecular block copolymers by the dynamic dimerization of

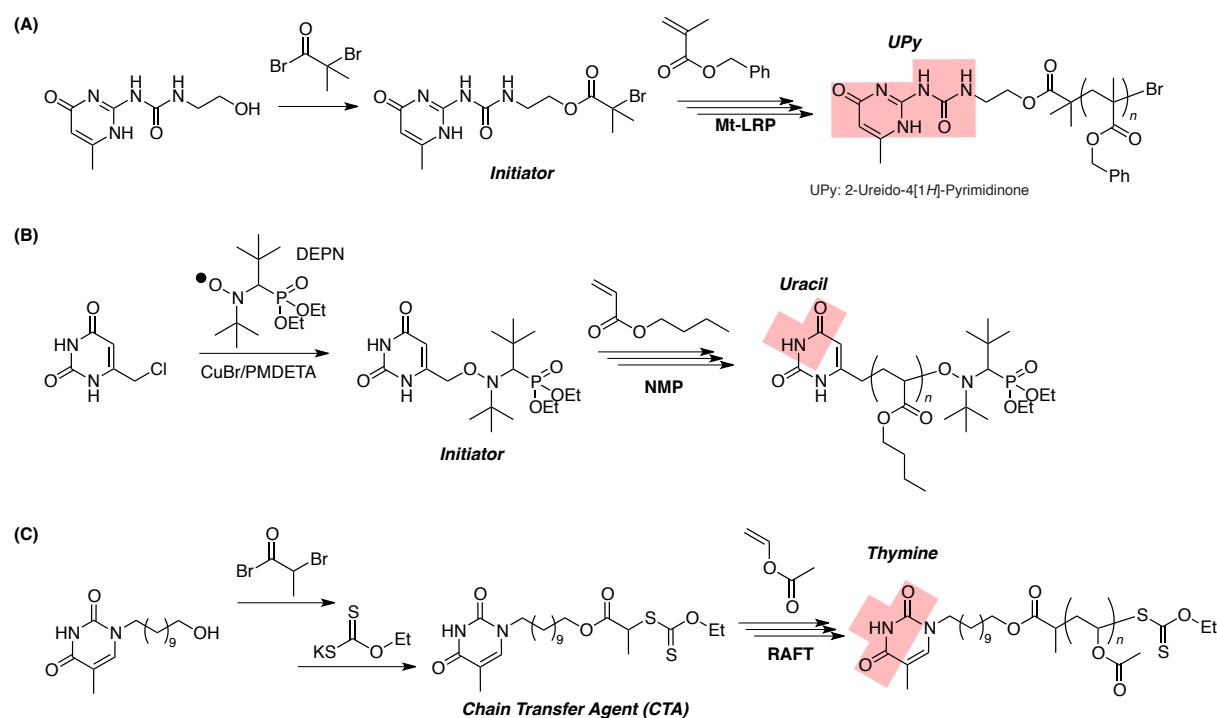


Figure 6. Examples of introduction of multiple hydrogen bonding sites into polymer chain with Mt-LRP, NMP, and RAFT systems.

end-functionalized polymers (Figure 6A).⁴¹⁻⁴³ Two Upy-capped polymers have separately been synthesized from different monomers and then blended in solution. The strong end-to-end connection through hydrogen bonds give AB-diblock supramolecular polymers that undergo phase separation similar to that found for covalently linked conventional diblock copolymers of the same set of segments.

Long et al. first reported the modification of NMP initiators for supramolecular block polymers. They employed *N-tert-butyl-N*-(1-diethylphosphono-2,2-dimethylpropyl)-*N*-oxyl (DEPN) with a uracil group for the synthesis of uracil-terminated polymers with controlled molecular weights and end functionalities (Figure 6B).⁴⁴ For RAFT polymerization, a thymine-decollated chain transfer agent has been designed for thymine-functionalized poly(vinyl acetate)s (Figure 6C).^{45,46} These polymers interact with polymeric partners carrying a multipoint hydrogen bonding unit complementary to each other.

Thus, designed initiators and chain transfer agents in living radical polymerization has provided a variety of terminally interactive polymers for supramolecular materials. However, the designs of segmental chains are yet unsatisfactory for effective chain-chain interaction or well-defined association. More elaborate polymer-polymer interaction for advanced functions can be achieved by the precision introduction of complementary interactive sites not only at segment terminals but at desired positions along the backbones of synthetic polymers. Such in-chain programmed interactive units will lead to more advanced and unique supramolecular structures.

Objectives

Given the above backgrounds, the author has directed his doctoral research to “positional program of complementary hydrogen bonding motifs into polymer chain” and “supramolecular self-assembly at the programmed positions” for which three research objects have been set:

- (1) Design of Functional Initiators for Living Radical Polymerization
- (2) Positional Programming of Hydrogen Bonding Sites into Polymer Chain
- (3) Supramolecular Self-Assembly at the Programmed Positions

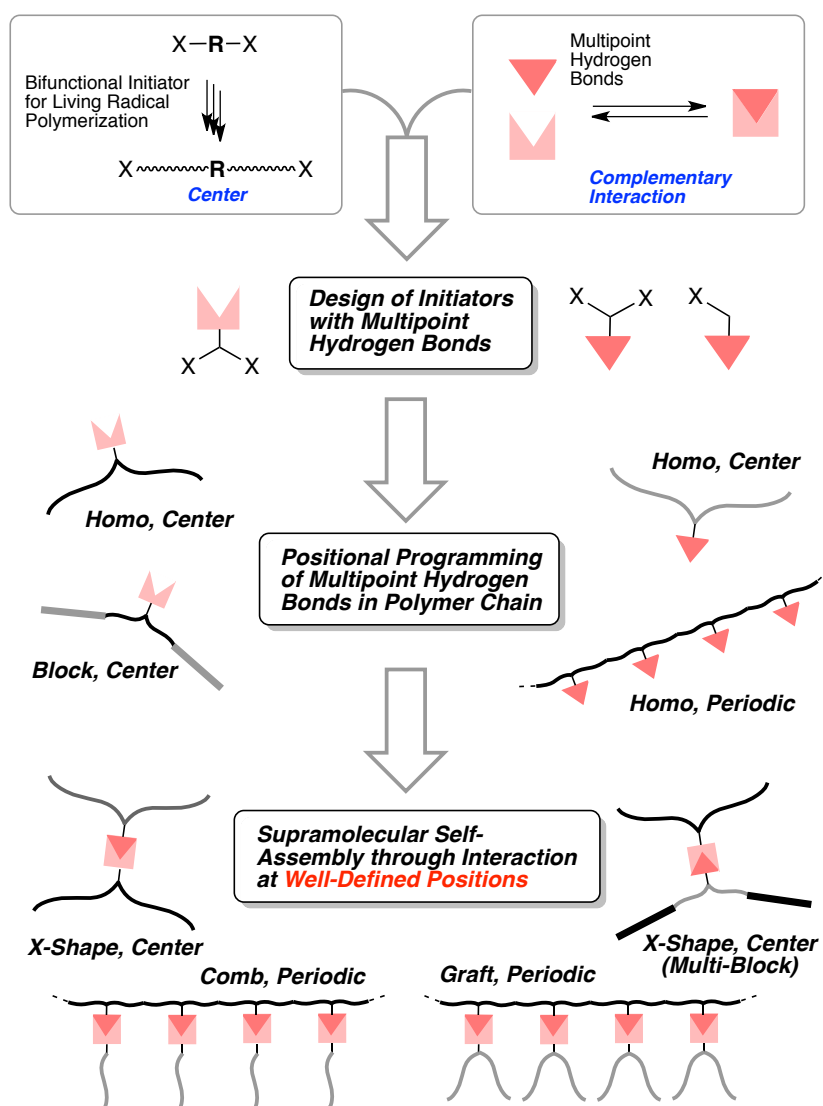


Figure 7. Supramolecular self-assembly at precisely programmed positions.

For these objectives, the author carefully devised “new initiators carrying complementary hydrogen bonding sites” for living radical polymerization, which may be placed at either a center or a terminal of a homo- or block copolymers (“center-programmed” and “terminal-programmed” polymers, respectively). The center-programmed polymers may be covalently chain extended by end-to-end reactions, thus forming “periodic-programmed” multiblock polymers in which a number of complementary hydrogen bonding sites may be placed in a regular interval. Combination of these *position-defined* functionalized polymers may lead to interesting supramolecular self-assemblies (Figure 7). These polymers by the author's *position-programmed approach* should clearly be differentiated from common supramolecular block copolymers, which were interacted at undefined positions.

(1) Design of Functional Initiators for Living Radical Polymerization. In the first part of this thesis research (Figure 8), the author designed a set of initiators bearing multiple complementary hydrogen bonding sites in which 3-3 and 6-5 point interaction sites are embedded in series. For the positional control of interactive sites in polymer chain, the “center” position has been targeted, because the functionalization of a mid segment in linear polymers may develop unique functions and properties relative to the end- or pendent-functionalized counterparts. In the two renderings in Figure 8, the terminal carbon–halogen (C-X) bond in an initiator is for metal-catalyzed living radical polymerization to construct a well-defined primary structure of the polymers. The center-programmed DAD motif of an –NH–C–N–C–NH– unit is derived from 2,6-diaminopyridine, and the ADA motif

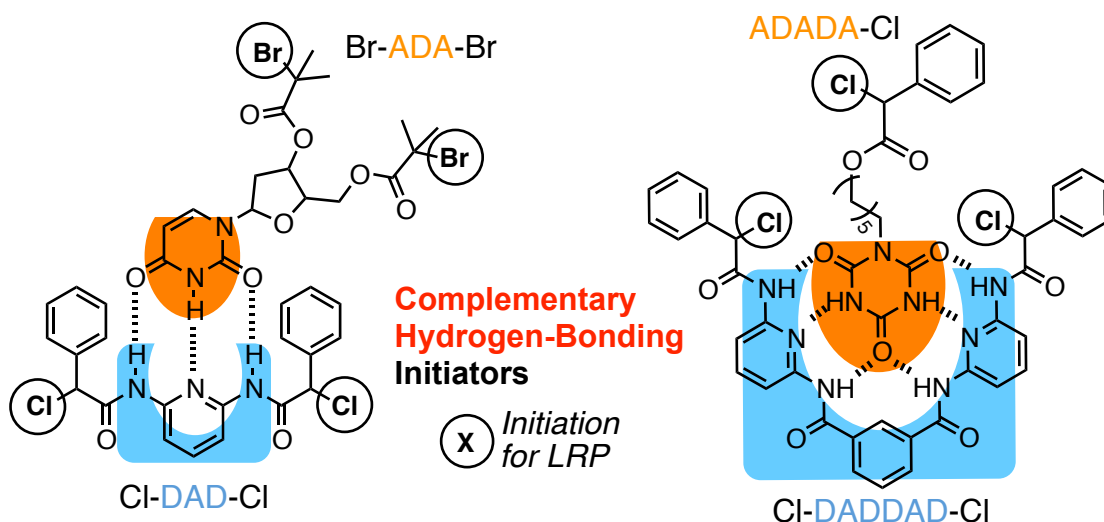


Figure 8. Designed sets of initiators carrying complementary H-bonding sites.

of a $-\text{CO}-\text{NH}-\text{CO}-$ unit from 2'-deoxyuridine.^{16,17} Another initiator pair is also designed; one is bifunctional and embeds the Hamilton receptor (DADDAD) and the other monofunctional with a cyanuric acid terminal (ADADA)⁴⁷; note that this combination will generate an extremely strong interaction (see above) suited for precisely controlled supramolecular self-assembly via complementary interactions at the programmed positions in polymer chains.

(2) Positional Programming of Interactive Sites into Polymer Chain. For the second objective of this thesis, the author employed bifunctional initiators (Cl-DAD-Cl, Br-ADA-Br, and Cl-DADDAD-Cl) and a monofunctional initiator (ADADA-Cl), complementary to each other, to achieve the “positional programming” of complementary hydrogen bonds in polymer chains. Metal-catalyzed living radical polymerization with these complementary initiators is promising to synthesize well-defined polymer structures that embed hydrogen bonds units at programmed positions (center or terminal) including not only homopolymers but also block copolymers with narrow molecular weight distributions (MWDs).

The periodic programmed complementary hydrogen bonds with regular interval into polymer chains are to be obtained by chain-extending controlled center-functional polymers

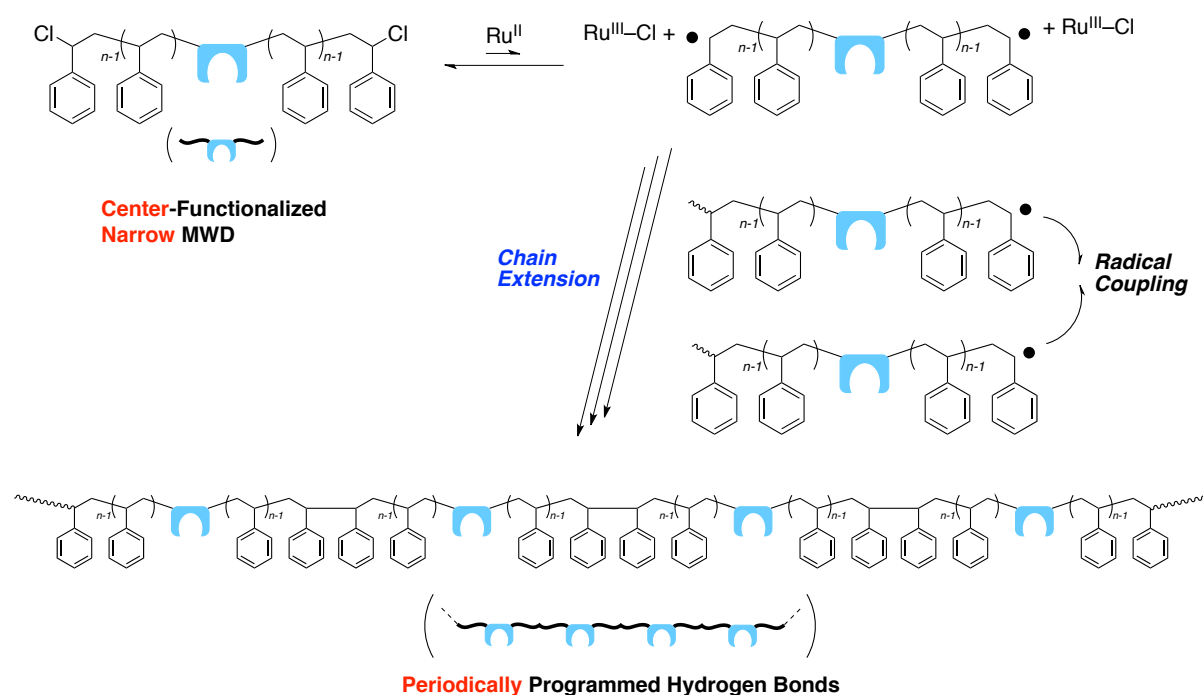


Figure 9. Periodically programmed hydrogen-bonding sites at regular interval in polystyrene chain.

(X $\sim$ Fn $\sim$ X; Fn = complementary hydrogen bonds unit; X = halogen) (Figure 9). Both halogen ends may be activated with a Ru^{II} catalyst, and the resulting radicals could be terminated by coupling with a chain end of other position programmed polymer (X' $\sim$ Fn' $\sim$ X') in the absence of monomer.⁴⁸⁻⁵¹ Thus, the “periodic-programming” of complementary hydrogen bonding sites, $-\sim$ [Fn $\sim$]_n-, may be accomplished.

(3) Supramolecular Self-Assembly at the programmed positions. The final objective involves the supramolecular self-assemblies via complementary hydrogen bonding interactions at well-programmed positions in polymer chains. As described above, various position-programmed polymers carrying complementary hydrogen bonds should be obtained from Mt-LRP with designed complementary initiators or by chain extension of controlled center-functional polymers. The variety combinations of position-programmed polymers can lead to interesting supramolecular self-assembly (T-shape, X-shape, multi block star, and grafted copolymer with regular interval). Furthermore, various supramolecular self-assemblies can be obtained not only by simple blending of position-programmed polymers but also by the compositional change in polymer chains to introduce "concerted" self-assembly systems such as hydrophilic/hydrophobic interaction coupled with complementary interaction.⁵²⁻⁵⁵

For example, inspired from biopolymers, the author considered center-functional amphiphilic triblock copolymer with interactive sites at the center, *hydrophilic–hydrophobic–hydrophilic* combinations programmed for supramolecular polymer assemblies in aqueous media (Figure 10). The hydrogen bonding interaction of an amphiphilic polymer with a center-functional complementary hydrophobic partner could also involve the formation of a “hydrophobic pocket” by the mid-chain hydrophobic segment around recognition sites in aqueous condition.

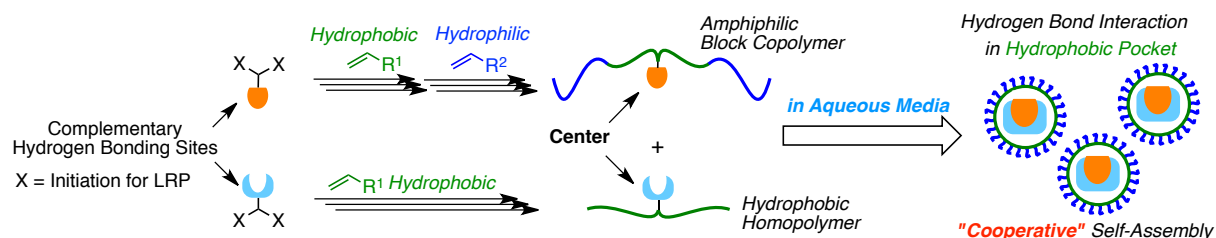


Figure 10. Cooperative supramolecular self-assembly in aqueous media.

Outline of This Study

The present thesis consists of two parts: **Part I** (Chapter 1-3) deals with the design of bifunctional initiators carrying complementary hydrogen bonding sites to introduce interactive sites at programmed positions (center or periodic introduction with regular interval) into polymer chain. From these controlled positions of complementary bonding sites, interesting supramolecular assembly will be discussed in organic environment as well as aqueous media. **Part II** (Chapter 4-5) focused on higher associatable complementary hydrogen bonding site as the functional group, which is embedded so-called Hamilton receptor to improve their association.

Chapter 1 presents X-shaped supramolecular block copolymer connected by complementary hydrogen bonding at the center position of polymer backbone. The author has specifically designed a pair of bifunctional initiators (e.g., Cl-DAD-Cl and Br-ADA-Br; D: hydrogen donor; A: hydrogen acceptor) in which the two initiating sites are connected via a H-bond forming group (–DAD– or –ADA–) that is complementary to each other. These initiators are then employed to initiate metal-catalyzed living radical polymerizations of different monomers (X and Y), to give a pair of block polymers that, when mixed together, would form four-armed (or cross-shaped) star-block polymers of an XXYY configuration. Note that, for such complimentary mid-chain-functionalized copolymers, the block architecture is based on a reversible, stimuli-responsive self-assembly and, in turn, that their micro-phase separation also inherits these characteristics (Figure 11).

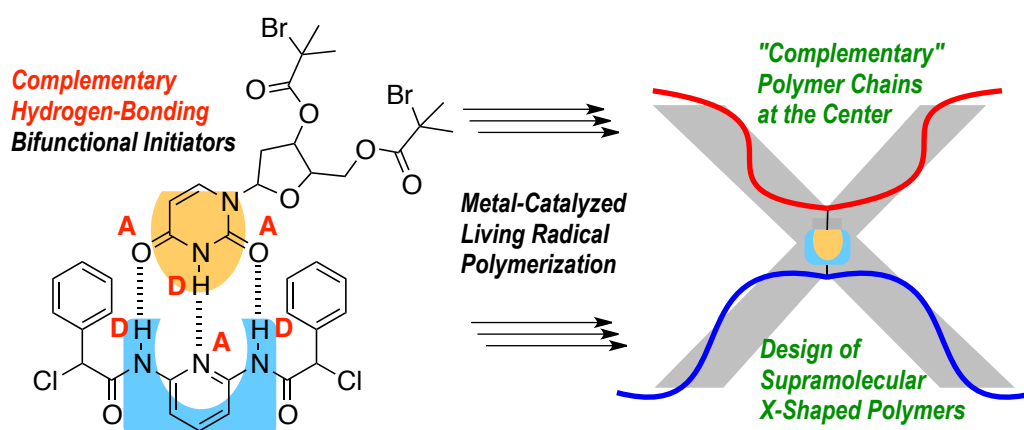


Figure 11. X-shaped supramolecular block copolymer via center-center complementary interaction from designed bifunctional initiators.

Chapter 2 describes “concerted” self-aggregation of center-functionalized amphiphilic block copolymer via complementary hydrogen bonding and *hydrophobic* interaction in aqueous media. The *hydrophobic* segment of designed amphiphilic triblock copolymer (ABA type block copolymer; A = *hydrophilic*; B = *hydrophobic*) bearing multiple hydrogen bonding sites (ADA; D = hydrogen donor; A = hydrogen acceptor) at the center of polymer backbone would be promoted complementary H-bonding interaction with DAD-functionalized polymer (*hydrophobic*) at the middle position in water supported by *hydrophobic* interaction. The aggregates in aqueous media were relatively stable and uniform in size, which most likely stems from the intermolecular complementary hydrogen-bond interaction at polymer chain centers (Figure 12).

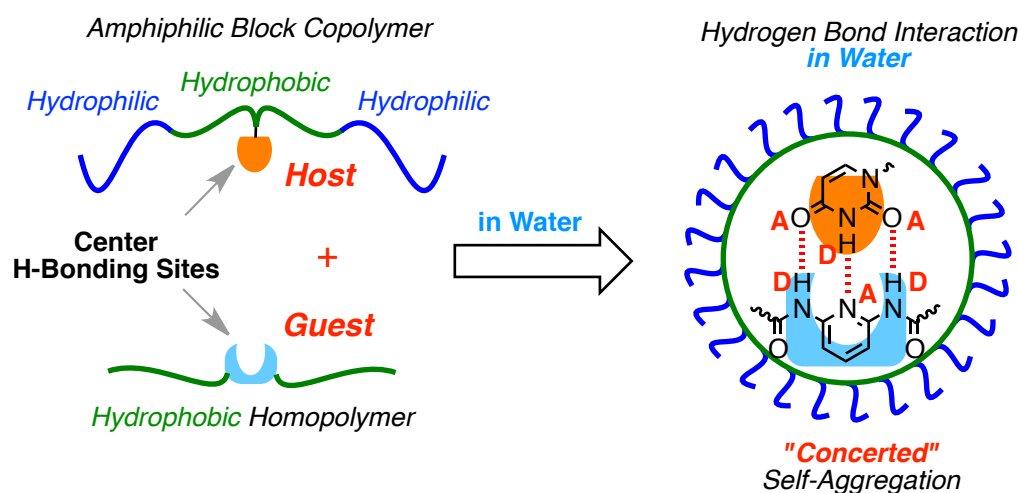


Figure 12. Concerted self-aggregation of center-functionalized amphiphilic block copolymer in aqueous solution.

Chapter 3 discusses periodic introduction of complementary hydrogen bonding interaction sites on polymer chain via radical chain extension of narrowly controlled center-functional oligomer. The ruthenium-catalyzed living radical polymerization with bifunctional initiator carrying interactive sites at the center position is promising to well-defined oligomer with narrow MWD and quantitative halogen ends in the oligomer chain should participate in radical coupling polymerization under similar condition with Mt-LRP (Figure 13). Herein, the author demonstrates activity enhancement of radical coupling polymerization by tuning of Ru catalyst system with phosphine ligand, amine co-catalyst, and alcohol as additive.

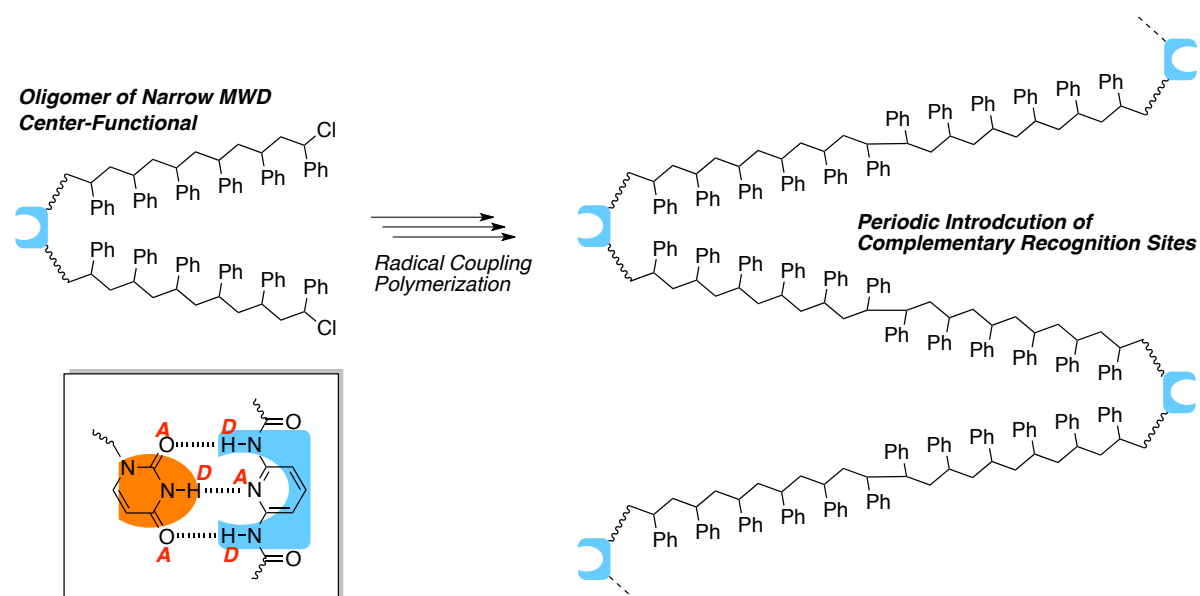


Figure 13. Introduction of multiple hydrogen bonding sites into polymer chain at regular interval via chain extension of center-functionalized oligomer with narrow MWD.

Chapter 4 focuses on a multiple hydrogen-bonding site of higher association constant (Figure 14: Hamilton receptor), which was precisely introduced at the central position of a vinyl polymer chain by the use of bi-headed functional initiating systems (bifunctional initiator) in living radical polymerization. Thus obtained polystyrene fairly recognized associable molecules and polymers carrying the complementary unit to form self-assemblies of high association constant.

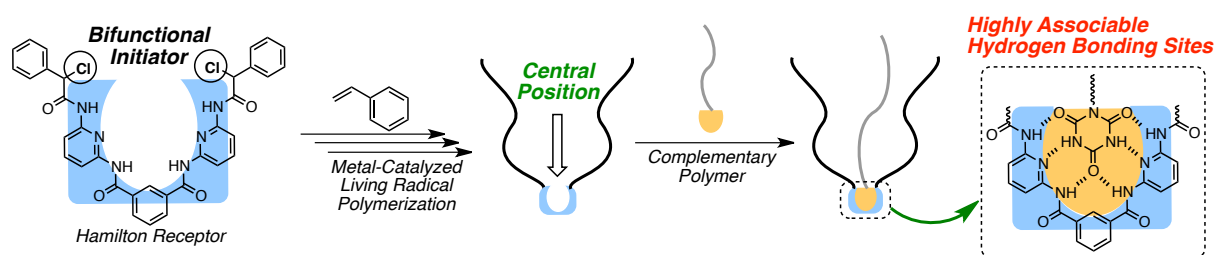


Figure 14. Self-assembly of center-functionalized polymer carrying highly associable H-bonding sites.

Chapter 5 deals with the supramolecular graft copolymer with periodically programmed polystyrene chain with Hamilton receptor (–DADDAD–), which was prepared

from chain extension of narrow MWD polystyrene carrying Hamilton receptor (–DADDAD–) at the center of polymer chain. The unique chain tightly interacted with the complementary interaction site-functionalized PMMA (ADADA–PMMA) to form supramolecular graft copolymer in which the graft was periodically arrayed (Figure 15). The periodic interaction site allowed an enhancement of association ability, which was evaluated by the association constant and thermal analyses.

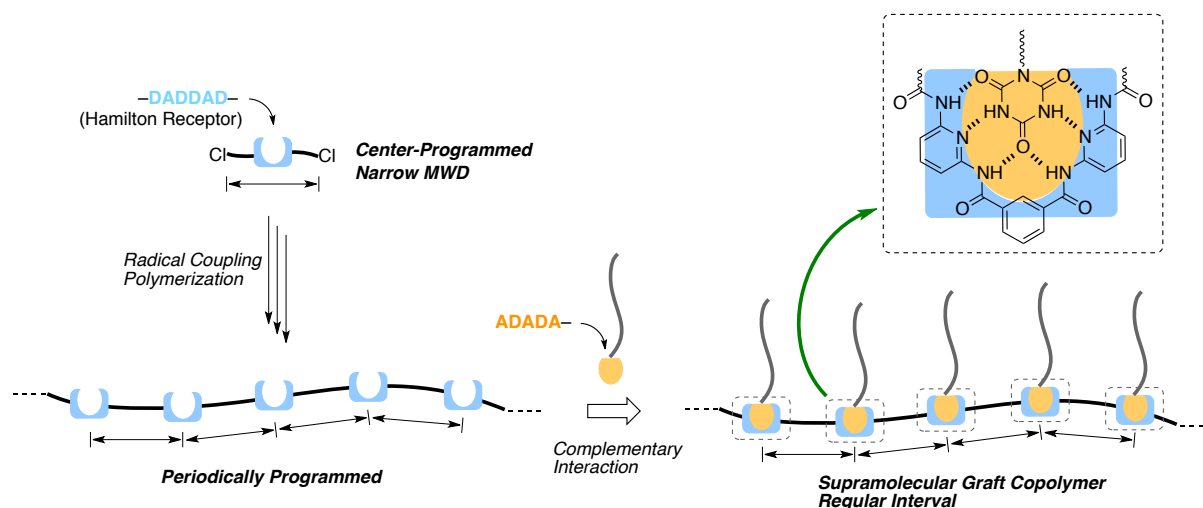


Figure 15. Supramolecular self-assembly via complementary hydrogen bonding at the periodic positions.

In conclusion, this thesis presents precisely controlled positions of complementary hydrogen bonding sites (positional programming) toward effective and specific supramolecular self-assembly of synthetic polymers. The position programming of multiple hydrogen bonding sites into polymer chains were achieved from design of initiators and chain extension of precisely controlled oligomers with narrow MWD in conjunction with ruthenium catalysts. For the center-programmed polymers, molecular recognition and selective interaction with different position-programmed polymers were successively occurred at the center of polymer chain without changing main structure: the associated products behave as single polymer chain; and periodic introduced hydrogen bonding sites with regular interval improved complementary interaction ability, thus advanced supramolecular self-assemblies were observed.

This study is the beginning to the structural design of artificial polymers by

supramolecular self-assembly via complementary hydrogen bonding interaction at the programmed positions (well-defined positions) in the polymer chain. The author believes that our ultimate position control of interactive sites would approach the essence of natural macromolecules, and he hopes this thesis contributes to the further developments in polymer science.

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PART I

Design of Positional Programming System with Complementary 3-3 Points Hydrogen Bonding Motifs

Chapter 1

Supramolecular X-Shaped Homo and Block Polymers by Mid-Segment Complementary Hydrogen-Bonds: Design of Bifunctional Initiators with Interactive Sites for Metal-Catalyzed Living Radical Polymerization

Abstract

Two polymer chains, each carrying a complementary multiple hydrogen-bonding site at the center, led to supramolecular block copolymers where two segments are connected in an X-shaped configuration. For the precision synthesis of the pairing precursor polymers, a set of bifunctional initiators were designed, X-DAD-X and Y-ADA-Y, that consist of three hydrogen bond-forming sites in series (DAD or ADA; D = hydrogen donor; A = hydrogen acceptor) and two initiating sites (X or Y) for ruthenium-catalyzed living radical polymerization; thereby DAD and ADA units are complementary to each other upon supramolecular association. Typically, DAD is of an -NH-C-N-C-NH- unit derived from 2,6-diaminopyridine, and ADA is of a -CO-NH-CO- unit from 2'-deoxyuridine. These functionalized initiators initiated living radical polymerizations of methyl methacrylate and styrene to give homopolymers (PMMA and PS, respectively) with a DAD or an ADA unit at the backbone center. Upon mixing in CDCl₃, for example, a pair of "complementary" polymers, such as PMMA-DAD-PMMA and PS-ADA-PS, formed supramolecular X-shaped "block" polymers via the multiple hydrogen bond association between their mid-chain DAD and ADA sites, as demonstrated by in-situ ¹H NMR (association constant ~ 10²). ¹H DOSY analysis also supported the interaction: the association products gave a single diffusion constant, thus behaving as one polymer chain, while each component chain had different diffusion constants.

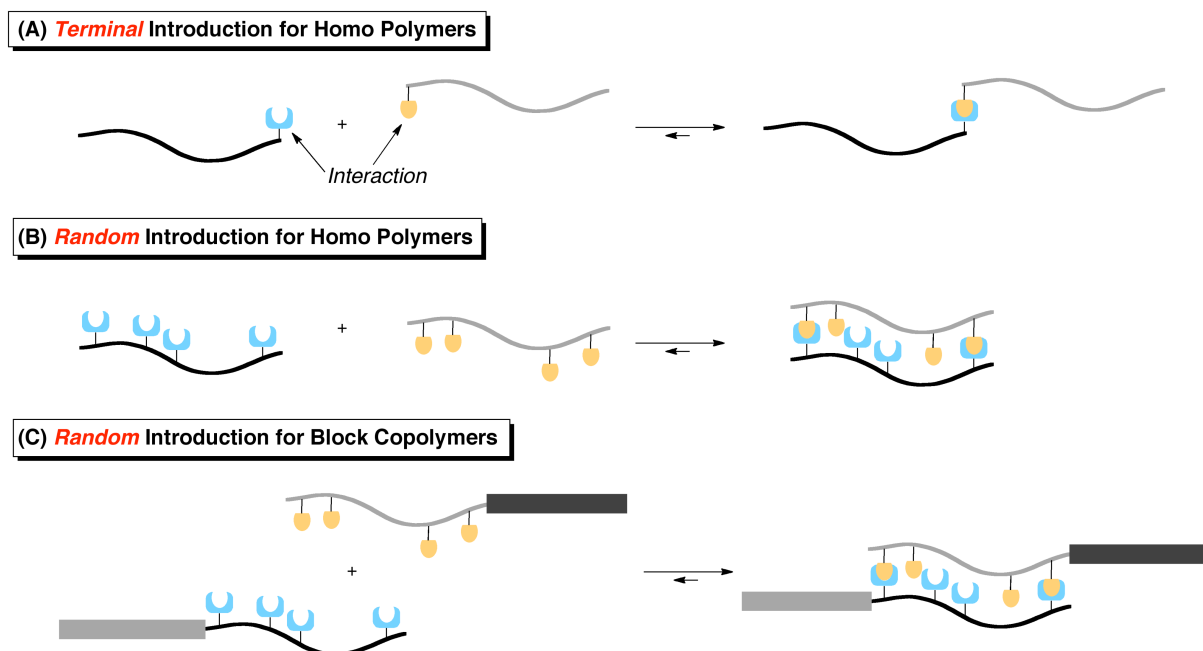
Introduction

In nature, the recognition between macromolecular chains through selective non-covalent bond interaction is essential to the “central dogma”, i.e., the replication, transcription, and expression of genes, peptides, and other biomacromolecules. A typical example is of course a DNA double helix, in which two polymeric strands interact with each other through a series of complementary hydrogen bonds. The elegant shapes, precise higher-order architecture, and the superb functions of natural polymers tell us the importance of selective and dynamic interactions at *well-defined positions* between macromolecular chains.

In synthetic polymers, on the other hand, intermolecular interaction between different homopolymers is more or less repulsive, rather than attractive, and thereby they are generally incompatible and undergo macro-phase separation. Block copolymers do form macroscopically homogeneous micro-phase separated structures (lamella, rod, cylinder, etc.),¹ but the patterns are limited and strongly dependent on segment combination and composition. Equally serious, the intermolecular interaction therein is mostly static and non-responsive to external stimuli.

Over the past few years, efforts have been directed to introduce dynamic interactive sites into polymer chains to induce specific aggregation behaviors (Scheme 1). A simple strategy is to attach a pair of complementary interactive sites at terminals of two different homopolymers (Scheme 1A).² Their blends (e.g., homopolymers A and B) led to micro-phase separation akin to those in conventional covalently linked diblock copolymers (A–B) of the same homopolymer segments. As first demonstrated by Meijer,³ a strong dynamic interaction of an extremely large association constant, such as multiple complementary hydrogen bonds, generates “covalent bond-like” linkages between end-functionalized polymeric segments that in turn form supramolecular polymers behaving nearly identically to the corresponding diblock and multiple block copolymers. Related variants of this approach include random incorporation with interactive monomers (via pendent groups) for homo (Scheme 1B)⁴ or block copolymers (Scheme 1C)⁵ to induce specific aggregation, though specially designed non-common monomers are required.

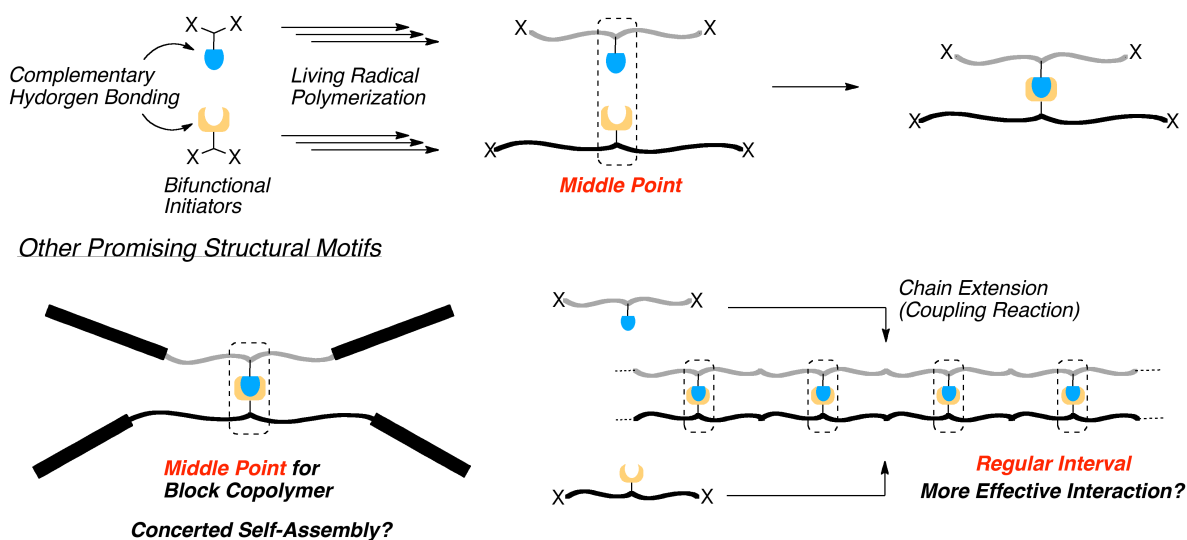
Despite successful formation of supramolecular and dynamic polymers, however, the structural designs in these examples are yet inferior to those for natural polymers. In particular, the complementary interactive sites are mostly at chain termini or at randomly



Scheme 1. Previous researches on interactions between polymers through introduction of dynamic interaction sites on the chains.

placed pendent groups, while those in natural polymers are built in far more precisely in both position and sequence. Precise introduction of interactive sites at well-defined positions on synthetic polymers should lead to more advanced and versatile regular structures derived from effective and unique self-assembling.

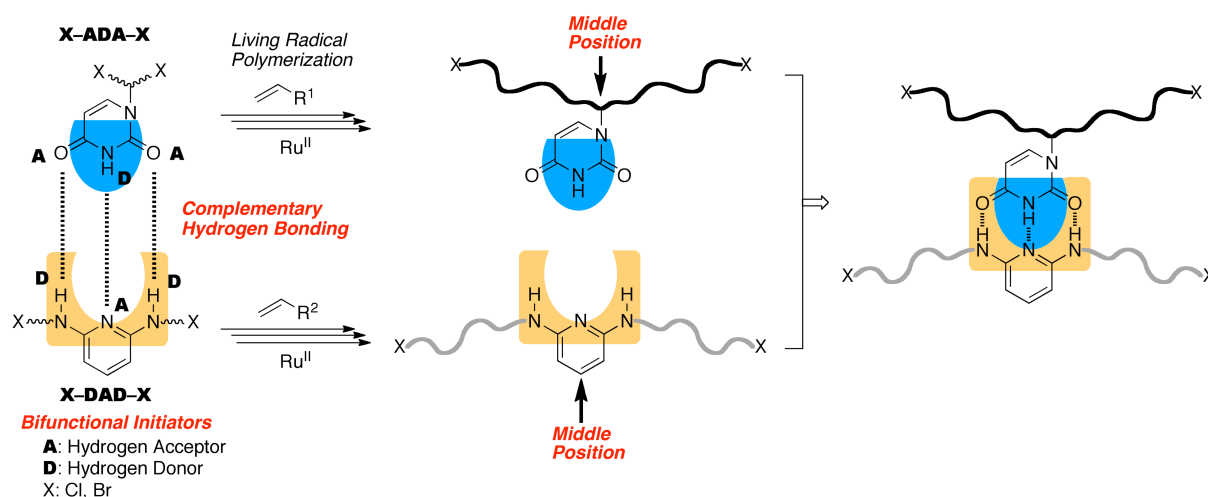
To approach this idea, my strategy is directed to design bifunctional initiators for living radical polymerization that carry a complementary hydrogen-bond units ($X \sim D \sim X$ and $X \sim A \sim X$; X: initiating site; D and A: complementary H-bond units; $\sim$: polymer chain) (Scheme 2). Given quantitative initiation from the two X sites, such initiators would generate “well-defined” polymers bearing an in-chain interactive site at the middle or center of a backbone. Additionally, sequential block copolymerization from these initiators would give similar central functions now embedded into an ABA-block architecture, which would induce cooperative self-aggregation by hydrogen bonds and by microphase separation inherent of block copolymers. Alternatively, periodic introduction of interactive units along the main chain in a regular interval might also be achieved through the chain extension of homotelechelic and mid-chain functionalized oligomers with narrow molecular weight distributions (MWDs): e.g., $nX \sim D \sim X \longrightarrow -(\sim D \sim)_n$.

Introduction at **Well-Defined Position** for Polymer Chains

Scheme 2. Bifunctional initiators for living radical polymerization carrying complementary H-bond and polymers from the initiators.

Thus, in this paper, the author reports the design of a sets of bifunctional initiators (Cl-DAD-Cl and Br-ADA-Br; Scheme 3), for metal-catalyzed living radical polymerization⁶ in which three complementary hydrogen bonding sites are embedded in series: Cl-DAD-Cl is a 2,6-diamide pyridine-based dichloride of a *donor*(D)-*acceptor*(A)-*donor*(D) configuration, and Br-ADA-Br is a thymine-based dibromide of an *acceptor*(A)-*donor*(D)-*acceptor*(A) configuration.⁷ Obviously, metal-catalyzed living radical polymerization from these initiators will give various well-defined homo- and block polymers with mid-chain complementary hydrogen bonding sites through which interesting supramolecular assembly would form.

Herein the author presents the precision control of radical polymerizations with these designed initiators, as well as the complementary interaction between resultant homopolymers of methyl methacrylate (MMA) and styrene (St). Quite recently, Lourtie and Bernard have reported a similar design of bifunctional initiators for reversible addition-fragmentation chain transfer polymerization,⁸ but mine is perhaps the first example for metal-catalyzed living radical polymerization or atom transfer radical polymerization. Note that my focus is to introduce interaction sites at well-defined internal positions on different polymer chains for the effective interaction without changing the main polymer structures, as well as to synthesize supramolecular miktoarm star polymers (or X-shaped block polymers).



Scheme 3. Living radical polymerization with 2,6-diamide pyridine-based chlorine initiator of a *donor*(D)-*acceptor*(A)-*donor*(D) configuration (Cl-DAD-Cl) and thymine-based bromine one of an *acceptor*(A)-*donor*(D)-*acceptor*(A) counterpart (Br-ADA-Br).

Experimental Section

Materials

Monomers (MMA and styrene: Aldrich; purity > 99 %) were dried overnight over calcium hydride and purified by distillation from calcium hydride before use. 2,6-Diaminopyridine (Wako; >97%), (+)-2'-deoxyuridine (Wako; >98%), 2-boromoisobutyryl bromide (Wako; >95%), triethylamine (Wako; 99%), 4-dimethylaminopyridine (Aldrich; 99%), $Ru(Cp^*)Cl(PPh_3)_2$ (Cp^* : cyclopentadienyl, Aldrich), α -chlorophenylacetylchloride (Aldrich; 90%), and 2-bomoisobutyric acid (TCI; >98%) were used as received. Dichloromethane (Wako; dehydrated) and pyridine (Wako; dehydrated) were bubbled with dry argon for more than 15 min immediately before use. Toluene and THF (Kishida Kagaku; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use. *n*-Monobutylamine (TCI; >98%) was degassed by reduced pressure before use. *n*-Octane and tetralin (internal standard for gas chromatography) were dried over calcium chloride and distilled from calcium hydride.

Synthesis of Cl-DAD-Cl Initiator

Dry dichloromethane (130 mL) and triethylamine (7.4 mL, 0.053 mol, 2.5 equiv) and were mixed, sequentially in this order, to 2,6-diaminopyridine (2.3 g, 0.020 mol, 1.0 equiv) placed in an argon-filled 250-mL round-bottom flask. The solution was cooled to 0 °C, and α -chlorophenylacetyl chloride (8.0 mL, 0.050 mol, 2.4 equiv) was added slowly under argon atmosphere. The solution was allowed to reach room temperature and stirred for overnight. An excess amount of distilled water (200 mL) was introduced to quench the reaction, and the organic layer was washed with NaHCO₃ saturated solution (100 mL, twice). The organic layer was dried over MgSO₄ for several hours, and the filtered solution was evaporated, followed by silica gel chromatography with ethylacetate/hexane mixture eluent. Finally, the product was purified by recrystallization with dichloromethane and hexane mixture (Cl-DAD-Cl: 4.7 g, 54 % yield). ¹H NMR (CDCl₃, r.t.) δ (ppm): 8.72 (s, 2H), 7.95 (d, 2H), 7.73 (t, 1H), 7.51 (m, 4H), 7.40 (m, 6H), 5.49 (s, 2H).

Synthesis of 2-Bromo-2-Methylpropanoic Anhydride⁹

A mixture of 2-bromoisobutyric acid (20 g, 0.12 mol, 1.0 equiv), dehydrated THF (200 mL), and triethylamine (20 mL, 0.15 mol, 1.2 equiv) were placed in an argon-filled 250-mL round-bottom flask. The solution was cooled to 0 °C, and 2-bromoisobutyryl bromide (18.05 mL, 0.146 mol, 1.2 equiv) was slowly added under argon. The solution was then stirred for 3 h at room temperature and filtered. The filtrated solution was evaporated to dryness, and the residue was dissolved in methylene chloride, followed by washing with NaHCO₃ saturated solution (100 mL; three times). The organic layer was dried over Na₂SO₄ for several hours, and the filtered solution was evaporated. Finally, the product was purified by recrystallization with hexane (21.20 g, 55 % yield). ¹H NMR (CDCl₃, r.t.) δ (ppm): 2.00 (s, 12H).

Synthesis of Br-ADA-Br initiator

A mixture of 2-bromo-2-methylpropanoic anhydride (21 g, 0.067 mol, 5.0 equiv), 4-dimethylaminopyridine (2.4 g, 0.020 mol, 1.5 equiv), 2-deoxyuridine (3.0 g, 0.013 mol, 1.0 equiv) and dry pyridine (40 mL) were introduced into an argon-filled round-bottom flask. The solution was stirred for 20 h and then evaporated, followed by silica gel chromatography with an ethylacetate/hexane (4/6 v/v) mixed eluent. Finally, the product was purified by recrystallization with a dichloromethane and hexane mixture (Br-ADA-Br: 5.40 g, 77 %

yield). ^1H NMR (CDCl_3 , r.t.) δ (ppm): 8.97 (s, 1H), 7.66 (d, 1H), 6.34 (m, 1H), 5.79 (m, 1H), 5.34 (m, 1H), 4.60-4.32 (m, 3H), 2.68-2.58 (m, 2H), 1.96 (m, 12H).

Polymerization Procedures

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. A typical procedure for MMA with Cl-DAD-Cl/ $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2/n\text{-BuNH}_2$ is given. In a round-bottom flask (50 mL) filled with argon was placed $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (9.3 mg, 0.012 mmol), toluene (0.43 mL), *n*-octane (0.16 mL), MMA (1.28 mL, 12.0 mmol), *n*-BuNH₂ solution (0.30 mL, 400 mM in toluene) and a solution of Cl-DAD-Cl (0.83 mL, 145.3 mM in THF) were sequentially added; the total volume was 3.00 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at 80 °C. In predominant intervals, the polymerization mixture was terminated by cooling to –78 °C in dry-ice-methanol. Monomer conversion was determined from residual monomer concentration measured by gas chromatography with *n*-octane (for MMA) or tetralin (for St) as an internal standard. The quenched solutions were evaporated to dryness to give the products, which were subsequently dried overnight under vacuum at room temperature.

Cleavage of PMMA Obtained from Br-ADA-Br

A baked glass tube was charged with 0.064 g (1.02×10^{-5} mol) of PMMA ($M_{n, \text{SEC}} = 6260$, $M_w/M_n = 1.13$) and 0.055 g of sodium methoxide (1.02×10^{-3} mol) with 9.0 mL of THF and 1.0 mL of dry methanol. The tube was sealed and heated at 80 °C for 17 h. The solvent was evaporated, followed by reprecipitation in methanol from THF solution. The product was subsequently dried overnight under vacuum and analyzed with SEC.

Cleavage of PS from Cl-DAD-Cl

A baked glass tube was charged with 0.04 g (2.05×10^{-5} mol) of PS ($M_{n, \text{SEC}} = 2180$, $M_w/M_n = 1.05$), 4.0 mL of 1,4-dioxane, and 2.0 mL of 12 mol/L HCl solution in 1,4-dioxane. The tube was sealed and heated at 100 °C for 48 h. The product was reprecipitated in methanol and dried overnight under vacuum for SEC analysis.

Measurement

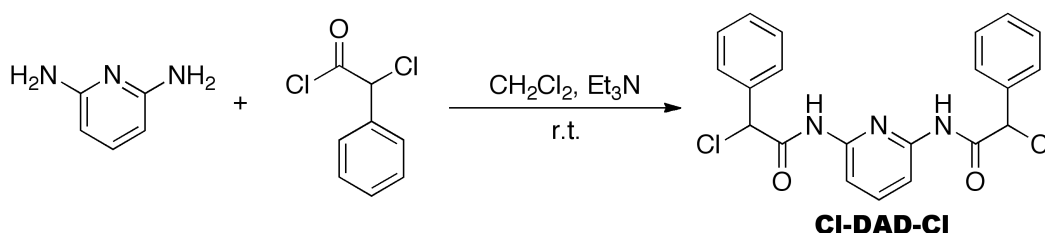
M_n and M_w/M_n of polymers were measured by size exclusion chromatography (SEC) at 40 °C in THF or CHCl_3 as an eluent. For the THF-SEC, three polystyrene-gel columns [LF-404 (from Shodex); pore size, 3000 Å; 4.6 mm i.d. $\times$ 250 cm] were connected to a DU-H2000 pump, a 74S-RI refractive-index detector, and a 41-UV ultraviolet detector (all from Shodex) and flow rate was set to 0.3 mL/min. For the CHCl_3 -SEC, three polystyrene gel columns [K-805L (from Shodex); pore size 20–1000Å; 8.0 mm i.d. $\times$ 30 cm] were connected to a PU-980 pump and a 930-RI refractive-index detector, and a 970-UV ultraviolet detector (all from Jasco) and flow rate was set to 1.0 mL/min. The columns were calibrated against 13 standard poly(MMA) (PMMA) samples (Polymer Laboratories; M_n = 620–1,200,000; M_w/M_n = 1.06–1.22) for obtained PMMA samples, and 13 standard polystyrene (PS) samples (Polymer Laboratories; M_n = 500–3,840,000; M_w/M_n = 1.01–1.14) for obtained PS samples, respectively. Polymer samples were purified by preparative SEC in CHCl_3 at room temperature on polystyrene gel preparative column [K-5002 (from Shodex); exclusion limit = 5×10^3 ; particle size = 15 μm ; 5.0 cm i.d. $\times$ 30 cm; flow rate = 10 mL/min] that were connected to a PU-2086 precision pump, a RI-2031 refractive-index detector, and UV-2075 ultraviolet detector (all from Jasco). ^1H NMR and ^1H DOSY were recorded in CDCl_3 at room temperature or 30 °C on JEOL JNM-ECA500 spectrometer, operating at 500.16 (^1H) MHz.

Results and Discussion

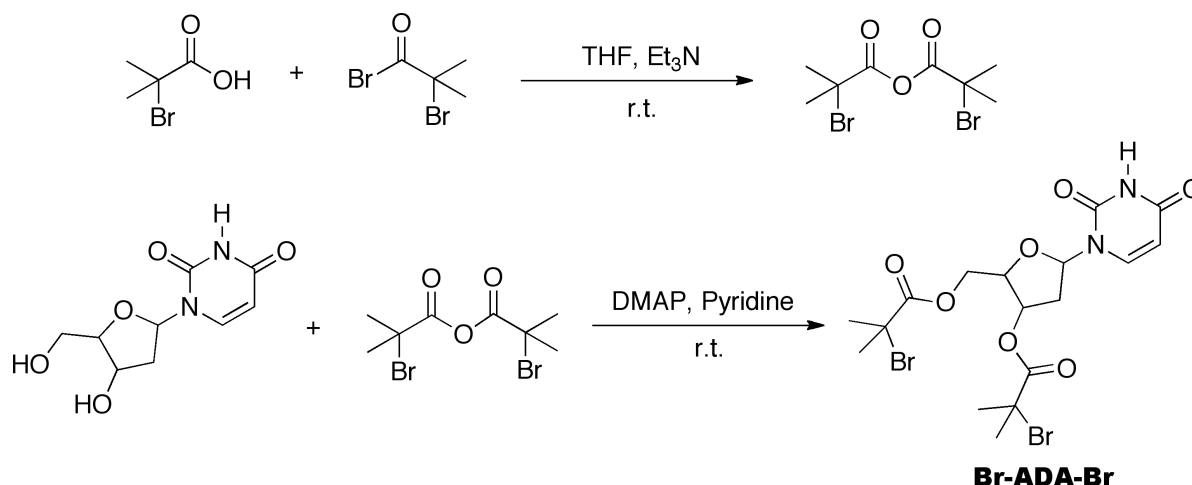
1. Design of Complementary Hydrogen-Bonding Bifunctional Initiators

Cl-DAD-Cl and Br-ADA-Br were prepared via the acylation of 2,6-diaminopyridine and 2'-deoxyuridine, respectively, as illustrated in Scheme 4. For the latter, an anhydride (2-bromo-2-methylpropanoic anhydride) was employed for the acylation, because it turned out more effective and less prone to side reactions than the corresponding acid bromide (2-bromoisobutyryl bromide).

(a) Synthesis of **Cl-DAD-Cl**



(b) Synthesis of **Br-ADA-Br**



Scheme 4. Syntheses of bifunctional initiators, Cl-DAD-Cl (a) and Br-ADA-Br (b).

The complementary interaction between Cl-DAD-Cl and Br-ADA-Br was evaluated by ^1H NMR to determine the association constant (K_a) (Figure 1).¹⁰ From the same stock solutions of the components in CDCl_3 , a series of mixtures were prepared at varying ratios ($[\text{Cl-DAD-Cl}]/[\text{Br-ADA-Br}] = 0.5, 1, 2, 4, 8, 12$, and 16 molar ratio). The chemical shift of the NH proton in Br-ADA-Br progressively shifted downfield, from 7.98 to 11.03 ppm, as the Cl-DAD-Cl amount was increased. From these changes, K_a was estimated to be 83.3 M^{-1} (Table 1), comparable to those for similar three-point complementary hydrogen bond pairs.¹¹ The two initiators were therefore found to undergo relatively strong complementary

interaction via their DAD and ADA units.

Table 1. Parameters for K_{ass} Calculation in This Work

Combination	[ADA] and [DAD]	δ_{mix} / ppm	δ_{ADA} / ppm	δ_{∞} / ppm
Br-ADA-Br and Cl-DAD-Cl ^a	2.0×10^{-3} mol/L	8.42	7.98	11.44 ^b
ADA_PS and DAD_PS-1 ^a	2.0×10^{-3} mol/L	8.26	7.88	12.08 ^b
ADA_PS and DAD_PMMA ^a	2.0×10^{-3} mol/L	8.45	7.88	11.34 ^b

^asee Figure 1 and Figure 6 for the interaction analyses by ^1H NMR ; ^bCalculated from curve fitting with third degree polynomial for plots with various mixing ratios.

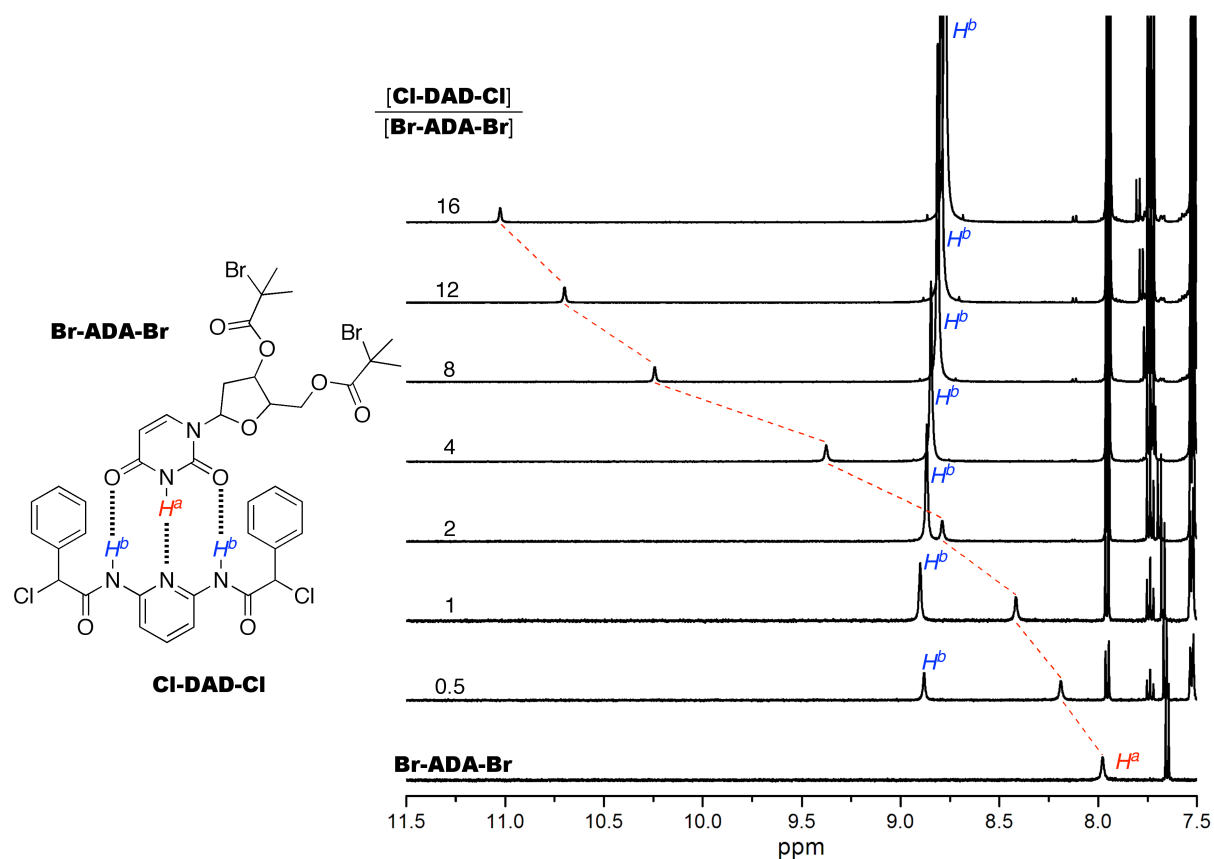


Figure 1. ^1H NMR spectra (CDCl_3 , room temperature) from 7.5 to 11.5 ppm of Br-ADA-Br (bottom) and the mixtures with Cl-DAD-Cl of various ratios ($[\text{Cl-DAD-Cl}]/[\text{Br-ADA-Br}] = 0.5, 1, 2, 4, 8, \text{ and } 16$) for calculation of K_{ass} : $[\text{Br-ADA-Br}] = 2.0 \text{ mM}$ (constant); $[\text{Cl-DAD-Cl}] = 0, 1, 4, 8, 16, 24, \text{ and } 32 \text{ mM}$.

2. Ruthenium-Catalyzed Living Radical Polymerization

Cl-DAD-Cl and Br-ADA-Br were then employed for living radical polymerizations of MMA and styrene (Table 2). Two ruthenium complexes, Ru(Cp*)Cl(PPh₃)₂ (RuCp*)¹² and Ru(Ind)Cl(PPh₃) (RuInd),¹³ were examined as catalysts in conjunction with an amine cocatalyst (*n*-BuNH₂, *n*-Bu₂NH, or *n*-Bu₃N). Both complexes catalyzed living polymerization to give fairly controlled polymers (Figure 2). However, RuCp* obviously gave narrower MWDs ($M_w/M_n < 1.2$: entries 1-3, 7-12, 16-18 in Table 2), and this Cp* catalyst was used throughout this study for polymer preparation, because molecular weight control, or quantitative initiation from both halogens, is vital in placing the interactive site at the chain center.

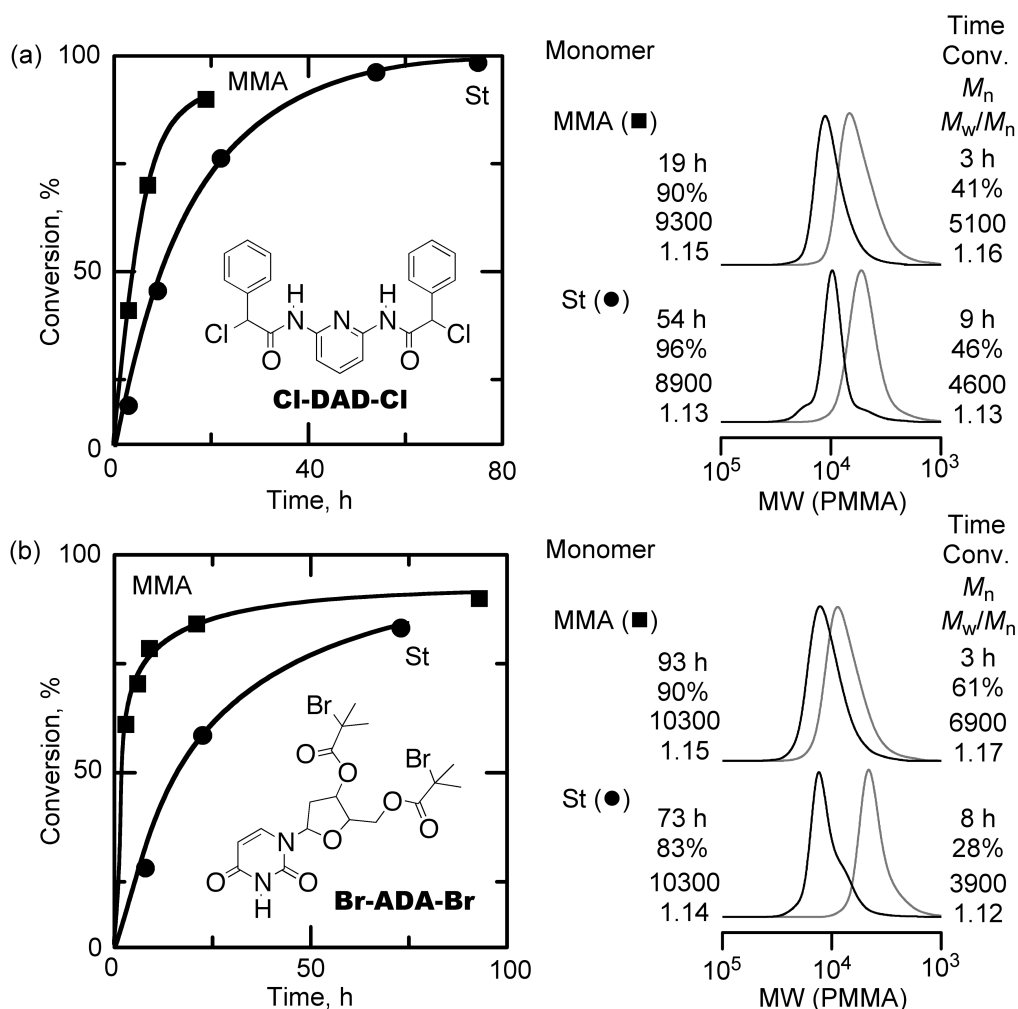


Figure 2. Time-conversion plots and SEC curves for the homopolymerization of MMA (■) and St (●) with (a) Cl-DAD-Cl or (b) Br-ADA-Br/Ru(Cp*)Cl(PPh₃)₂/Amine in toluene at 80 (MMA) or 100 °C (St): [Monomer]₀ = 4000 mM; [Initiator]₀ = 40 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ = 4mM; [Amine]₀ = 40 mM.

Table 2. Living Radical Polymerizations of MMA or St with Cl-DAD-Cl or Br-ADA-Br^a

Entry	Initiator	Monomer	Catalyst	Cocatalyst	Temp. °C	Time h	Conv. %	M_n^b	M_w/M_n^b
1	Cl-DAD-Cl	MMA	RuCp*	<i>n</i> -BuNH ₂	80	3	41	5100	1.16
2						7	70	7900	1.13
3						19	90	9300	1.11
4			RuInd	<i>n</i> -Bu ₃ N	80	3	24	2400	1.31
5						7	41	4200	1.57
6						48	99	9200	1.27
7		St	RuCp*	<i>n</i> -BuNH ₂	100	9	46	4600	1.13
8						22	76	7300	1.11
9						75	98	9200	1.14
10	Br-ADA-Br	MMA	RuCp*	<i>n</i> -BuNH ₂	80	3	61	6900	1.17
11						9	78	9400	1.15
12						93	90	10300	1.15
13			RuInd	<i>n</i> -Bu ₃ N	80	3	73	7900	1.21
14						6	95	11800	1.24
15						9	100	12900	1.24
16		St	RuCp*	<i>n</i> -Bu ₂ NH	100	8	28	3900	1.12
17						22.5	59	7800	1.13
18						75	98	9200	1.14

^a[Monomer]₀ = 4.0 M; [Initiator]₀ = 40 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ or [Ru(Ind)Cl(PPh₃)₂]₀ = 4.0 mM; [Cocatalyst]₀ = 40 mM in toluene. ^bBy size exclusion chromatography calibrated with PMMA or PS standards.

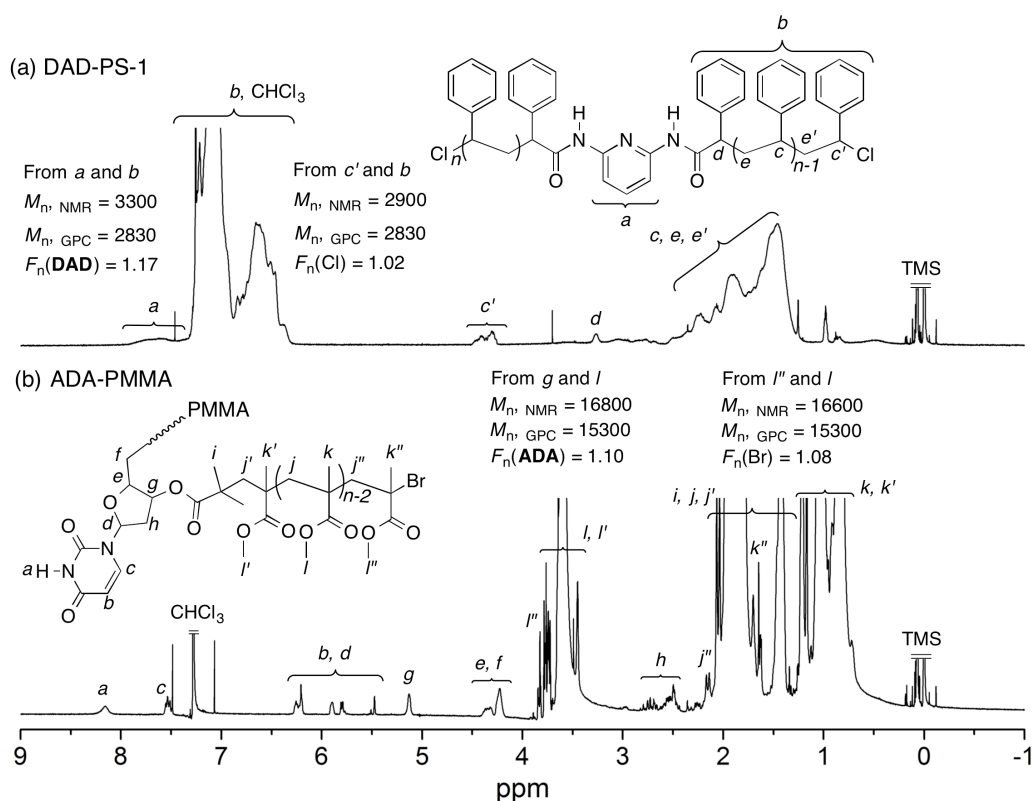
3. Structural Analysis of Obtained Polymers

Five samples of PMMA or PS were thus prepared to study the interaction between pairs of polymers (Table 3). All the samples were purified with preparative SEC, and the functionality (F_n) in terms of DAD or ADA was determined by ¹H NMR. For example, a PS sample from Cl-DAD-Cl (DAD-PS-1: $M_{n, SEC} = 2830$, $M_w/M_n = 1.08$) exhibited the characteristic peak of a pyridine (3H) (Figure 3a). Peak integration led to $M_{n, NMR} = 3300$,

Table 3. Samples of ADA- or DAD-Functionalized Polymers in This Work^a

Sample Code	$M_{n, SEC}^d$	M_w/M_n^d	$M_{n, NMR}^f$	F_n (DAD or ADA) ^g
DAD-PS-1 ^b	2830 ^e	1.08 ^e	3300	1.17
DAD-PS-2 ^b	2870	1.05	2770	0.96
DAD-PMMA ^b	2830	1.18	2060	0.73
ADA-PS ^b	4080	1.06	3850	0.94
ADA-PMMA ^c	15400 ^e	1.17 ^e	16800	1.10

^aAll polymer samples were purified by preparative SEC to remove low molecular weight residues. ^b[Monomer]₀ = 4.0 M, [initiator]₀ = 40 mM, [Ru(Cp*)Cl(PPh₃)₂]₀ = 4.0 mM, [*n*-BuNH₂]₀ = 40 mM in toluene at 80 °C for MMA and 100 °C for St. ^c[MMA]₀ = 4.0 M, [Br-ADA-Br]₀ = 20 mM, [Ru(Cp*)Cl(PPh₃)₂]₀ = 2.0 mM, [*n*-BuNH₂]₀ = 20 mM in toluene at 80 °C. ^dMeasured by size-exclusion chromatography calibrated with PMMA or PS standards in THF. ^eCHCl₃ was used as an eluent. ^fCalculated with ¹H NMR. ^gDetermined by $M_{n, NMR}/M_{n, SEC}$.

**Figure 3.** ¹H NMR spectra (CDCl₃, room temperature) of (a) DAD-PS-1 and (b) ADA-PMMA.

and the number-average functionality of DAD [$F_n(\text{DAD}) = M_{n,\text{NMR}}/M_{n,\text{SEC}}$] was estimated to be 1.17, indicating near quantitative introduction of the central unit. Similarly, for a PMMA sample from Br-ADA-Br (ADA-PMMA: $M_{n,\text{SEC}} = 15400$, $M_w/M_n = 1.17$), a peak derived from the methine proton adjacent to the deoxyribose ester [$-\text{CH}(\text{OCO}-)-$] was detected (Figure 3b), to give $M_{n,\text{NMR}} = 16800$ and in turn $F_n(\text{ADA}) = 1.10$. Overall, all the samples obtained in this study had nearly one mid-chain ADA or DAD unit per chain.¹⁴

The samples were then treated to cleave the bifunctional initiator moiety from the polymer backbones; if the former is in fact placed in the center of backbone as designed, molecular weight should decrease by half after the cleavage. To perform the cleavage experiment, two polymer samples were employed: PMMA obtained from Br-ADA-Br ($M_{n,\text{SEC}} = 6260$, $M_w/M_n = 1.13$) and PS from Cl-DAD-Cl ($M_{n,\text{SEC}} = 2180$, $M_w/M_n = 1.05$). The former was treated with sodium methoxide (NaOCH_3) in THF/MeOH (9/1 v/v) (80 °C, 17 h) for transesterification of alkyl esters into methyl esters. Note that this procedure cleaves the two ester-linkages in the ADA residue, whereas the pendent methyls in the PMMA chains remain unchanged. For the latter, the amide linkages in the DAD moiety were cleaved with trifluoroacetic acid in dioxane at 100 °C for 48 h. After these cleavage experiments, the overall molecular weights of the two samples (the peak tops of SEC curves) were indeed reduced by half (Figure 4).

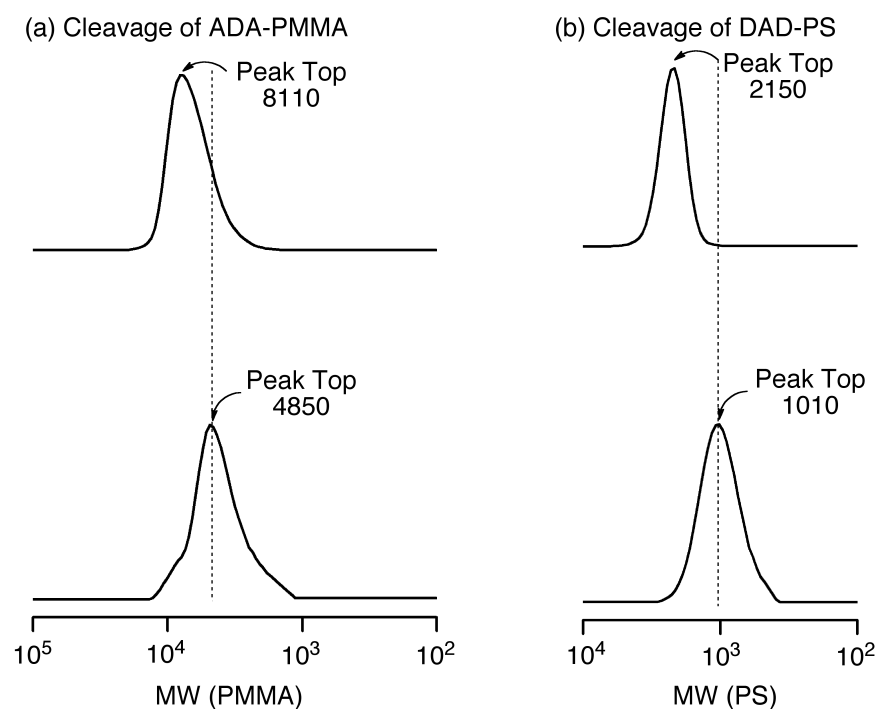


Figure S9. SEC analyses for the cleavage experiment with (a) ADA-PMMA and (b) DAD-PS.

4. Interaction between "Complementary" Polymer Chains

The interaction between the ADA- and DAD-functionalized polymers was examined by ^1H NMR (Figure 5). For example, equimolar amounts of ADA-PMMA ($M_{n, \text{SEC}} = 15400$, $M_w/M_n = 1.17$) and DAD-PS-1 ($M_{n, \text{SEC}} = 2830$, $M_w/M_n = 1.08$) were mixed in CDCl_3 at 10 mM each, and the solution was stirred overnight at room temperature. Figure 5 shows the magnified ^1H NMR spectra in the 7.9–8.6 ppm range for DAD-PS-1 (a), ADA-PMMA (b), and their mixture (c). Upon mixing, the thymine NH proton of ADA-PMMA clearly shifted downfield from 8.14 (Figure 5b) to 8.33 ppm (Figure 5c), indicating an interaction between the DAD and the ADA units. On the other hand, no such a shift occurred when ADA-PMMA was mixed with a DAD-free, commercial PS standard sample of a similar molecular weight ($M_n = 2630$, $M_w/M_n = 1.05$) (Figure 5d).

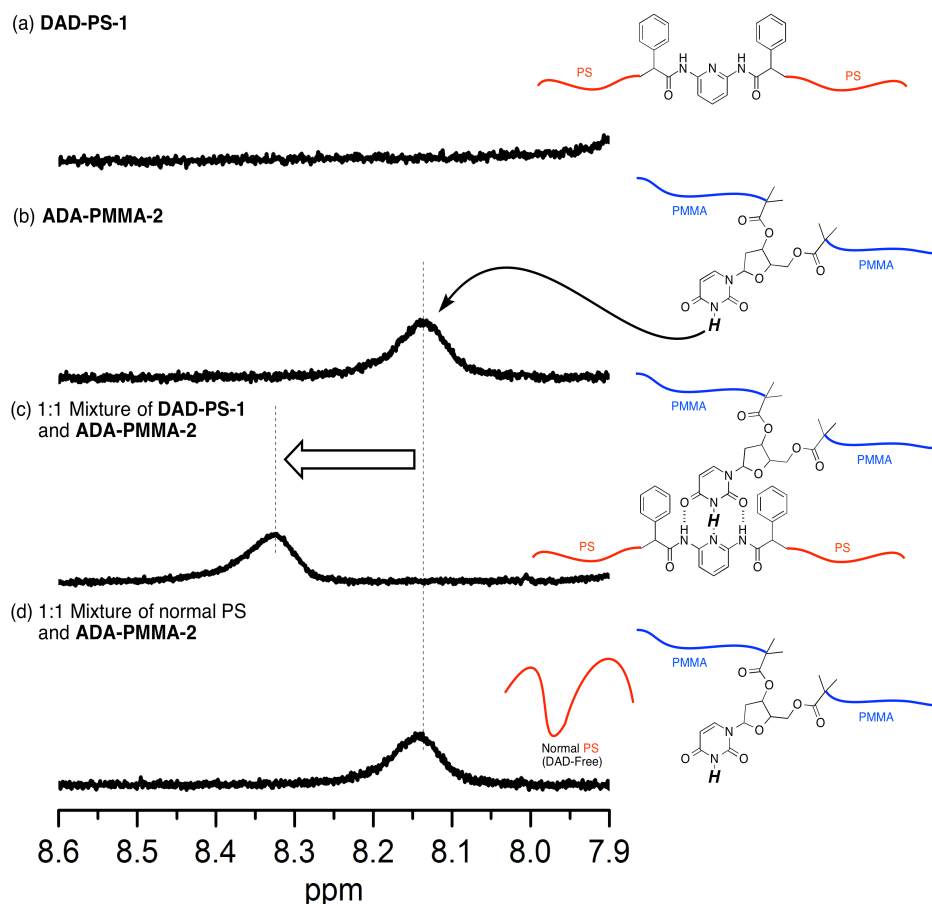


Figure 5. ^1H NMR spectra (CDCl_3 , room temperature) from 7.9 to 8.6 ppm of (a) DAD-PS-1 ($[\text{DAD-PS-1}] = 2.0 \text{ mM}$), (b) ADA-PMMA ($[\text{ADA-PMMA}] = 2.0 \text{ mM}$), (c) 1:1 mixture of DAD-PS-1 and ADA-PMMA ($[\text{DAD-PS-1}] = [\text{ADA-PMMA}] = 2.0 \text{ mM}$), and (d) 1:1 mixture of normal PS and ADA-PMMA ($[\text{normal PS}] = [\text{ADA-PMMA}] = 2.0 \text{ mM}$).

As with the ADA- and the DAD-initiators (see Section 1 above), a series of mixtures of the two complementary polymers at varying molar ratios (0.50 to 12) were further analyzed by ^1H NMR in CDCl_3 , to confirm their supramolecular interaction and further to determine their association constant (K_a) (Figure 6). For two pairs of polymers, ADA-PS/DAD-PS-2 (Figure 6a) and ADA-PS/DAD-PMMA (Figure 6b), the ADA's NH signals gradually and consistently shifted to downfield from 7.88 ppm to 10.53 ppm as the relative amount of the ADA unit increased, giving $K_a = 54.3 \text{ M}^{-1}$ and 116.2 M^{-1} , respectively (see also Table 1). Both values are similar to those for the initiator pairs ($K_a = 83.3 \text{ M}^{-1}$; Section 1), but it is interesting that the hetero-polymer pair ADA-PS/DAD-PMMA is more associative than the homo-polymer pair and even the initiator pair, though all the three systems involve the identical ADA–DAD complementary functions.

Further analysis is now being conducted for this intriguing phenomenon with a wider variety of polymer pairs, but it seems no doubt that complementary hydrogen-bonding interactions work well in solution even at the centers of polymer chains, which are also strong enough to overcome repulsion between different polymers such as PS and PMMA.

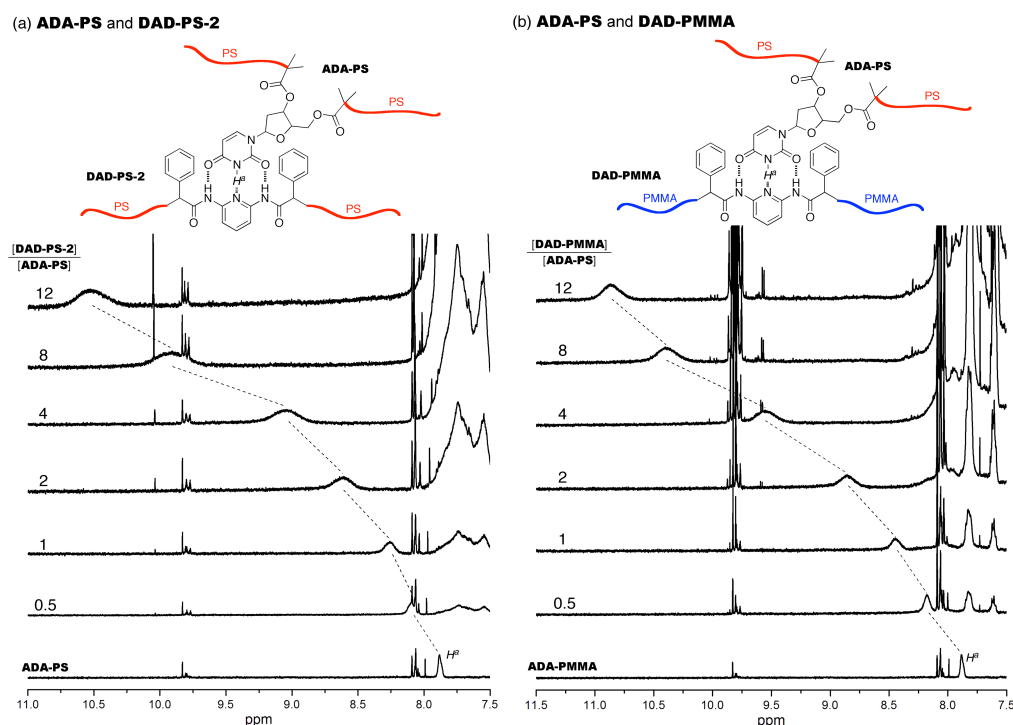


Figure 6. ^1H NMR spectra (CDCl_3 , room temperature) from 7.5 to 11.5 ppm for calculation of K_{ass} between ADA- and DAD-functionalized polymers, (a) ADA-PS and DAD-PS-2 and (b) ADA-PS and DAD-PMMA: ADA-functionalized polymer (bottom) and the mixtures with DAD-counterpart of various ratios ($[\text{DAD-polymer}]/[\text{ADA-polymer}] = 0.5, 1, 2, 4, 8,$ and 12); $[\text{ADA-polymer}] = 2.0 \text{ mM}$ (constant), $[\text{DAD-polymer}] = 0, 1, 4, 8, 16,$ and 24 mM .

5. ^1H DOSY Analyses for Interaction between Polymer Chains

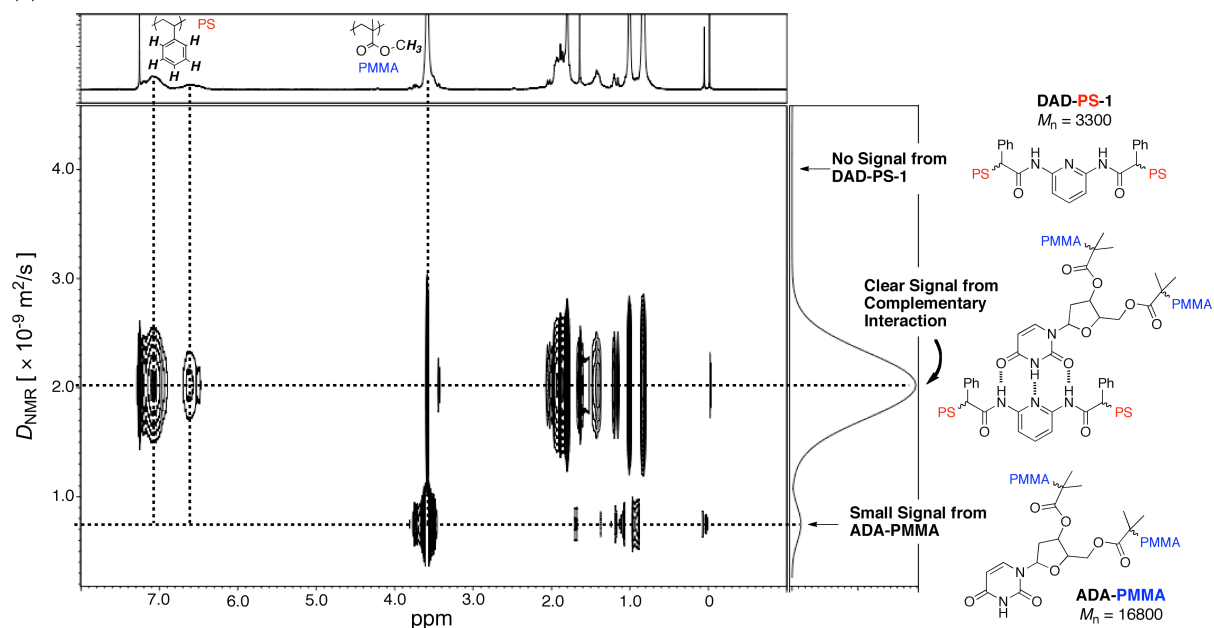
As discussed in the preceding section, ^1H NMR spectroscopy is indeed a convenient way to examine polymer-polymer interactions, but obviously it is less effective and sensitive for higher molecular weight polymers where signals of mid-chain functional groups (like ADA and DAD, one per long backbone) are usually too weak for quantitative measurement. Thus, diffusion-ordered ^1H NMR spectroscopy (DOSY) was employed, which conveniently gives diffusion coefficients (D_{NMR}) of multiple solutes in solution.

In a typical run, a sample of ADA-PMMA of a relatively high molecular weight ($M_{\text{n,SEC}} = 15400$) was mixed with an equimolar complementary sample DAD-PS-1 of a shorter length ($M_{\text{n,SEC}} = 2830$) in CDCl_3 , and their interaction was directly followed by ^1H DOSY analysis. Figure 7 illustrates a 2D correlation diagram of ^1H NMR signals (abscissa) and D_{NMR} distribution (ordinate).

The diffusion data consist of two populations, and their correlations with NMR signals indicate that the larger and predominant distribution is for the expected supramolecular PS-PMMA pair ($D_{\text{NMR}} = 2.00 \times 10^{-9} \text{ m}^2/\text{s}$), whereas the very minor peak for non-associating (free) ADA-PMMA chains (Figure 7(a), $D_{\text{NMR}} = 8.70 \times 10^{-10} \text{ m}^2/\text{s}$); the latter is probably due to a minor deviation from a perfectly stoichiometric mixture upon sampling. Importantly, no population was detected for non-associating DAD-PS, which should have a larger $D_{\text{NMR}} = 4.00 \times 10^{-9} \text{ m}^2/\text{s}$ according to separate measurements. On the other hands, the mixture between commercial PS standard ($M_{\text{n}} = 2630$, $M_{\text{w}}/M_{\text{n}} = 1.05$) and ADA-PMMA ($M_{\text{n,SEC}} = 15400$) did not behave as a single molecule in D_{NMR} (Figure 7 (b)). The peak of phenyl group from PS and methoxy group from PMMA had clearly different mobility in that solution. This result indicates that there was no interaction between ADA-PMMA and unfunctionalized PS in this system.

The virtually single, very large population with D_{NMR} clearly different from those for the two components demonstrates the efficient complementary pairing of PS and PMMA chains by which the supramolecular structure thus formed could move as a single large (supra)molecule. Further examination is needed to clarify why the paired assembly is apparently more movable than non-associating PMMA.

(a) 1:1 Mixture of ADA-PMMA and DAD-PS-1



(b) 1:1 Mixture of ADA-PMMA and Normal PS (DAD-Free)

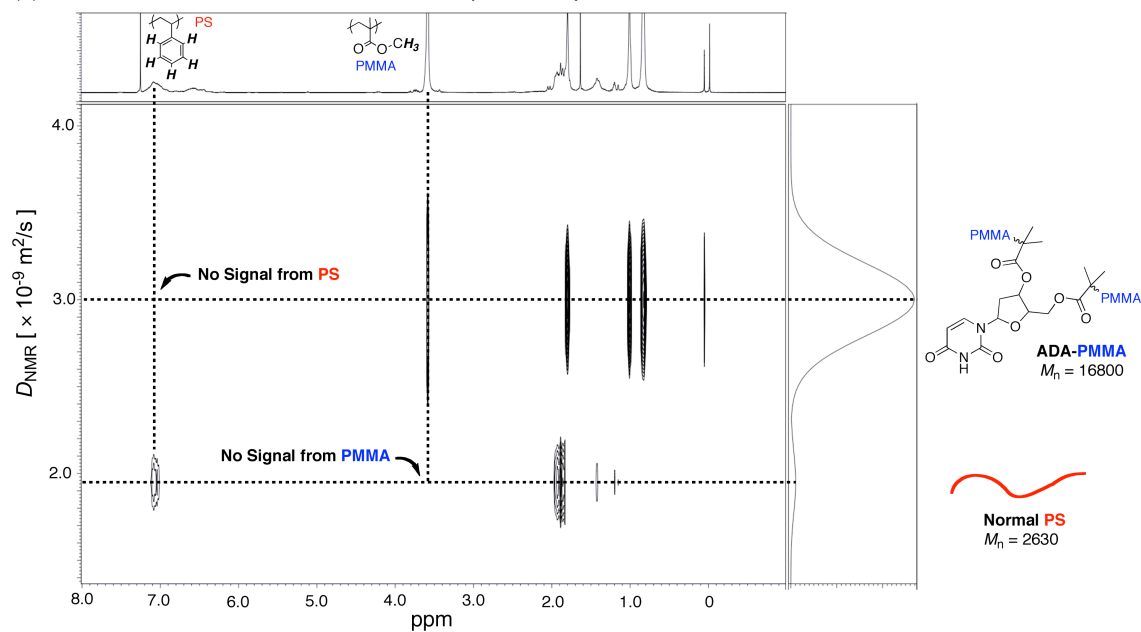


Figure 7. ^1H DOSY spectra (CDCl_3 , 30°C) of (a) 1:1 mixture of ADA-PMMA and DAD-PS-1 ($[\text{ADA-PMMA}] = [\text{DAD-PS-1}] = 2.0 \text{ mM}$) and (b) 1:1 mixture of ADA-PMMA and normal PS ($[\text{ADA-PMMA}] = [\text{normal PS}] = 2.0 \text{ mM}$).

Conclusion

A pair of bifunctional initiators (Cl-DAD-Cl and Br-ADA-Br), bearing complementary hydrogen bonding interactive sites, was designed for the precision synthesis of complementary associative polymers. The ruthenium-catalyzed living radical polymerization with these initiators led to well-defined polymers (PS and PMMA) that almost quantitatively carried DAD or ADA at the center of the backbone. ^1H NMR analyses revealed that the pair of polymers with DAD and ADA undoubtedly interacted with each other in CDCl_3 , and the association constants were comparable to that between initiators, even with a pair of different polymers (PMMA and PS). ^1H DOSY analyses also supported such a polymer-polymer interaction, in which one molecular behavior was observed. The author is now studying advanced interaction behaviors between polymers in terms of cooperative self-aggregation by “hydrogen bond” and “block copolymer” or periodic introduction of interaction sites.

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$$\delta_{mix} = \delta_{ADA} + \frac{(\delta_{\infty} - \delta_{ADA}) \left[\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right) - \sqrt{\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right)^2 - 4[ADA][DAD]} \right]}{2[ADA]}$$

, where the experimental parameters are as follows,

[ADA] and [DAD]: molar concentrations of ADA- and DAD-functionalized compounds (i.e., initiators or polymers)

δ_{mix} : a chemical shift for NH proton of ADA-functionalized compound for an equimolar mixture with DAD counterpart in ^1H NMR spectrum (a in Figure 1);

δ_{ADA} : a chemical shift for NH proton of ADA-functionalized compound;

K_{ass} : an association constant;

δ_{∞} : a saturated chemical shift for NH proton of ADA-functionalized compound when an excess molar of DAD counterpart was mixed. The value was calculated from curve fitting with third degree polynomial for plots with various mixing ratios.

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- (14) Only functionality of DAD-PMMA was lower than those of other samples. The theoretical M_n of DAD-PMMA was calculated to be about 1700 from the conversion (12.8%) and the ratio of monomer to initiator ($[\text{MMA}]_0/[\text{Cl-DAD-Cl}]_0 = 100$). This is much lower than the value by SEC ($M_{n, SEC} = 2830$). Thus, the lower F_n (DAD) might be caused by an inexactness of the SEC analysis. For such a low molecular weight polymer carrying a DAD unit at the middle point, a calibration curve with PMMA standard might not be applicable.

Chapter 2

Chain Center-Functionalized Amphiphilic Block Polymers: Complementary Hydrogen-Bond Self-Assembly in Aqueous Solution

Abstract

Hydrogen-bonding self-assemblies formed in an aqueous medium from a pair of an amphiphilic ABA triblock copolymer and a hydrophobic homopolymer, both with a triple hydrogen-bonding site that was complementary to each other and precisely placed at the main-chain center: $(\text{PEGMA})_m-(\text{MMA})_n-\mathbf{ADA}-(\text{MMA})_n-(\text{PEGMA})_m$ and $(\text{MMA})_p-\mathbf{DAD}-(\text{MMA})_p$ (**A** = hydrogen acceptor; **D** = hydrogen donor; PEGMA: PEG methacrylate; MMA: methyl methacrylate). The polymers were synthesized by the ruthenium-catalyzed living radial polymerization with bifunctional initiators (**Br-ADA-Br** and **Cl-DAD-Cl**) aiming at pinpoint chain-center functionalization to give a symmetric segmental sequence; **ADA** and **DAD** initiators were derived from 2,6-diaminopyridine and thymine, respectively. Upon mixed equimolar in THF, both polymers spontaneously associated, and the apparently 1:1 assembly further grew into higher aggregate particles on subsequent addition of water. The aggregates in water/THF were relatively stable and uniform in size, which most likely stems from the intermolecular complementary hydrogen-bond interaction at polymer chain centers. In sharp contrast, an equimolar mixture of **ADA**-block polymer and **DAD**-free poly(MMA) in water/THF resulted in larger and irregular particles, so short-lived to eventually collapse. These results indicate that, however structurally marginal, precise pinpoint functionalization of macromolecular chains allows stable self-assemblies via complementary hydrogen-bond interaction even in aqueous media.

Introduction

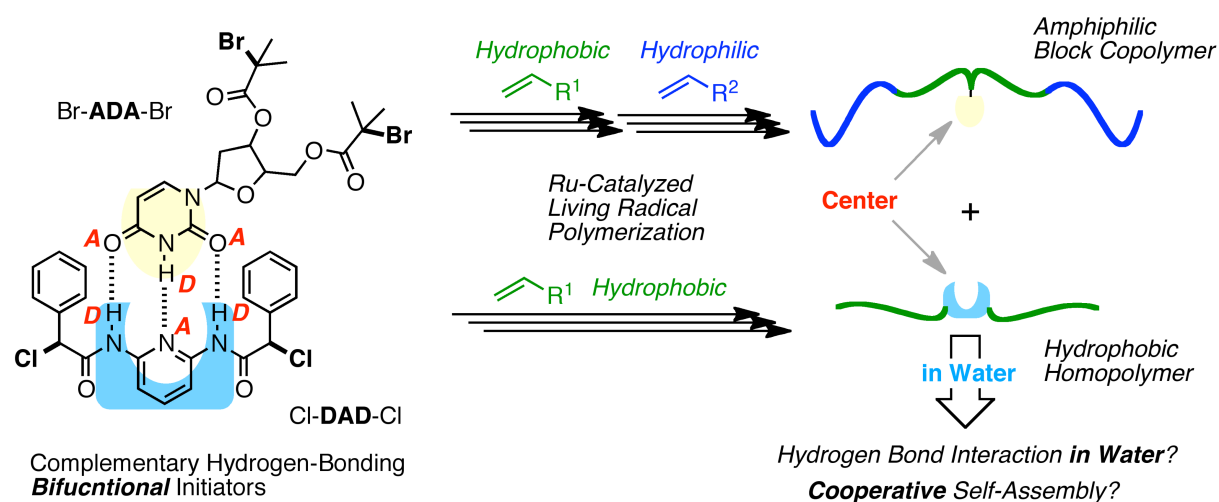
Complementary hydrogen bonds are crucial in regular structures and specific functions of nucleic acids such as DNA and RNA¹. Though dissociative, the interaction in these genes is partner-selective by definition and moderately tight, allowing well-defined helical structures and the genetic transcription into proteins. Similarly, the proteins – another type of biomacromolecules – also utilize hydrogen bonds for higher-ordered architectures and selective guest recognition. Rather surprisingly, the hydrogen bond interaction in biopolymers effectively works in water, one of the most polar solvents, although, in principle, hydrogen bonds are stronger in nonpolar media. A key factor for the effective hydrogen bonding in water is of course a hydrophobic environment generated in biopolymers by Van der Waals and other weaker interactions, and the aqueous H-bonding is promoted particularly by interactive sites precisely embedded at specific positions in macromolecules.

In parallel with the development of living radical polymerizations to control structures of synthetic polymers²⁻⁵, synthetic interest has been directed to “weak” interactions into block copolymers, such as hydrogen bond⁶⁻⁸, metal-ligand⁹, and π - π stacking¹⁰, so as to modify their regular structures (e.g., micro-phase separation) via “cooperating” self-assembly. In most cases, however, weakly interactive functions were randomly introduced primarily by copolymerization¹¹⁻¹³, eventually resulting in seemingly less effective and less specific intermolecular interaction and structures therefore.

My efforts have therefore been directed to precise introduction of weak interaction sites at well-defined positions on block copolymers. As recently reported¹⁴, the author has designed polymers that are position-specifically functionalized with complementary interactive multiple hydrogen-bonding units, **DAD** and **ADA** (**D**: hydrogen donor from 2,6-diaminopyridine; **A**: hydrogen acceptor from thymine) (see Scheme 1). The synthesis is based on ruthenium-catalyzed living radical polymerization with new bifunctional initiators, Cl-**DAD**-Cl and Br-**ADA**-Br, to give poly(methyl methacrylate) (PMMA) and polystyrene (PSt), homopolymers symmetrically functionalized at the backbone center: **DAD**-PMMA [= (MMA)_m-**DAD**-(MMA)_m] and **ADA**-PSt [= (styrene)_n-**ADA**-(styrene)_n]. Upon mixed equimolar in chloroform, the polymer pair spontaneously formed X-shaped supramolecular block copolymers via their complementary hydrogen-bonding, and the unique structure is certainly derived from DAD and ADA sites precisely positioned at the chain centers. Note,

however, that the self-assembling occurred only in a nonpolar organic solvent, different from similar phenomena of biopolymers in water.

As inspired from natural macromolecules as mentioned above, this work is therefore focused on precision polymers that allow complementary hydrogen-bonding interaction *in water* and related aqueous media where it is less favored (Scheme 1). For this the author has designed and synthesized an amphiphilic ABA block copolymer, (PEGMA)_m-(MMA)_n-**ADA**-(MMA)_n-(PEGMA)_m (PEGMA: PEG methacrylate), that is pinpoint functionalized at the backbone center with a symmetrical segmental sequence, so as to generate hydrophobic pockets for hydrogen bonding under aqueous conditions. Additionally, another hydrophobic partner, (MMA)_p-**DAD**-(MMA)_p, was prepared that mimics the center segment of the **ADA** block copolymer but with a complementary **DAD** central function. To my knowledge, there are limited examples to see hydrogen-bonded interaction in water with designer synthetic molecules, including not only polymers¹⁵⁻¹⁶ but also oligomers¹⁷⁻¹⁸.



Scheme 1. Living radical polymerization with bifunctional initiators (**Cl-DAD-Cl** and **Br-ADA-Br**) and cooperative self-aggregation of supramolecular block copolymer in aqueous solution.

Experimental Section

Materials

Methyl methacrylate (MMA) and styrene (St) (TCI; >99 %) were dried overnight over calcium chloride and purified by double distillation from calcium hydride before use. PEGMA [$\text{CH}_2=\text{CMeCO}_2(\text{CH}_2\text{CH}_2\text{O})_n\text{Me}$; $n = 8.5$ on average] (Aldrich) was purified by passing through an inhibitor removal column (Aldrich) and was subsequently degassed by triple vacuum-argon bubbling cycles before use. Ruthenium catalysts $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]$ (Cp^* : pentamethylcyclopentadienyl, Aldrich) and $\text{Ru}(\text{Ind})\text{Cl}(\text{PPh}_3)_2$ (Ind: indenyl, Aldrich) were used as received. Toluene and THF (Kishida Kagaku; purity 99.5 %) was dried and purified by passing through purification columns (Solvent Dispensing System, Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use. *n*-Monobutylamine (TCI; >98 %) and *n*-tributylamine (TCI; >98 %) was degassed by reduced pressure before use. *n*-Octane and tetralin (internal standard for gas chromatography) were dried over calcium chloride and distilled from calcium hydride. The bifunctional initiators (Cl-**DAD**-Cl and Br-**ADA**-Br) were synthesized from 2,6-diaminopyridine and thymine derivative, as recently reported.¹⁴

Ruthenium-Catalyzed Living Radical Polymerizations

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. Typical procedures for block copolymerization of MMA and PEGMA with Br-**ADA**-Br are given below. In a round-bottom flask (50 mL) filled with argon was placed $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (7.9 mg, 0.01 mmol), toluene (0.71 mL), *n*-octane (0.14 mL), MMA (1.07 mL, 10 mmol), *n*-BuNH₂ solution (0.25 mL, 400 mM in toluene) and a solution of Br-**ADA**-Br (0.33 mL, 302.6 mM in THF) was sequentially added in argon atmosphere; the total volume was 2.5 mL. The reaction mixture was placed in an oil bath kept at 80 °C. After 3 h, the polymerization mixture was terminated by cooling to room temperature. In an another round-bottom flask (50 mL) filled with argon was placed $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (6.4 mg, 0.008 mmol) and 2 mL of the quenched solution was added. The mixture was evaporated during overnight to remove unreacted MMA. Monomer conversion was determined from residual monomer concentration measured by gas chromatography with *n*-octane as an internal standard

(conversion = 47 %) from remained solution and the obtained polymer was measured with SEC ($M_n = 6500$, $M_w/M_n = 1.14$). To evaporated mixture, toluene (11.0 mL), tetralin (1.08 mL), *n*-BuNH₂ solution (0.4 mL, 400 mM in toluene) and PEGMA (3.41 mL, 8.0 mmol) were introduced in argon atmosphere; the total volume was 16.0 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at 80 °C. In predominant intervals, the polymerization mixture was terminated by cooling to –78 °C in dryice-methanol. The conversion of PEGMA was determined from residual monomer concentration measured by ¹H NMR spectra with tetralin as an internal standard. The quenched solutions were evaporated to dryness for SEC characterization. Samples for self-aggregation experiments were purified by dialysis with MeOH, followed by silicagel column with toluene for quantitative removal of ruthenium residue.

Measurement

M_n and M_w/M_n of polymers were measured by size exclusion chromatography (SEC) at 40 °C in THF or DMF eluent, the latter containing 10 mM LiBr: (THF-SEC) triple polystyrene-gel columns (Shodex LF-404; pore size, 3000 Å; 4.6 mm i.d. × 250 cm), a DU-H2000 pump, a 74S-RI refractive-index detector, and a 41-UV ultraviolet detector (all from Shodex); flow rate 0.3 mL/min. (DMF-SEC) triple polystyrene gel columns (Shodex K-805L; pore size 5000 Å; 8.0 mm i.d. × 30 cm), a PU-2080 pump, a RI-2031 refractive-index detector, and a UV-2075 ultraviolet detector set at 270 nm (all from Jasco); flow rate 1.0 mL/min. The columns were calibrated against 13 standard samples of poly(MMA) (Polymer Laboratories; $M_n = 620$ –1,200,000; $M_w/M_n = 1.06$ –1.22) or polystyrene (Polymer Laboratories; $M_n = 500$ –3,840,000; $M_w/M_n = 1.01$ –1.14). Samples were purified by preparative SEC in CHCl₃ at room temperature on a polystyrene gel column (Shodex K-5002; exclusion limit = 5×10^3 ; particle size = 15 µm; 5.0 cm i.d. × 30 cm; flow rate = 10 mL/min) connected to a PU-2086 precision pump, a RI-2031 refractive-index detector, and a UV-2075 ultraviolet detector (all from Jasco).

Proton nuclear magnetic resonance (¹H NMR) spectra were recorded in CDCl₃ or THF-*d*₈ at room temperature on a JEOL JNM-ECA500 spectrometer operating at 500.16 MHz. Dynamic light scattering (DLS) was measured at 25 °C on an Otsuka Photol ELSZ-0 spectrometer equipped with a semiconductor laser (658 nm). The measuring angle was 165°.

and data were analyzed by the CONTIN fitting method. In the DLS analyses in H₂O/THF (1/1 v/v) mixed solvent, values of viscosity (0.7097) and refractive index (1.3663) were estimated from the averaged values for H₂O (0.8900 and 1.3300, respectively) and THF (0.5402 and 1.4073, respectively). Cryogenic transmission electron microscopy (Cryo-TEM) was performed at ca. 90 K on Cryo-Tecnaï F20 instrument (acceleration voltage 200 kV) equipped with a cryo-transfer holder (626.DH, Gatan).

Sample Preparation for DLS and Cryo-TEM

ADA-block ($M_{n,NMR} = 42700$; $M_w/M_n = 1.32$) and **DAD**-MMA ($M_{n,NMR} = 13400$; $M_w/M_n = 1.15$) were separately dissolved in THF at 2.5 mM. For self-assembly analysis, 0.10 mL aliquots of these stock solutions were mixed and then diluted with 2.3 mL of THF into total 2.5 mL of 100 μ M nominally equimolar mixtures of the two polymers. The mixtures were stirred overnight at room temperature and diluted with 2.5 mL of ultrapure water (Wako Chemicals) into 50 μ M solutions (final concentration of both polymers = 2.8 mg/mL) that were further stirred for 1 h and filtered on a 0.45 μ m-pore syringe filter (Aldrich). DLS was measured on solutions immediately after filtration and 5 and 20 h thereafter.

The 20 h specimen was also employed for cryo-TEM. A drop (~ 2 μ L) of the filtered solution was placed on a lacey carbon-coated copper TEM grid (300 mesh, PolyScience) set in an automated sample vetrifier (VitrobotTM Mark III; FEI). The excess solution over the grid was blotted with a filter paper to leave a thin sample layer, and the grid was quickly immersed into liquid ethane cooled with liquid nitrogen. The vitrified specimen was kept in liquid nitrogen until mounted onto the cryo-transfer holder. Sample temperature was monitored and kept constant throughout the preparation steps.

Results and Discussion

1. Synthesis of Amphiphilic Block Copolymers Carrying Complementary Hydrogen Bonding Sites

Amphiphilic block copolymers consisting of poly(MMA) as a hydrophobic segment and poly(PEGMA) as a hydrophilic counterpart were synthesized with the **ADA**-functionalized bifunctional initiator (Br-**ADA**-Br): the **ADA** site is consequently embedded at the center of the triblock copolymers. The order of the block segment was targeted as “*hydrophilic-hydrophobic-hydrophilic*” to make hydrophobic environment around the **ADA** center. Hereby, it is expected that hydrogen-bonding interaction with **DAD**-functionalized molecules would be promoted even in water.

Thus, MMA was first polymerized with Br-**ADA**-Br as an initiator. A Cp*-based ruthenium complex [Ru(Cp*)Cl(PPh₃)₂] was used as a catalyst, in conjunction with *n*-BuNH₂ cocatalyst, for the polymerization (Figure 1). The polymerization was well controlled to give poly(MMA) of narrow molecular weight distribution ($M_n = 6500$, $M_w/M_n = 1.14$ for 47 % conversion: Figure 1). After an evaporation of the polymerization solution for removal of remained MMA monomer, PEGMA was injected for second polymerization from the Br-capped poly(MMA) as a macroinitiator. Even in the second polymerization, the PEGMA monomer was also smoothly consumed. SEC curves of obtained polymers shifted to higher molecular weight keeping the monodispersed distributions ($M_w/M_n \sim 1.3$) without any tailing peaks, indicating control of the block copolymerization.

Then, structure of the obtained block copolymer (**ADA**-block) was analyzed with ¹H NMR (Figure 2). In addition to characteristic peaks to the side chain of poly(MMA) (*f*) and that of poly(PEGMA) (*c-e*), minor but characteristic peaks from the **ADA** unit were clearly observed (*g-p*). The M_n of the block copolymer was calculated from the integration ratio of the methine proton adjacent to the deoxyribose ester [*l*: -CH(OCO-)-] in the **ADA** unit to the main chain polymer peaks (*d*, *e*, and *f*) and the given molecular weight of the PMMA segment [$M_{n, \text{GPC}} = 6500$, $DP_{n, \text{MMA}} (m) = 60$]: $M_{n, \text{NMR}} = 42700$, $DP_{n, \text{PEGMA}} (n) = 76$. On the other hand, the molecular weight was also calculated from the PEGMA conversion (conv. = 75 %): $M_{n, \text{conv}} = 42540$. Thus, the $M_{n, \text{NMR}}$ based on **ADA** moiety agreed well with $M_{n, \text{conv}}$, indicating almost quantitative introduction of the **ADA** site for one block chain: $F_n(\text{ADA}) \sim 1.00$ ($M_{n, \text{NMR}}/M_{n, \text{conv}}$).

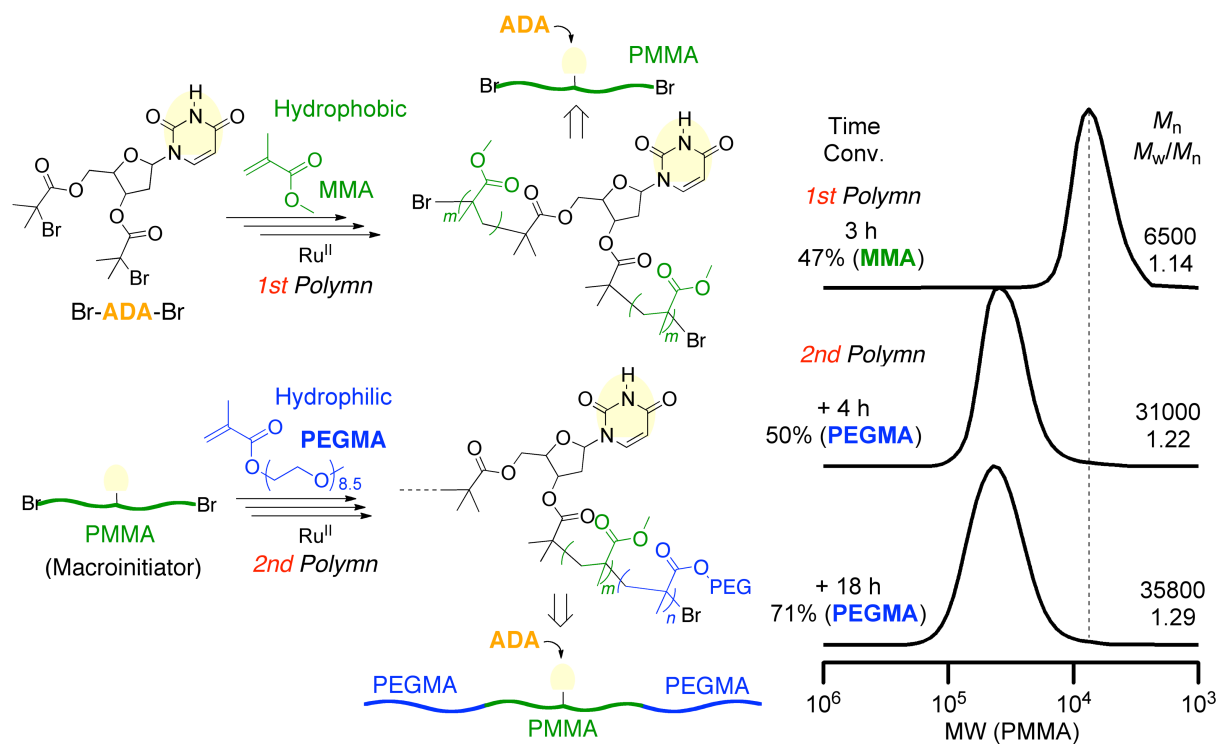


Figure 1. SEC curves for block copolymerizations of MMA and PEGMA with Br-**ADA**-Br. 1st polymerization: [MMA]₀ = 4.0 M; [Br-**ADA**-Br]₀ = 40 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ = 4 mM; [*n*-BuNH₂]₀ = 40 mM in toluene at 80 °C for 3 h; 2nd polymerization: [PEGMA]₀ = 0.5 M; [PMMA macroinitiator]₀ = 5 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ = 1 mM; [*n*-BuNH₂]₀ = 10 mM in toluene at 80 °C.

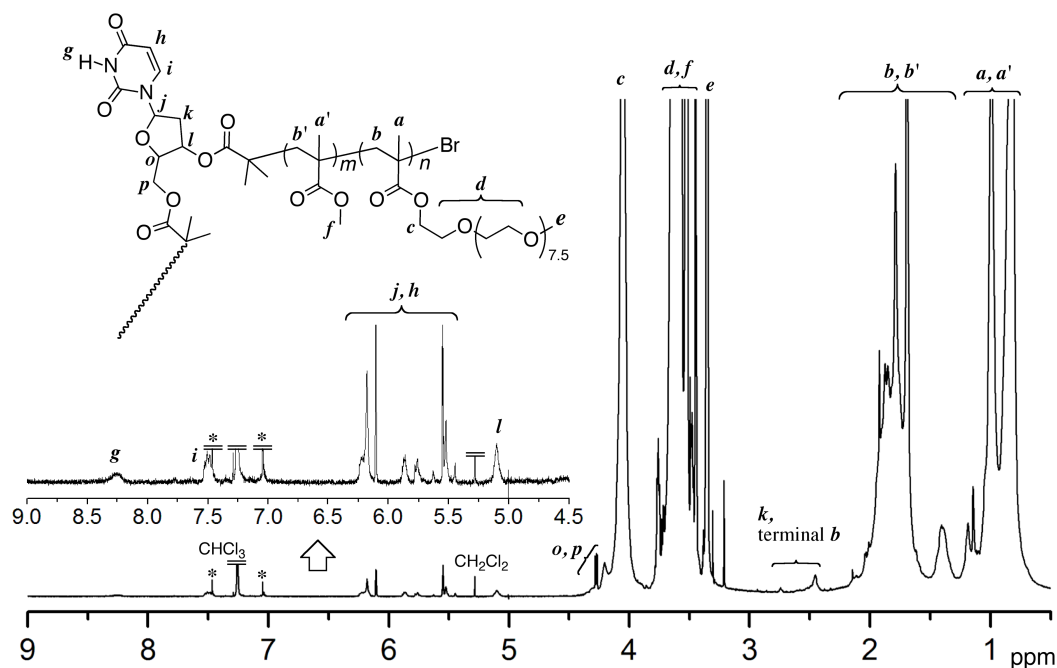


Figure 2. ^1H NMR Spectra (CDCl_3 , room temperature) for structural analysis of ADA-block.

2. Molecular Recognition in Aqueous Solution via Complementary Hydrogen-Bonding

To promote hydrogen-bonding interaction of **ADA**-block with some **DAD**-based molecule or polymer in water, they were first mixed in organic solvent to associate each other, followed by dilution with an excess of water. For this strategy, THF was selected as the organic solvent because it is miscible with water.

Prior to using **ADA**-block, an interaction between initiators (**Cl-DAD-Cl** and **Br-ADA-Br**) in THF was analyzed with ^1H NMR to evaluate the association constant (K_{ass}) between **DAD** and **ADA**.¹⁴ From the same stock solutions of the components in $\text{THF-}d_8$, a series of mixtures were prepared at varying ratios ($[\text{Cl-DAD-Cl}]/[\text{Br-ADA-Br}] = 1, 2, 4, 8, 12$, and 16 molar ratio). As the **Cl-DAD-Cl** amount was increased, the chemical shift of the NH proton in **Br-ADA-Br** gradually shifted downfield from 10.39 to 10.55 ppm, indicating an interaction in THF (Table 1 and Figure 3). The association constant (K_{ass}) was estimated as 20.2 M^{-1} . The value is a little lower than that in less polar solvent, CDCl_3 ($K_{\text{ass}} = 83.3 \text{ M}^{-1}$), but the interaction was certainly confirmed in $\text{THF-}d_8$.

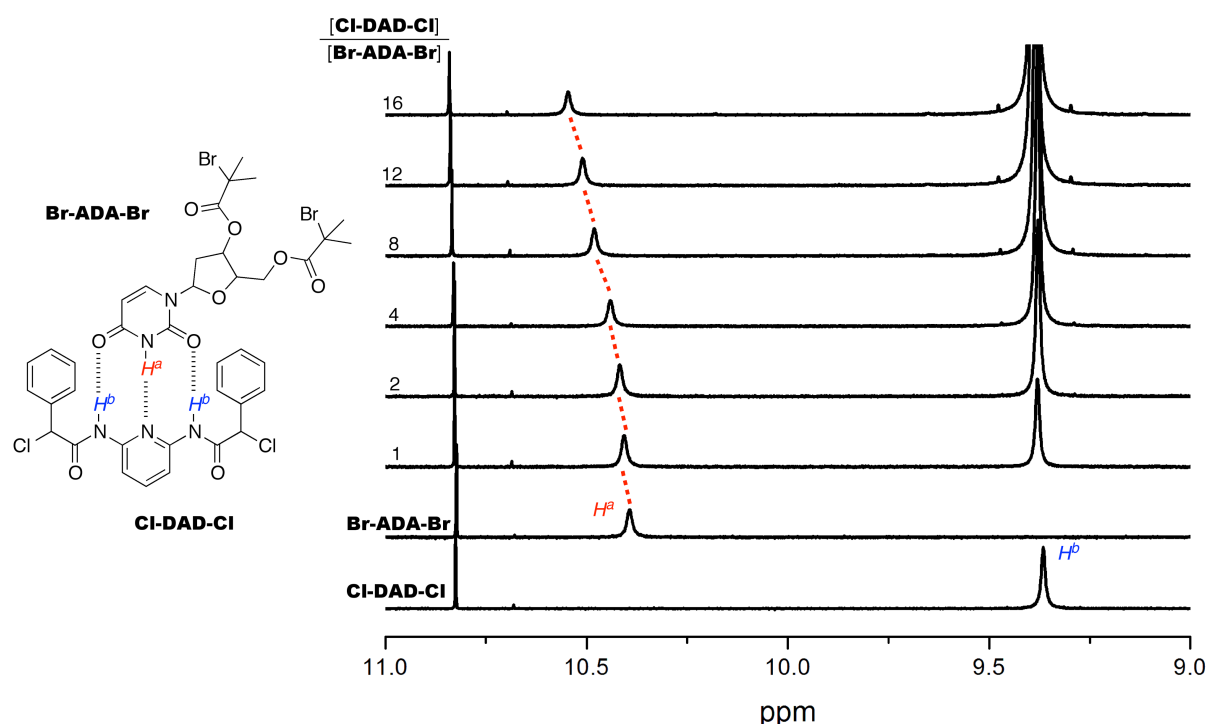


Figure 3. Calculation of K_{ass} between **Br-ADA-Br** and **Cl-DAD-Cl** with ^1H NMR spectra (9.0-11.0 ppm, $\text{THF-}d_8$, room temperature) of mixtures with varying concentrations of **Cl-DAD-Cl**: $[\text{Cl-DAD-Cl}]/[\text{Br-ADA-Br}] = 1, 2, 4, 8, 12$ and 16; $[\text{Br-ADA-Br}] = 2.0 \text{ mM}$ (constant), $[\text{Cl-DAD-Cl}] = 0, 2, 4, 8, 16, 24$, and 32 mM.

Table 1. Parameters for K_{ass} Calculation in This Work

Combination	[ADA] and [DAD]	δ_{mix} / ppm	δ_{ADA} / ppm	δ_{∞} / ppm
Br- ADA -Br and Cl- DAD -Cl ^a	2.0×10^{-3} mol/L	10.41	10.39	10.73 ^b

^asee Figure 3 for the interaction analyses by ^1H NMR ; ^bCalculated from curve fitting with third degree polynomial for plots with various mixing ratios.

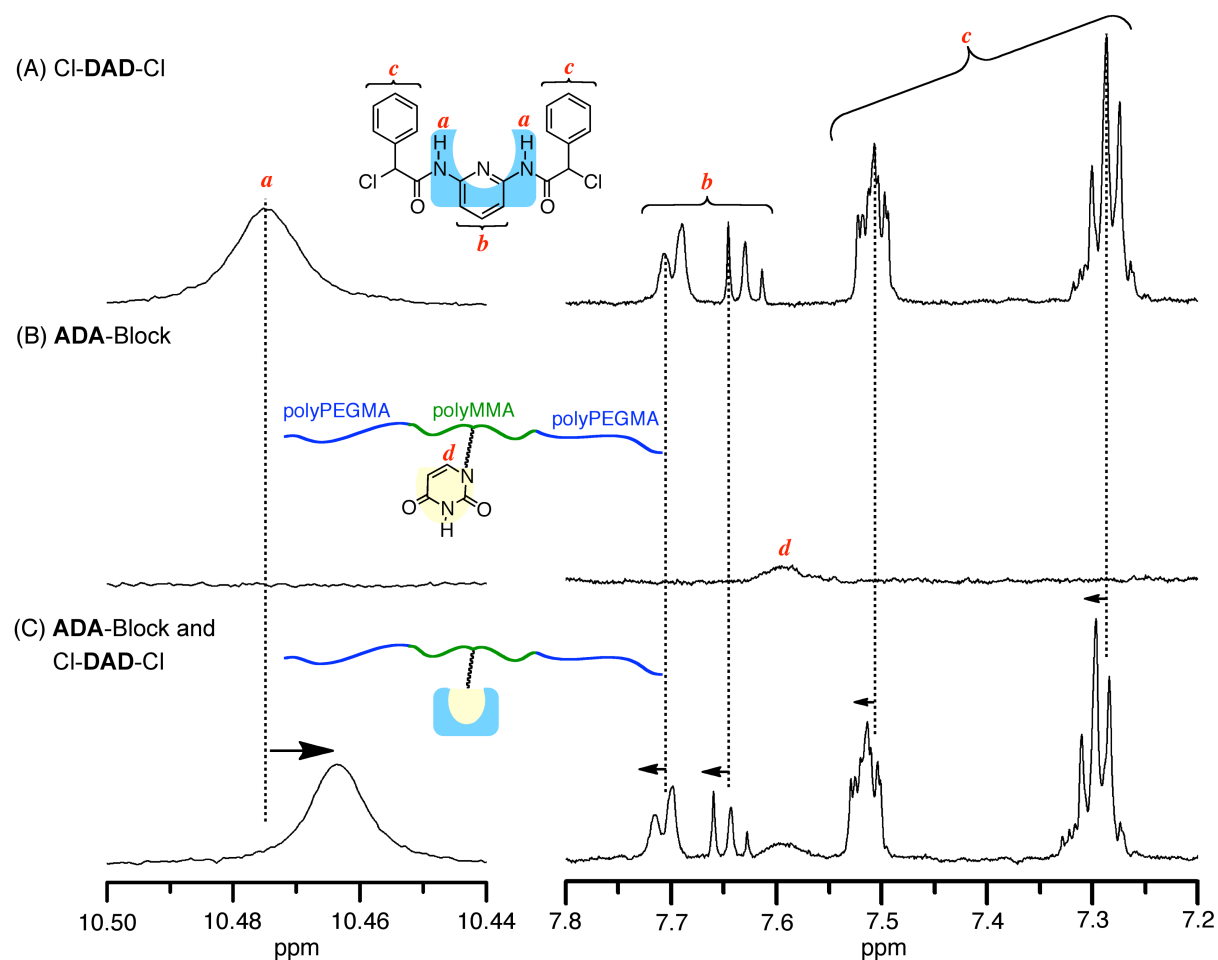


FIGURE 3. ^1H NMR analyses (25°C) for interaction between **ADA-Block** and **Cl-DAD-Cl** in H_2O and $\text{THF-}d_8$ (1/1 v/v): (A) **Cl-DAD-Cl**, (B) **ADA-Block** (C) 1:1 mixture of **Cl-DAD-Cl** and **ADA-Block**. All the samples were prepared with 1 mM concentration in $\text{H}_2\text{O/THF-}d_8$.

Next, a recognition ability of **ADA**-block for **DAD** unit in water was examined (Figure 4): here the initiator (Cl-**DAD**-Cl) was used as the model of **DAD**-based molecule. They both were first mixed in THF-*d*₈ (2 mM for each), followed by overnight stirring at room temperature. Then, the mixed solution was diluted with the same volume of water to make 1 mM solution in THF-*d*₈ and H₂O (1/1 v/v). Figure 4C shows the expanded spectra in the range of 10.44–10.50 ppm and 7.20–7.80 ppm, along with those for single component, Cl-**DAD**-Cl (Figure 4A) and **ADA**-block (Figure 4B), which were also prepared in the identical way with the mixture sample. Upon mixing, peaks from amine (*a*), benzene (*c*) and pyridine (*b*) protons in **DAD** unit clearly shifted, indicating both the complementary sites interact with each other even in water. These results indicate that **ADA**-block can recognize a **DAD**-based molecule even in water via the complementary interaction. This is likely due to a formation of “hydrophobic pocket” by the poly(MMA) segment around **ADA**, i.e., a recognition site for the **DAD** molecule.

3. Hydrogen Bonding Interaction between Polymers in Aqueous Solution

My effort was then directed to an aqueous interaction between polymers whose center was modified with **ADA** and **DAD** sites. For the **DAD**-based polymer, MMA was polymerized with Cl-**DAD**-Cl and ruthenium catalyst to prepare well-defined poly(MMA) (**DAD**-PMMA: $M_{n, GPC} = 12700$, $M_w/M_n = 1.15$). From the ¹H NMR analysis, a quantitative introduction of **DAD** at the center was confirmed ($M_{n, NMR} = 13400$, $F_n(\text{DAD}) = 1.06$). This polymer was mixed with an equimolar **ADA**-Block in THF, followed by the addition of same amount of water to prepare 1/1 v/v water and THF solution (see experimental section). The dispersed solution was filtered and the resultant aggregation was characterized with dynamic light scattering (DLS) and cryo-TEM (see Experimental section for detail). In these analyses, two samples were also prepared for the comparison: a mixture of **ADA**-Block and **DAD**-free PMMA (normal PMMA: $M_n = 12700$, $M_w/M_n = 1.03$); **ADA**-Block only (without **DAD**-PMMA).

The obtained aqueous solutions for the three samples were analyzed with DLS on predetermined times (0, 5, 20 h) after the water addition (Table 2). With the combination of **ADA**-Block and **DAD**-PMMA, some aggregated particles of about 180 nm of R_H were observed, and the size was almost constant afterward (5 and 20 h), suggesting “stable” aggregation (entry 1-3). These phenomena were quite different from the comparative samples. The combination of **ADA**-Block with **DAD**-free PMMA gave larger and scattering

sizes at the beginning, and the particles subsequently grew bigger in 5 h but likely collapsed in 20 h giving much smaller particles (entry 4–6). At the initial stage, the hydrophobic PMMA chains can exist with the assistance of **ADA-Block** under some aggregation even without any clear interaction, but the instability would cause secondary aggregation and decomposition in the end. On the other hand, only **ADA-block** was much smaller than common micelles, which is likely due to the condition with higher content of THF (entry 7-9). From these results, the aggregation behaviors with **ADA-Block** and **DAD-PMMA** were characteristic to the central introduction of complementary hydrogen bond, and herein the couple of polymer chains were mutually recognized even in aqueous solution to stabilize the aggregation for long time.

Table 2. DLS Analyses of THF/Water Solutions^a for Three Samples with **ADA-Block**

Entry	Samples	Time after Preparation, h	R_H^b , nm (n = 5)					Averaged R_H , nm
1	ADA-Block + DAD-PMMA	0	172.4	180.8	187.8	173.4	187.3	180.3
2		5	185.7	185.8	173.8	190.7	196.0	186.4
3		20	191.2	194.5	186.3	174.3	195.3	189.5
4	ADA-Block + Normal PMMA	0	140.0	273.1	584.7	293.2	406.8	339.6
5		5	1112.4	1061.7	352.5	1231.7	396.3	830.9
6		20	25.5	20.5	25.6	25.7	25.7	24.6
7	ADA-Block only	0	<i>Not Aggregated^c</i>					—
8		5						—
9		20						—

^aSee experimental section for preparation of the solutions. ^bNumber averaged values

^cPeaks for less than 2 nm were observed

Finally, for the samples measured 20 h after the preparation, the resultant structures were directly observed with cryo-TEM. The couple of **ADA-Block** and **DAD-PMMA** gave almost uniform shapes, although partial secondary aggregations were also observed (Figure

5A). On the other hand, the combination **ADA-Block** with **DAD-free PMMA** gave clearly different image (Figure 5B), where the aggregates seem to be further associated giving irregular structures. In the case with only **ADA-Block**, the main image consists of very small dots. Thus, the TEM observation also supports specific aggregation in water to the central interaction between the amphiphilic chain and hydrophobic one.

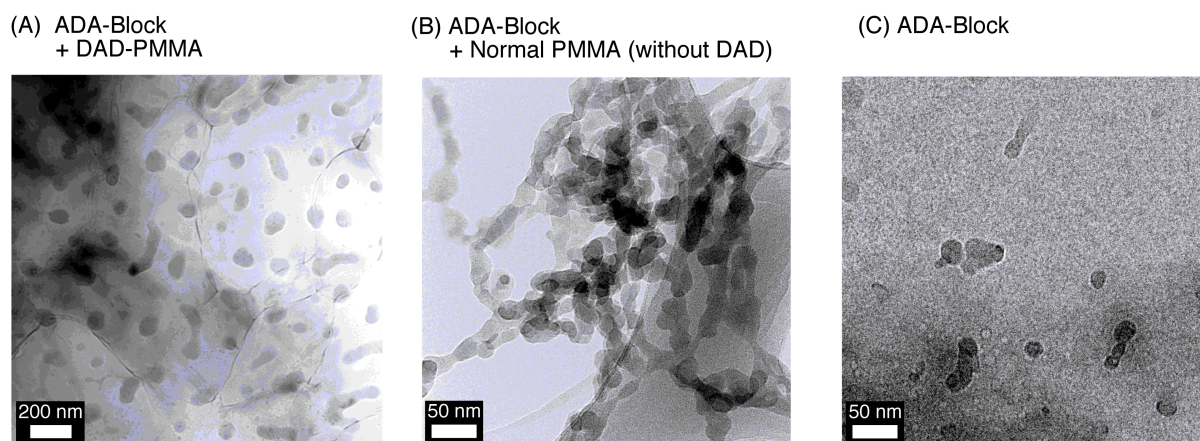


Figure 5. Cryo-TEM images of three samples in THF/H₂O with **ADA-Block**: (A) **ADA-block** and **DAD-PMMA**, (B) **ADA-block** and normal PMMA (C) **ADA-block** only. See experimental section for preparation of the solutions.

Conclusion

The complementary interaction between middle points of “amphiphilic block copolymer” and “hydrophobic homopolymer” gave stable and uniform particles in water, whereas the combination absent of the complementary interaction resulted in unstable aggregation. The two polymer chains would interact with each other via the complementary hydrogen bond even in water, as supported by the NMR analyses with the model combination. Presumably, the well-defined position of the interaction site in the chains contributed to the interaction efficiency: indeed, the couple of chains recognized each other, despite of only “one” set of the interaction sites, to induce the unique aggregation. These results would indicate an importance of position control for polymer functionalization.

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$$\delta_{mix} = \delta_{ADA} + \frac{(\delta_{\infty} - \delta_{ADA}) \left[\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right) - \sqrt{\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right)^2 - 4[ADA][DAD]} \right]}{2[ADA]}$$

, where the experimental parameters are as follows,

[ADA] and [DAD]: molar concentrations of ADA- and DAD-functionalized compounds (i.e., initiators or polymers)

δ_{mix} : a chemical shift for NH proton of ADA-functionalized compound for an equimolar mixture with DAD counterpart in ^1H NMR spectrum (H^a in Figure 3);

δ_{ADA} : a chemical shift for NH proton of ADA-functionalized compound;

K_{ass} : an association constant;

δ_{∞} : a saturated chemical shift for NH proton of ADA-functionalized compound when an excess molar of DAD counterpart was mixed. The value was calculated from curve fitting with third degree polynomial for plots with various mixing ratios.

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Chapter 3

Chain Extension of Center-Functionalized Polystyrene via Radical-Radical Coupling: Periodic Introduction of Complementary Interaction Site on Polymer Chain

Abstract

In this work, my purpose was directed to syntheses of polymer periodically carrying complementary interaction sites in chain without significantly changing the main structure. First, oligostyrene was precisely prepared via ruthenium-catalyzed living radical polymerization with a bifunctional (bi-headed) initiator (Cl-DAD-Cl) carrying three-point complementary hydrogen bonding sites (DAD: D = hydrogen donor; A = hydrogen acceptor). Radical species was then generated from the C-Cl bonds at the both terminals without monomers to induce “chain extension” through radical-radical coupling reaction between styryl radical species. The resultant polymer chains periodically carried the DAD sites, which were supported by ^1H NMR analyses, since molecular weight distribution the starting oligomer was enough narrow ($M_w/M_n = 1.06$) and the complementary interaction site was incorporated at the central position. The polymer can be regarded as novel polystyrene in which complementary hydrogen bonding are regularly embedded, although irregular head-to-head structure ($\sim\sim\sim\text{CH}_2\text{-CH(Ph)-CH(Ph)-CH}_2\sim\sim\sim$; Ph = phenyl, $\sim\sim\sim$ = polystyrene). Certainly, the extended polystyrene can interact with poly(methylmethacrylate) whose center was functionalized with the complementary couple or ADA array to give unique supramolecular graft copolymer, where two PMMA chains were dynamically grafted at regular intervals.

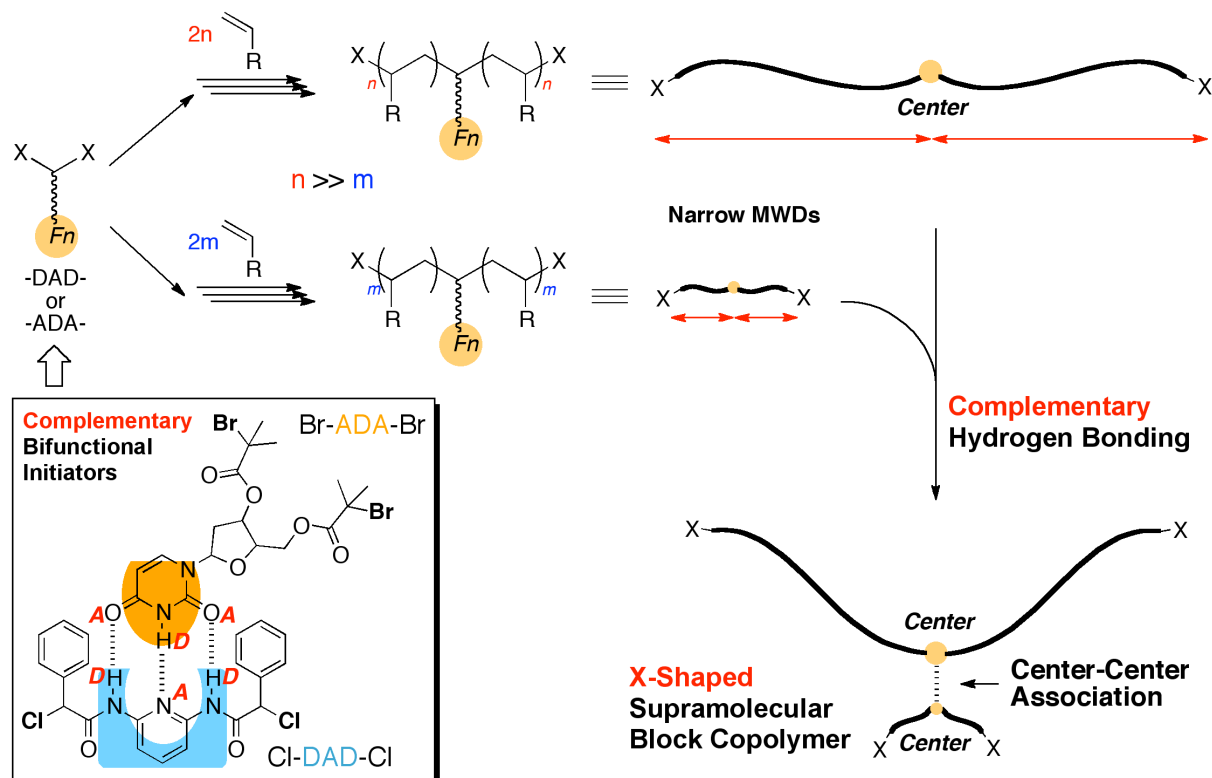
Introduction

Natural polymers such as DNA and proteins have inspired us to control position or sequence of functional groups for synthetic polymers. Some approaches toward such precisely controlled polymers have been recently presented,¹ however it is still hard to express novel functions derived from the control over position/sequence. Among functional groups for the control, dynamic or weak interaction site should be interesting, since the position or sequence control can affect the resultant chain conformation and the complexation behaviors with other molecules. For example, in nature, peptide chains are folded to form higher order structures depending on some weak but selective interactions at well-defined positions, and advanced or smart functions are realized on the basis of the structures.

Some efforts have been reported to introduce dynamic interaction sites on synthetic polymer chains. For example, Meijer et al. have presented some examples that oligomers or molecular chains carrying strong multiple hydrogen bonding interaction sites at terminals can express physical properties or phase separation like conventional polymers or block copolymers.² Some studies have been also studied on random introduction of interaction sites in segment of random copolymers³ or block copolymers⁴ to control aggregation or self-assembled behaviors. As seen in these examples, the positions of interaction sites were limited to chain ends and random sites in chains. If interaction sites can be incorporated at well-defined positions in chain except the terminals, additional or more advanced properties might be prospective. In terms of position to be controlled, periodic introduction of interaction sites on chain should be interesting toward effective chain-chain association. For example, Wagner's group has presented preparation polyethylene in which functional groups were incorporated at regular intervals via acrylic diene metathesis polymerization (ADMET) of center-functionalized diene molecules.⁵ The functionalized polyethylenes expressed peculiar crystalline structures and functions to the functional groups and interval carbon numbers.

Quite recently, the author presented an introduction of complementary hydrogen bonding interaction site at the center of vinyl polymer chains with a couple of "bi-headed" (bifunctional) initiators carrying the interaction site for metal-catalyzed living radical polymerizations.⁶ The initiators (Scheme 1: Cl-DAD-Cl and Br-ADA-Br) carry complementary array (DAD and ADA; D: H-donor; A: H-acceptor) of three points hydrogen bonding sites, and polymerizations with the initiators gave a couple of center-associative

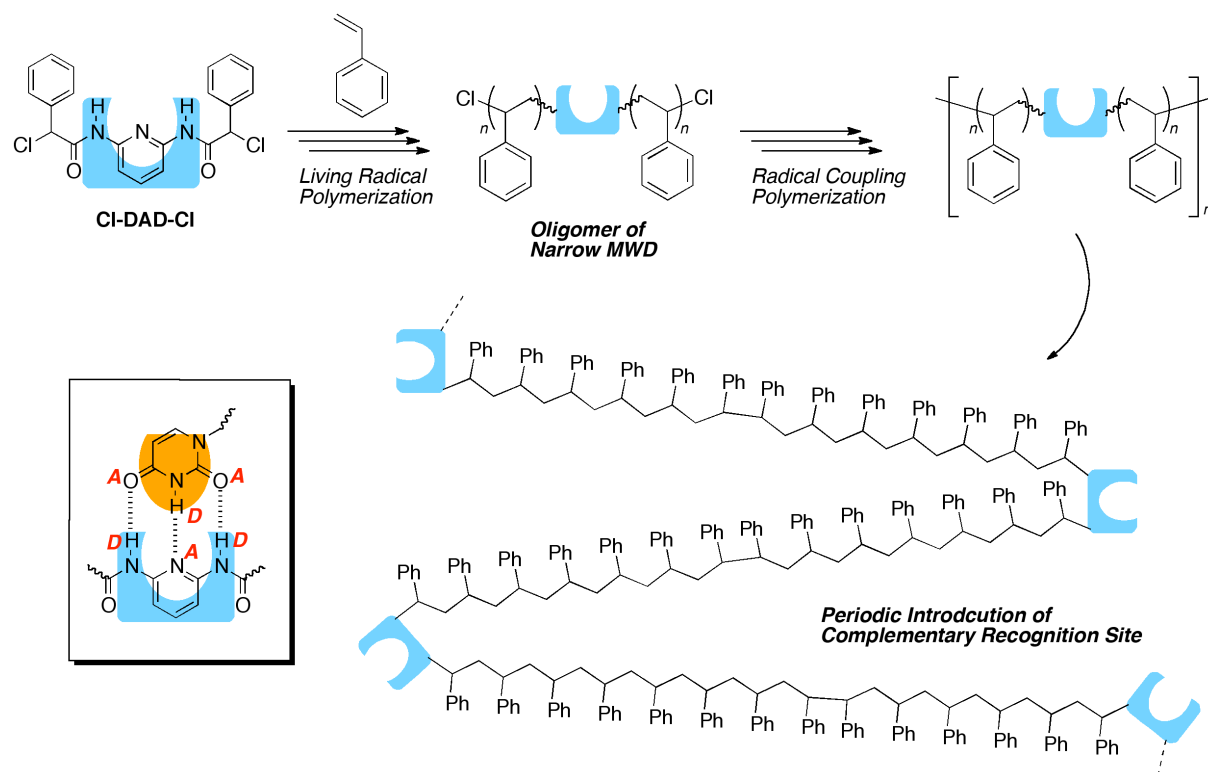
polymers of well-controlled molecular weights. The couple of different polymers [e.g., polystyrene (PSt) and poly(methyl methacrylate) (PMMA)] were certainly associated with each other at the center to give X-shaped supramolecular block copolymer.



Scheme 1. Bifunctional initiators carrying complementary H-bonding sites for living radical polymerization and X-shaped supramolecular block copolymer via center-association.

In this work, the author expanded polymerizations with the complementary couple of bifunctional initiators for “center-associative polymers” to chain extension for “periodically associative polymers” in which interaction sites are periodically introduced on polymer chains. More specifically, styrene was polymerized with Cl-DAD-Cl under Ru(II) catalysis to prepare bi-headed oligostyrene of narrow molecular weight distribution. Subsequently, the ruthenium catalysis was switched from “living radical polymerization” to “radical coupling reaction” for chain extension reaction. Note that styryl radical species are prone to incur coupling reaction rather than disproportionation in the absence of monomer and thus head-to-head structure ($\sim\sim\sim\text{CH}_2\text{--CH(Ph)--CH(Ph)--CH}_2\sim\sim\sim$; Ph = phenyl, $\sim\sim\sim$ = polystyrene) is introduced in the junction of chain extension. Ideally, as narrower the molecular weight distribution of the starting oligomer or polymer, the DAD site would be precisely introduced on the resultant chain-extended polystyrene. Thus, the strategy would allow periodic

introduction of the DAD site without introducing other polar groups in the polystyrene, which is favorable to study effects of the interaction sites. In this work, the interaction with ADA-functionalized polymers was also characterized (Scheme 2).



Scheme 2. Periodic introduction of complementary interaction sites into polymer chain via radical coupling polymerization of well-defined precursor with narrow MWD.

Experimental Section

Materials

Monomers (MMA and styrene: Aldrich; purity > 99 %) were dried overnight over calcium hydride and purified by distillation from calcium hydride before use. 2,6-Diaminopyridine (Wako; >97%), (+)-2'-deoxyuridine (Wako; >98%), 2-bromoisobutyryl bromide (Wako; >95%), triethylamine (Wako; 99%), 4-dimethylaminopyridine (Aldrich; 99%), $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (Cp^* : cyclopentadienyl, Aldrich), α -chlorophenylacetylchloride (Aldrich; 90%), and 2-bomoisobutyric acid (TCI; >98%) were used as received. Dichloromethane (Wako; dehydrated) and pyridine (Wako; dehydrated) were bubbled with dry argon for more than 15 min immediately before use.

Toluene and THF (Kishida Kagaku; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use. *n*-Monobutylamine (TCI; >98%) and 1,6-diaminohexane (1,6-DAH, TCI; >99%) was degassed by reduced pressure before use. *n*-Octane (internal standard for gas chromatography) was dried over calcium chloride and distilled from calcium hydride.

Synthesis of Complementary Hydrogen-Bonding Bifunctional Initiators

Cl-DAD-Cl (2,6-diamide pyridine-based dichloride of a *donor* (**D**) – *acceptor* (**A**) – *donor* (**D**) configuration) and Br-ADA-Br (thymine-based dibromide of an *acceptor* (**A**) – *donor* (**D**) – *acceptor* (**A**) configuration) were synthesized according to the literature.⁶

General Polymerization Procedures

Polymerization was carried out by the syringe technique under dry argon in baked round bottom flask equipped with a three-way stopcock. A typical procedure for styrene (St) or methyl methacrylate (MMA) with initiator/Ru(Cp*)Cl(PPh₃)₂/*n*-BuNH₂ is given. In a round-bottom flask (50 mL) filled with argon was placed Ru(Cp*)Cl(PPh₃)₂ (40.6 mg, 0.051 mmol), Cl-DAD-Cl (211.3 mg, 0.51 mmol), toluene (1.55 mL), THF (3.40 mL), *n*-octane (0.69 mL), *n*-BuNH₂ solution (1.27 mL, 400 mM in toluene) and St (5.84 mL, 51.0 mmol) were sequentially added; the total volume was 12.75 mL. Immediately after mixing, the solution was placed in an oil bath kept at 100 °C for 90 min. The polymerization mixture was terminated by cooling to –78 °C in dryice-methanol. Monomer conversion was determined from residual monomer concentration measured by gas chromatography with *n*-octane as an internal standard (conversion = 6 %) from remained solution and the obtained polymer was purified by fractional SEC in CHCl₃ to remove low molecular weight oligomer and catalyst. The final product was dried overnight under vacuum at room temperature and measured with SEC ($M_n = 1580$, $M_w/M_n = 1.05$).

Chain Extension Procedures

The chain extension reaction was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. A typical procedure for macroinitiator (PS_{tDAD}) with Ru(Cp*)Cl(PPh₃)₂/amine/P(*n*-Bu)₃/EtOH are

given. In a round-bottom flask (50 mL) filled with argon was placed PS_{DAD} (0.2947 g, 0.208 mmol), $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (49.7 mg, 0.062 mmol), toluene (2.65 mL), 1,6-DAH solution (0.42 mL, 1000 mM in toluene), $\text{P}(n\text{-Bu})_3$ solution (0.83 mL, 500 mM in toluene) and EtOH (1.30 mL) were sequentially added; the total volume was 5.20 mL. Immediately after mixing, the solution was placed in an oil bath kept at 100 °C for 48 h. The polymerization mixture was terminated by cooling to -78 °C in dryice-methanol. The quenched solution was evaporated and purified by fractional SEC in CHCl_3 to remove low molecular weight oligomer and catalyst. The final product was dried overnight under vacuum at room temperature and measured with SEC ($M_n = 8380$, $M_w/M_n = 1.48$).

Measurement

M_n and M_w/M_n of polymers were measured by size exclusion chromatography (SEC) at 40 °C in THF as an eluent. For the THF-SEC, three polystyrene-gel columns [LF-404 (from Shodex); pore size, 3000 Å; 4.6 mm i.d. $\times$ 250 cm] were connected to a DU-H2000 pump, a 74S-RI refractive-index detector, and a 41-UV ultraviolet detector (all from Shodex) and flow rate was set to 0.3 mL/min. The columns were calibrated against 13 standard polystyrene (PSt) samples (Polymer Laboratories; $M_n = 500\text{--}3,840,000$; $M_w/M_n = 1.01\text{--}1.14$) for obtained PSt samples, respectively. Polymer samples were purified by preparative SEC in CHCl_3 at room temperature on polystyrene gel preparative column [K-5002 (from Shodex); exclusion limit = 5×10^3 ; particle size = 15 μm ; 5.0 cm i.d. $\times$ 30 cm; flow rate = 10 mL/min] that were connected to a PU-2086 precision pump, a RI-2031 refractive-index detector, and UV-2075 ultraviolet detector (all from Jasco). ^1H NMR was recorded in CD_2Cl_2 or CDCl_3 at room temperature on JEOL JNM-ECA500 spectrometer, operating at 500.16 (^1H) MHz. MALDI-TOF-MS analysis was performed on a Shimadzu AXIMA-CFR instrument equipped with 1.2 m linear flight tubes and a 337 nm nitrogen laser; the matrix was dithranol. Differential scanning calorimetry (DSC) was performed on polymer samples under a dry nitrogen flow at heating or cooling rate of 10 °C/min on a DSCQ200 calorimeter (TA Instruments) equipped with a RCS 90 electric machine.

Results and Discussion

1. Ruthenium-Catalyzed Radical Coupling Condensation Polymerization

The author first studied conditions for ruthenium-catalyzed “radical coupling reaction” of the DAD-functionalized polystyrene. Efficient radical coupling systems have been developed in copper-catalyzed living radical polymerization (ATRP)⁷ and organotellurium-mediated living radical polymerization (TERP)⁸, but coupling condition under ruthenium catalysis is unknown. To promote coupling reaction, conditions are required for re-generation of radical generator (e.g., catalyst) as well as generation of radical species at high concentration.

Bi-headed polystyrene of DAD site was prepared via living radical polymerization with Cl-DAD-Cl as an initiator, in conjunction with Ru(Cp*)Cl(PPh₃)₂ (RuCp*: catalyst) and *n*-BuNH₂ (cocatalyst)⁹. The polymerization was quenched at earlier polymerization stage (conversion = 22% in 3 h) to ensure quantitative Cl-functionalization at both terminals. The obtained polymer was well controlled to give narrow molecular weight distribution ($M_w/M_n \sim 1.1$; Figure 1A). For screening of condition, the obtained polymer was directly employed for the coupling reaction without isolation: the quenched polymerization solution was evaporated to remove remained St, amine cocatalyst, and solvent without exposure to oxygen, followed by direct injection of compounds for the coupling. Note that the ruthenium catalyst remained in vessel through the procedure as well as obtained polystyrene.

First, phosphine ligand [PPh₃ or P(*n*-Bu)₃] and amine (*n*-BuNH₂) were added along with solvent (toluene) into the polymer solution upon heating (100 °C, 72 hours). Ligand exchange with the added phosphine or amine may be expected to enhance the catalytic activity as well as reduction of trivalent ruthenium (Ru^{III}).¹⁰ In SEC analyses of the obtained polymers under these conditions (Figure 1B and C), higher molecular weight peak likely from coupled polymer was observed, but the peak was very small.

However, co-injection of ethanol (EtOH) was found to promote the coupling reaction: the ratio of higher molecular weight peak was clearly increased (Figure 1D). It was reported that dichloride ruthenium (II) phosphine complex [Ru(Cp*)Cl(PPh₃)₂] is prepared through reduction of [Ru(Cp*)Cl₂(PPh₃)] with PPh₃ in EtOH. Therefore, accumulated Ru(III) species that are generated via coupling would be reduced to Ru(II) with phosphine and EtOH to activate C–Cl bond.¹¹ Furthermore, replacement of amine cocatalyst with diamine [NH₂-(CH₂)₆-NH₂: 1,6-DAH] that was known to significantly enhance catalytic activity of

RuCp* (Figure 1E)¹² and further addition RuCp* (Figure 1F) allowed more effective coupling reactions: higher molecular weight polymers were generated. The detailed data in the screening experiments were summarized in Table 1.

The radical coupling reaction with injection of RuCp*, P(*n*-Bu)₃, 1,6-DAH, and EtOH was traced with purified DAD-functionalized oligostyrene ($M_{n, SEC} = 1450$, $M_w/M_n = 1.05$). Molecular weight was gradually increased over time, and the change was saturated around 24 hours. Thus, the coupling reaction was almost quenched in 24 hours.

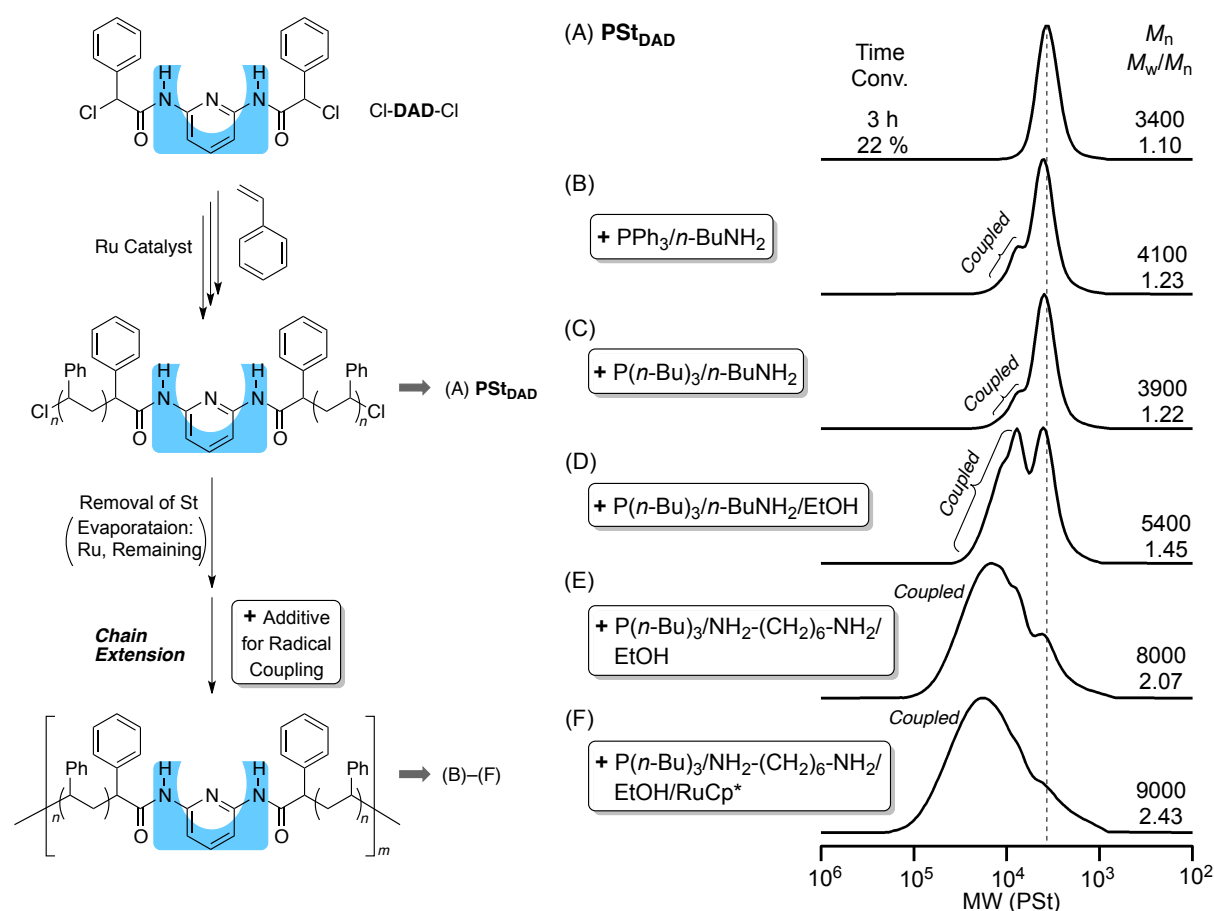


Figure 1. Screening of conditions for radical coupling reaction of bi-headed polystyrene carrying DAD (PSt_{DAD}). See Table 1 for details of the conditions. Living radical polymerization of styrene for PS_{DAD}: [St]₀ = 4.0 M; [Cl-DAD-Cl]₀ = 40 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ = 4.0 mM; [*n*-BuNH₂]₀ = 40 mM in toluene at 100 °C.

Table 1. Results of Chain Extension Reaction with Various Conditions

Entry	Coupling Condition						
	[MI] ^a (mM)	[Ru] _{add} (mM)	R-NH ₂	[R-NH ₂] _{add} (mM)	PR ₃	[PR ₃] _{add} (mM)	EtOH (v/v %)
1	40	0	<i>n</i> -BuNH ₂	40	PPh ₃	40	0
2	40	0	<i>n</i> -BuNH ₂	40	P(<i>n</i> -Bu) ₃	40	0
3	40	0	<i>n</i> -BuNH ₂	40	P(<i>n</i> -Bu) ₃	40	25
4	40	0	1,6-DAH	40	P(<i>n</i> -Bu) ₃	40	25
5	40	8	1,6-DAH	40	P(<i>n</i> -Bu) ₃	40	25

^a[St]₀ = 4.0 M; [Cl-DAD-Cl]₀ = 40 mM; [Ru(Cp*)Cl(PPh₃)₂]₀ = 4.0 mM; [*n*-BuNH₂]₀ = 40 mM in toluene at 100 °C for 3 h. Remained St, amine cocatalyst, and solvent was removed by evaporation for overnight.

2. Periodic Introduction of DAD Sites into Polystyrene

To introduce DAD units with regular interval into polymer chain by radical coupling polymerization, well-defined center functional precursor with narrow MWD is necessary. The narrowly controlled precursor will be promising regular interval in chain extended polymer between DAD units and specially, the polymer chain of obtained product from center functional oligo(St) with good terminal functionalities almostly akin to normal poly(St). Therefore, styrene was first oligomerized with Cl-DAD-Cl as an initiator via Ru-catalyzed living radical polymerization, in conjunction with RuCp* and *n*-BuNH₂ cocatalyst in toluene and it was quenched at lower conversion (6 %) to make sure quantitative terminal group (Cl). The obtained oligo PSt_{DAD} was purified with preparative SEC in CHCl₃ to prepare precisely controlled oligomer with narrow MWD (PSt_{DAD}2k-1; $M_{n, SEC} = 1580$, $M_w/M_n = 1.05$; Figure 4A).

In my previous paper, the author already discussed about low functionality of DAD based oligomer that might be caused by an inexactness of the SEC analysis. For such a low molecular weight oligomer carrying a DAD unit at the middle point, a calibration curve with PSt standard might not be applicable. Nevertheless, the functionality of DAD and

end-groups of oligomer (Cl-ends) were further studied by ^1H NMR spectra (Figure 2A). The $\text{PSt}_{\text{DAD}2\text{k}-1}$ precursor exhibited the characteristic peak of a pyridine (*a*, 3H). Peak integration led to $M_{\text{n,NMR}} = 1420$ and the number-average functionality of DAD [$F_{\text{n,DAD}} = M_{\text{n,NMR}}/M_{\text{n,SEC}}$] was estimated to be 0.89, indicating near quantitative introduction of the central unit. Similarly, for end-groups, a peak '*e*' derived from the methylene neighboring to end Cl of $\text{PSt}_{\text{DAD}2\text{k}}$ was detected around 4.3 ppm, to give $M_{\text{n,NMR}} = 1430$ and in turn $F_{\text{n,Cl}} = 0.90$. These results obviously indicate that $\text{PSt}_{\text{DAD}2\text{k}}$ quantitatively embed the DAD unit at the center position and Cl at the both ends.

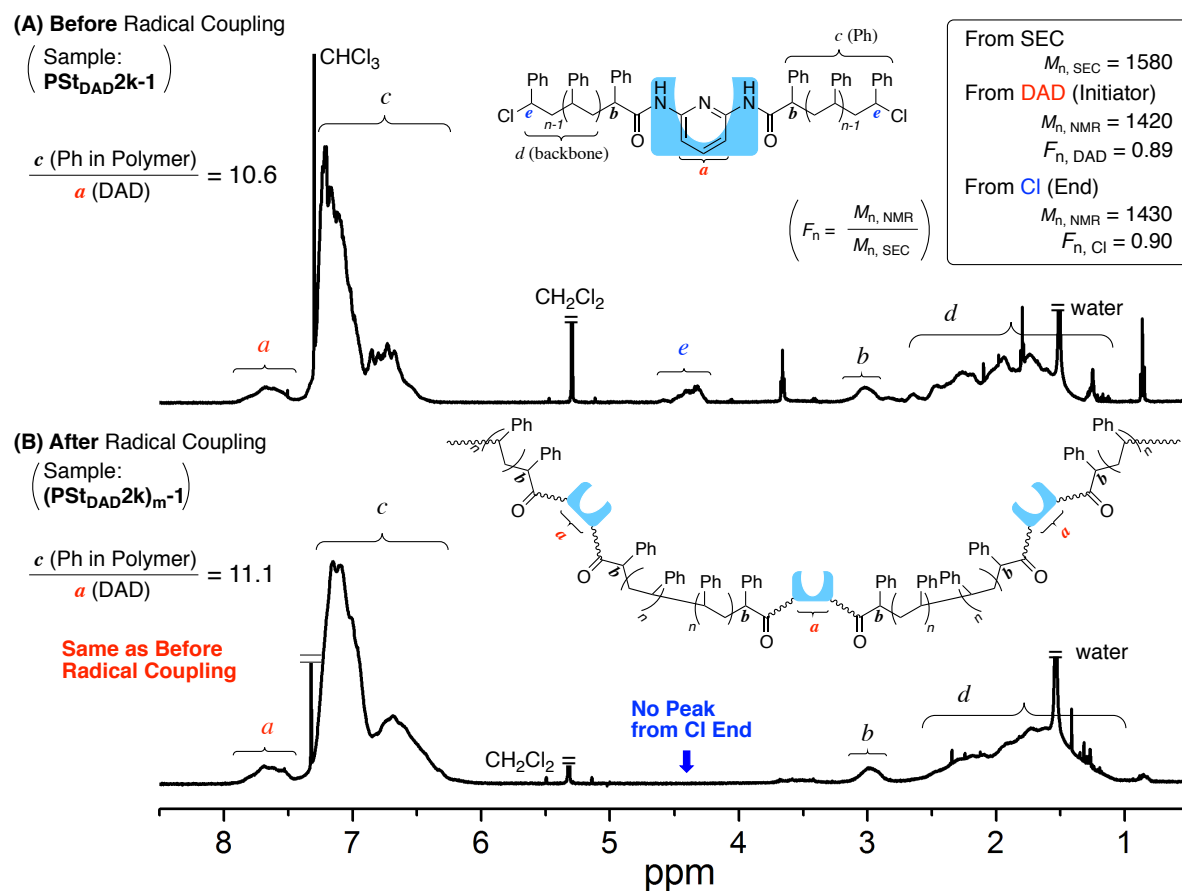


Figure 2. Structure analysis of (A) $\text{PSt}_{\text{DAD}2\text{k}-1}$ as precursor and (B) chain extended $(\text{PSt}_{\text{DAD}2\text{k}})_m-1$ by ^1H NMR spectra (CD_2Cl_2 , room temperature).

Moreover, the structure of obtained $\text{PSt}_{\text{DAD}2\text{k}}$ was further analyzed by MALDI-TOF-MS to support less functionality of halogen-ends ($F_{\text{n,Cl}}$) in the oligomer chain (Figure 3). For example, the major series was observed, which consist of regularly spaced peaks with styrene mass interval (104.12) and each peaks matched to linear oligomer with both Cl terminal ($\text{PSt}_{\text{DAD}2\text{k}} + \text{H}^+$). The minor series was also observed, which indicated

linear $\text{PSt}_{\text{DAD}2\text{k}}$ with Cl ends containing Na^+ [$\text{PSt}_{\text{DAD}2\text{k}} + \text{Na}^+$], respectively. This data certainly supported that the $\text{PSt}_{\text{DAD}2\text{k}}$ almost quantitative carry the chlorines at the terminal groups.

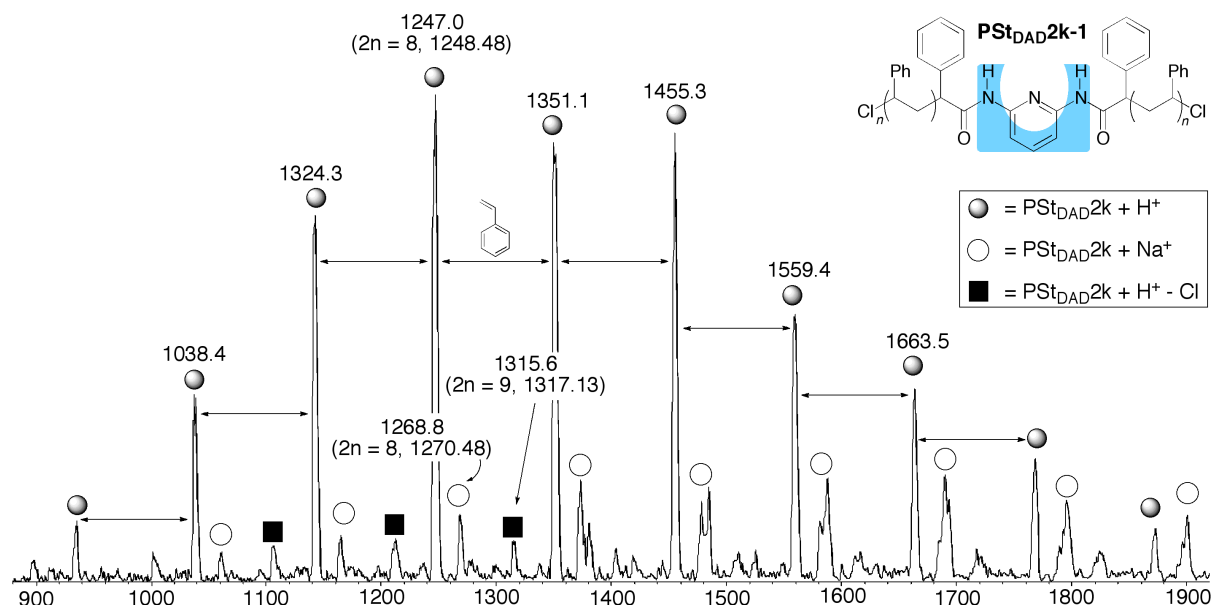


Figure 3. MALDI-TOF-MS analysis of $\text{PSt}_{\text{DAD}2\text{k}-1}$ precursor.

Chain extension of obtained well-defined precursor with narrow MWD via radical coupling polymerization was performed under designed RuCp^* catalyst system with $\text{NH}_2-(\text{CH}_2)_6-\text{NH}_2$ cocatalyst, in conjunction with $\text{P}(n\text{-Bu})_3$ in toluene/EtOH (25 v/v % EtOH) for 48 h and the final product was also purified with preparative SEC in CHCl_3 to remove low molecular weight oligomer and Ru catalyst ($M_{n,\text{SEC}} = 8380$, $M_w/M_n = 1.48$). The SEC curves of obtained product was clearly shifted to higher molecular weight with broad MWD indicating coupling condensation polymerization certainly occurred between precursors and poly(St) periodically carrying DAD units was successfully synthesized (Figure 4B, $(\text{PSt}_{\text{DAD}2\text{k}})_m-1$).

In order to confirm the structural change of obtained $(\text{PSt}_{\text{DAD}2\text{k}})_m-1$ after polycondensation reaction, ^1H NMR analysis was employed and ^1H NMR spectrum of product showed quite similar with the precursor ($\text{PSt}_{\text{DAD}2\text{k}-1}$) excepting the methylene peaks around 4.4 ppm from neighboring to terminal Cls on the precursor chain (Figure 2B). Here, the most important point is no structural change of the product after reaction that was provided from the comparison of integration ratios between obtained products before/after reaction. The peak integration ratio of chain extended poly(St) between poly(St) main peak

(*c*, 5H) and pyridine group (*a*, 3H) from DAD unit was shown as 11.1 which was closely similar with ratio of integration from precursor (10.6) indicating that designed poly(St) periodically carrying DAD units was successfully polymerized and spacer length between DAD units in polymer chain is apparently same with its precursor (regular intervals), respectively (Figure 2). In addition, the number average of DAD units in chain extended polymer chain was estimated as around 6 DAD units with regular intervals from molecular weight at the peak tops of each SEC curve (M_p of $(PSt_{DAD2k})_m$ / M_p of PSt_{DAD2k}).

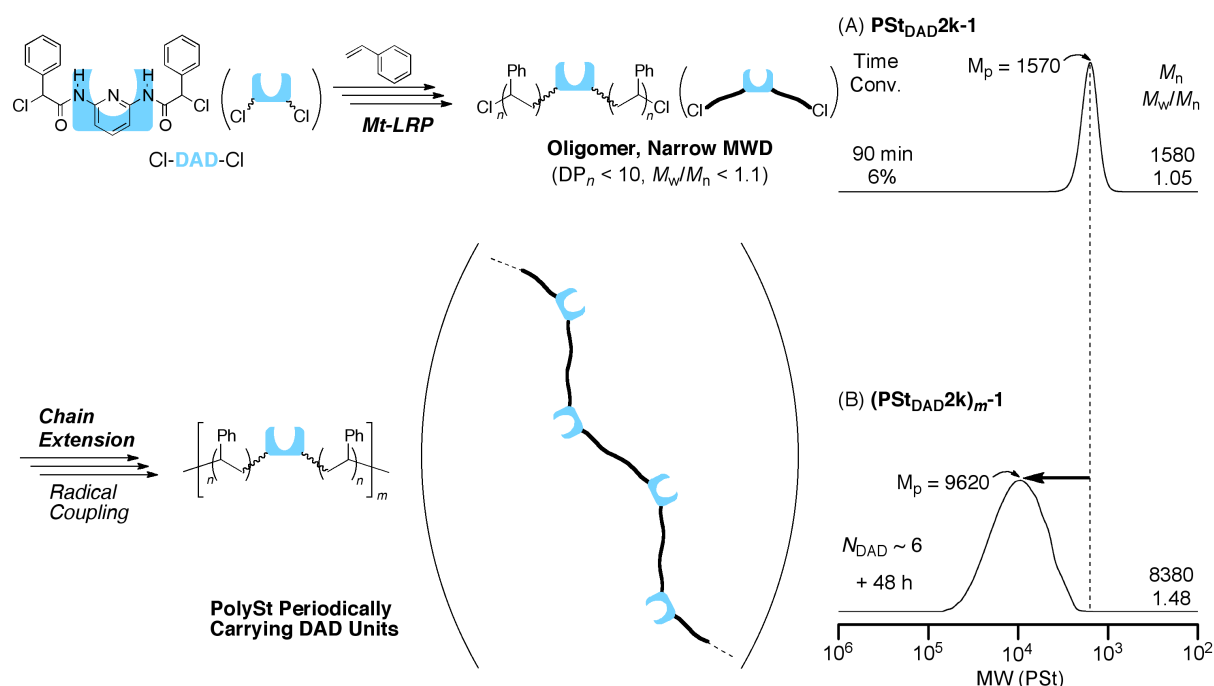


Figure 4. SEC curve of precursor ($PSt_{DAD2k-1}$) as macroinitiator (A) and chain extended poly(St) ($(PSt_{DAD2k})_m-1$) (B): Living radical polymerization for PS_{DAD} : $[St]_0 = 4.0$ M; $[Cl-DAD-Cl]_0 = 40$ mM; $[Ru(Cp^*)Cl(PPh_3)_2]_0 = 4.0$ mM; $[n-BuNH_2]_0 = 40$ mM in toluene at 100 °C; Chain extension reaction: $[(PSt_{DAD2k})_m] = 40$ mM, $[Ru(Cp^*)Cl(PPh_3)_2]_0 = 12.0$ mM, $[NH_2-(CH_2)_6-NH_2]_0 = 40$ mM, $[P(n-Bu)_3]_0 = 40$ mM in toluene/EtOH = 3/1 v/v % at 100 °C.

3. Influence of Periodic Positions in Polymer Chain

The center functional precursor and chain extended poly(St) from the well-defined precursor with narrow MWD are very similar with normal poly(St), thus their solid state properties were studied to confirm the influences of hydrogen bonding positions at the center or periodic positions in polymer chain by differential scanning calorimetry (DSC) (Figure 5; All samples measured on second heating at 10 °C/min). The center functional precursor

(PSt_{DAD}2k-2; $M_{n, \text{NMR}} = 1490$, $M_w/M_n = 1.07$) showed glass transition temperatures (T_g) near 88 °C and this value was much higher than normal poly(St) (n -PSt1k; $T_g \sim 18$ °C) with similar molecular weight due to rigid group (-DAD- unit) at the center position of the polymer chain (Figure 5A and 5B) and intermolecular hydrogen bonding interaction. Similarly, as an expect, the higher T_g of chain extended poly(St) ((PSt_{DAD}2k)_m-2; $M_{n, \text{SEC}} = 5540$, $M_w/M_n = 1.57$, $N_{\text{DAD}} \sim 5$) was observed around 134 °C compared with other normal polystyrenes ($T_g \sim 97$ °C and 102 °C), indicating that rigid group still influence to thermoproperties at periodic positions in polymer chain.

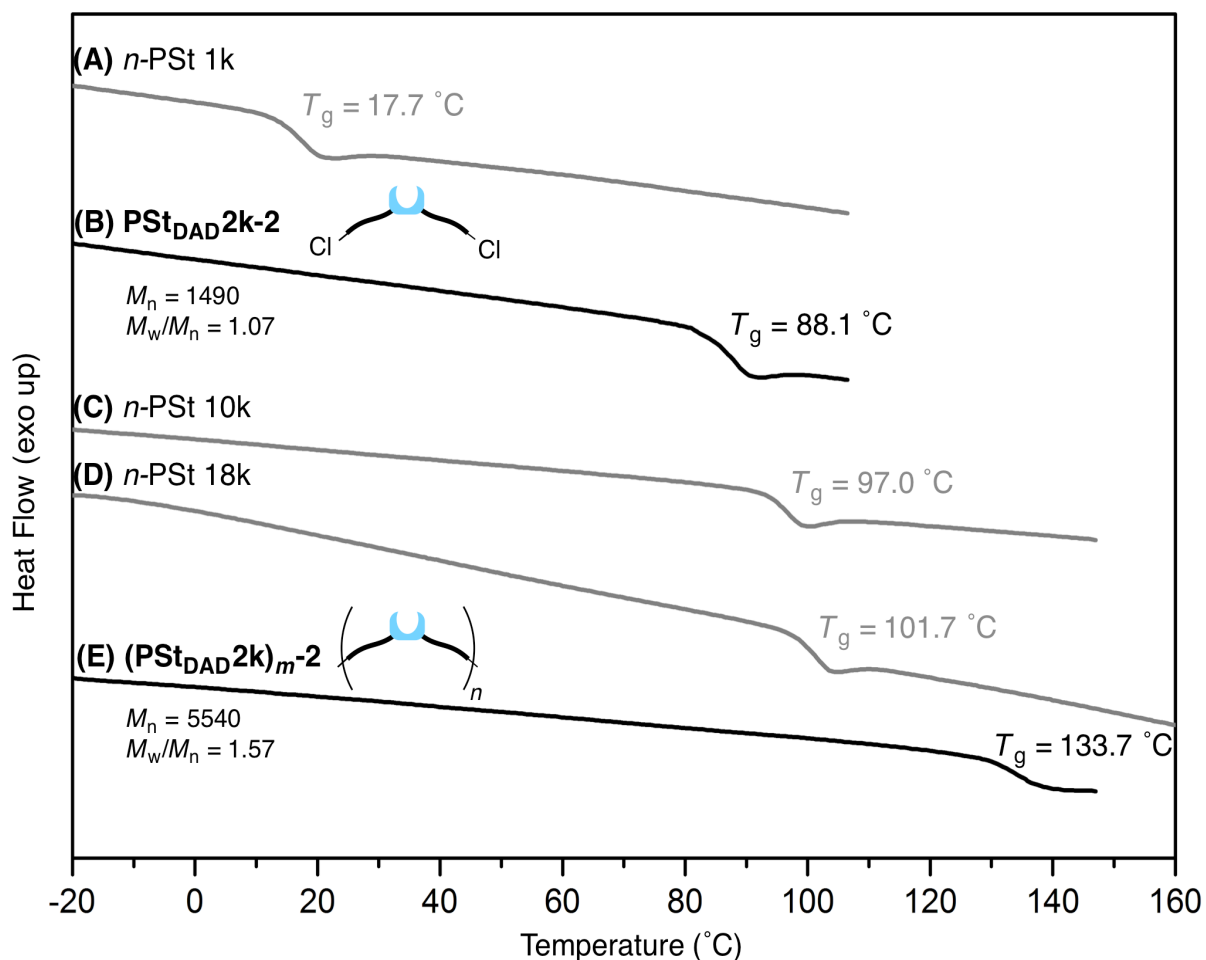


Figure 5. DSC traces (second run) of PSt_{DAD}2k-2 as precursor and chain extended (PSt_{DAD}2k)_m-2 compared with normal Poly(St)s.

The precursor (PSt_{DAD}2k-2; $M_{n, \text{NMR}} = 1050$, $M_w/M_n = 1.07$) and chain extended poly(St) ((PSt_{DAD}2k)_m-2; $M_{n, \text{SEC}} = 8690$, $M_w/M_n = 1.57$, $N_{\text{DAD}} \sim 5$) were employed to confirm the effect of precisely controlled positions of -DAD- units on (PSt_{DAD}2k)_m-2 chain with

PMMA_{ADA} ($M_{n,NMR} = 4090$, $M_w/M_n = 1.14$). For the chain extended poly(St), the interactive sites (-DAD- units) are densely located onto polymer chain with short distance, thus the ability of complementary hydrogen bonding with PMMA_{ADA} might be expected not only negative effect from steric hindrance between different polymer chains but also positive effect from spitting distance of DAD units to easily interact each other. Therefore, the precursor (PSt_{DAD2k-2}) and PMMA_{ADA} combination at varying molar ratios (0.5 to 12) was first

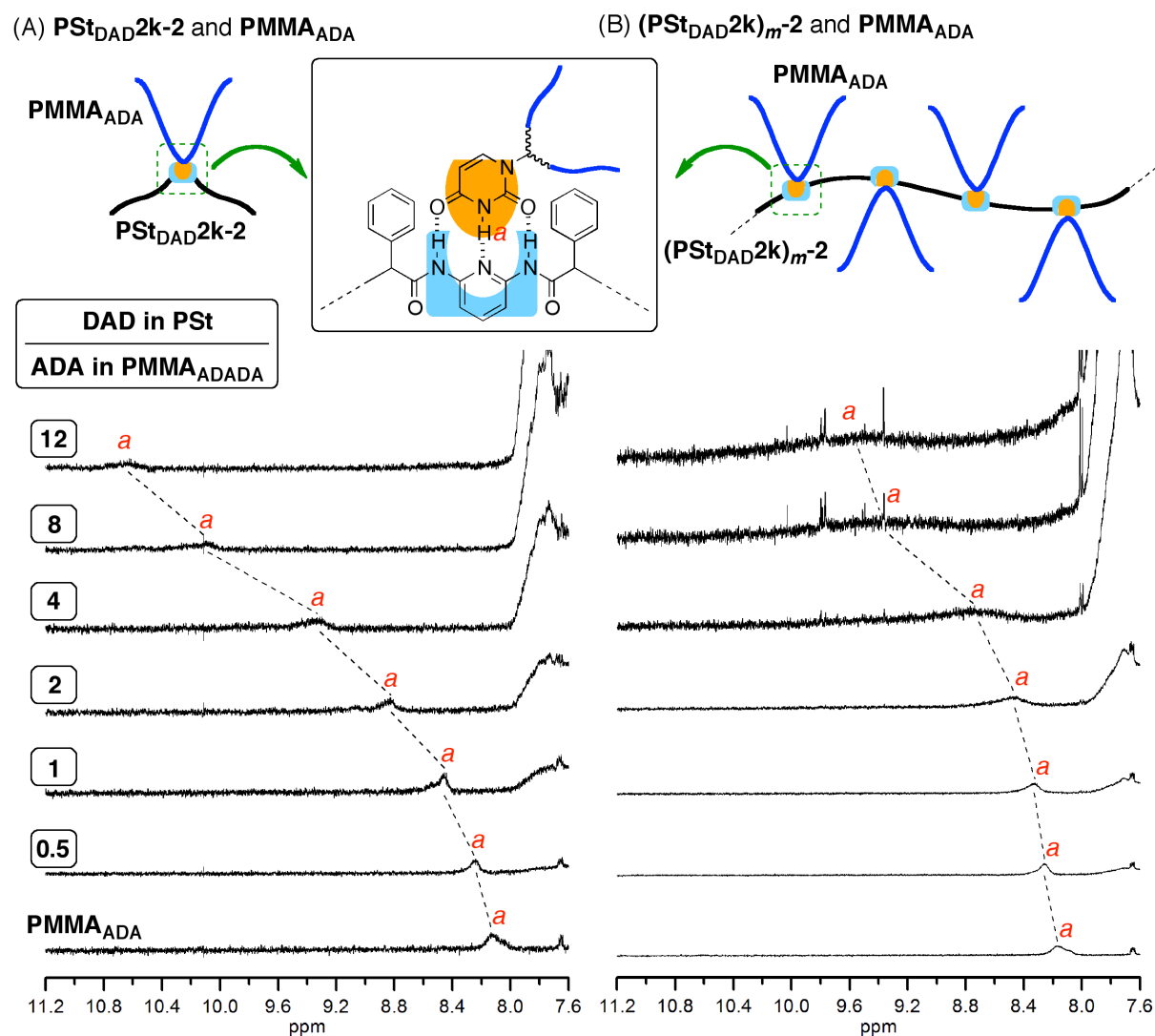


Figure 6. ^1H NMR spectra (CDCl_3 , room temperature) from 7.6 to 11.2 ppm of for calculation of K_a between DAD- and ADA-functionalized polymers, (A) precursor (PSt_{DAD2k-2}) and PMMA_{ADA} and (B) chain extended poly(St) ((PSt_{DAD2k})_{m-2}) and PMMA_{ADA}: PMMA_{ADA} (bottom) and the mixtures with DAD-counterpart of various ratios ($[\text{DAD-polymer}]/[\text{ADA-polymer}] = 0.5, 1, 2, 4, 8$, and 12); $[\text{ADA-polymer}] = 2.0 \text{ mM}$ (constant), $[\text{DAD-polymer}] = 0, 1, 4, 8, 16$, and 24 mM .

analyzed by ^1H NMR in CDCl_3 to determine binding constant between polymers.¹³ For a pairs of polymers, center-functional precursor/ PMMA_{ADA} (Figure 6A), the NH signals from ADA unit gradually and consistently shifted to downfield from 8.10 ppm to 10.6 ppm as the relative amount of the ADA unit increased, giving $K_a = 65.0 \text{ M}^{-1}$, respectively (table 2). With this controlled experiment, the polymer pair of chain extended poly(St)/ PMMA_{ADA} was also studied (Figure 6B). As a respect, the NH signals from ADA unit was shifted to downfield from 8.17 ppm to 9.47 ppm as increasing the molar ratio of DAD units and shown similar binding ability with precursor/ PMMA_{ADA} ($K_a = 61.6 \text{ M}^{-1}$, table 2). These phenomenon would come from offsetting between negative effect and positive effect for hydrogen bonding interaction in chain extended poly(St) chains. Moreover, these NH signals from pair of chain extended poly(St)/ PMMA_{ADA} are getting broader that are estimated due to the location of PMMA_{ADA} that stand closely together with $(\text{PSt}_{\text{DAD}2\text{k}})_m\text{-2}$ (Figure 6B).

Further research is now being conducted for efficient interactions of precisely controlled position of interactive sites with regular interval using different polymer pairs to increase association ability between hetero-polymer combinations. However, it is certain that complementary hydrogen-bonding interactions work well at the well-defined position.

Table 2. Parameters for K_a Calculation in This Work

Combination	[ADA] and [DAD]	δ_{mix} / ppm	δ_{ADA} / ppm	δ_{∞} / ppm
$\text{PSt}_{\text{DAD}2\text{k}-2}$ and PMMA_{ADA} ^a	$2.0 \times 10^{-3} \text{ mol/L}$	8.45	8.10	11.47 ^b
$(\text{PSt}_{\text{DAD}2\text{k}})_m\text{-2}$ and PMMA_{ADA} ^a	$2.0 \times 10^{-3} \text{ mol/L}$	8.36	8.17	10.10 ^b

^asee Figure 1 and Figure 6 for the interaction analyses by ^1H NMR ; ^bCalculated from curve fitting with third degree polynomial for plots with various mixing ratios.

Conclusion

A chain extended poly(St) ($(\text{PSt}_{\text{DAD}})_m$), carrying periodically introduced DAD units on the polymer chain, was designed from center-functional well-defined PSt_{DAD} with narrow MWD as a precursor. The author has demonstrated the ruthenium-catalyzed coupling condensation polymerization for chain extension of precisely controlled oligomer, which almost quantitatively carried DAD at the center of the backbone. Among the best

combination is the RuCp* coupled with P(*n*-Bu)₃, EtOH, and 1,6-DAH; particularly, EtOH and 1,6-DAH clearly increase the reactivity of catalyst and provide much higher efficiency by involving to reduction of Ru^{III}. To summarize, RuCp* in conjunction with P(*n*-Bu)₃, EtOH, and 1,6-DAH contribute to not only growing radical species from oligomer ends but also the regeneration of accumulated Ru^{III} effectively, although they are not perfect as the evidence yet. ¹H NMR analyses revealed that the pair of polymers with periodic DAD units and ADA unit interacted with each other in CDCl₃ without doubt, and the association constants were determined between hetero-polymer pair (PMMA_{ADA}/(PSt_{DAD})_m). The author is now studying advanced interaction behaviors between polymers in terms of supramolecular self-assembly by hydrogen bond and periodic introduction of interaction sites with different polymers.

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- (13) (a) Fielding, L. *Tetrahedron* **2000**, *56*, 6151-6170. (b) Thordarson, P. *Chem. Soc. Rev.* **2011**, *40*, 1305-1323. (c) Mathematical model chosen to determine K_a : The data were fitted to the following equation to provide K_a :

$$\delta_{mix} = \delta_{ADA} + \frac{(\delta_{\infty} - \delta_{ADA}) \left[\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right) - \sqrt{\left([ADA] + [DAD] + \frac{1}{K_{ass}} \right)^2 - 4[ADA][DAD]} \right]}{2[ADA]}$$

, where the experimental parameters are as follows,

[ADA] and [DAD]: molar concentrations of ADA- and DAD-functionalized compounds (i.e., initiators or polymers)

δ_{mix} : a chemical shift for NH proton of ADA-functionalized compound for an equimolar mixture with DAD counterpart in ^1H NMR spectrum (*a* in Figure 6);

δ_{ADA} : a chemical shift for NH proton of ADA-functionalized compound;

K_a : an association constant;

δ_{∞} : a saturated chemical shift for NH proton of ADA-functionalized compound when an excess molar of DAD counterpart was mixed. The value was calculated from curve fitting with third degree polynomial for plots with various mixing ratios.

PART II

Supramolecular Self-Assembly with Highly Associable 6-5 Points Hydrogen Bonds at the Programmed Position

Chapter 4

Functionalization at the Central Position of Vinyl Polymer Chains: Highly Associable Multipoint Hydrogen Bonds for Complementary Self-Assemblies

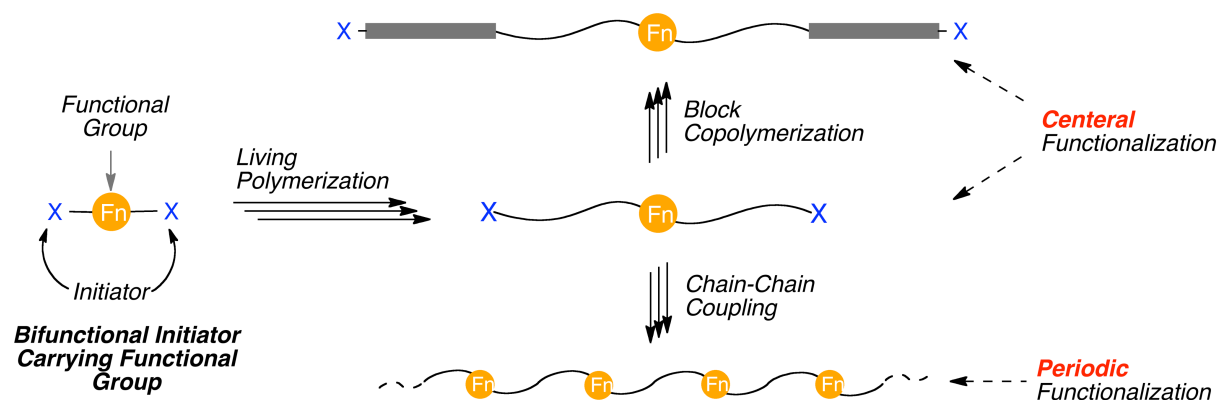
Abstract

This paper deals with the precision introduction of a multiple hydrogen-bonding site of a high association constant at the central position of a vinyl polymer chain for complementary self-assemblies. The interactive site consists of an array of hydrogen donors (D) and acceptors (A) to induce a multiple and highly associable interaction with a complementary counterpart. A bifunctional initiator (Cl–DADDAD–Cl) for metal-catalyzed living radical polymerization was thus designed and synthesized to embed a “Hamilton receptor” (DADDAD) between two terminal chlorides (Cl). In the presence of a ruthenium complex, the dichloride gave controlled polymers (Cl~~~DADDAD~~~Cl, ~~~: polymer backbone) of narrow molecular weight distributions ($M_w/M_n < 1.2$) from common monomers such as styrene and methyl methacrylate (MMA). The receptor-decorated polystyrene recognized complementary associable molecules and polymers carrying an ADADA unit (ADADA–Anthracene and ADADA–PMMA) to form self-assemblies where the association constant was as high as $K_{\text{ass}} \sim 8000 \text{ M}^{-1}$.

Introduction

Development of living polymerization has allowed precision control of molecular weight, end groups, and architectures of polymers.¹ Nowadays, interest in polymer science is directed to finer control beyond these, such as “position” and “sequence” of functionalities in polymer chains, to approach the structural precision and the intricate functions of biopolymers.²

In terms of the positional control in functionalities, the “center” should be targeted, because central functionalization in linear macromolecules may develop unique functions and properties relative to the terminally functionalized counterparts. One possible approach is, as recently reported by Lutz,³ to insert a non-homopolymerizable monomer preferring crossover propagation (e.g., maleimide derivatives) in living polymerization of styrene, though the backbone is currently limited to polystyrene. Another approach is to control living polymerization with a bifunctional initiator carrying a functional group (Scheme 1).⁴ This methodology could be more feasible and versatile, as is to be readily applicable to a variety of monomers and centrally functionalized block copolymers and also to be potentially extendable to “periodic” functionalization via the chain-chain coupling of center-functionalized telechelic polymers.

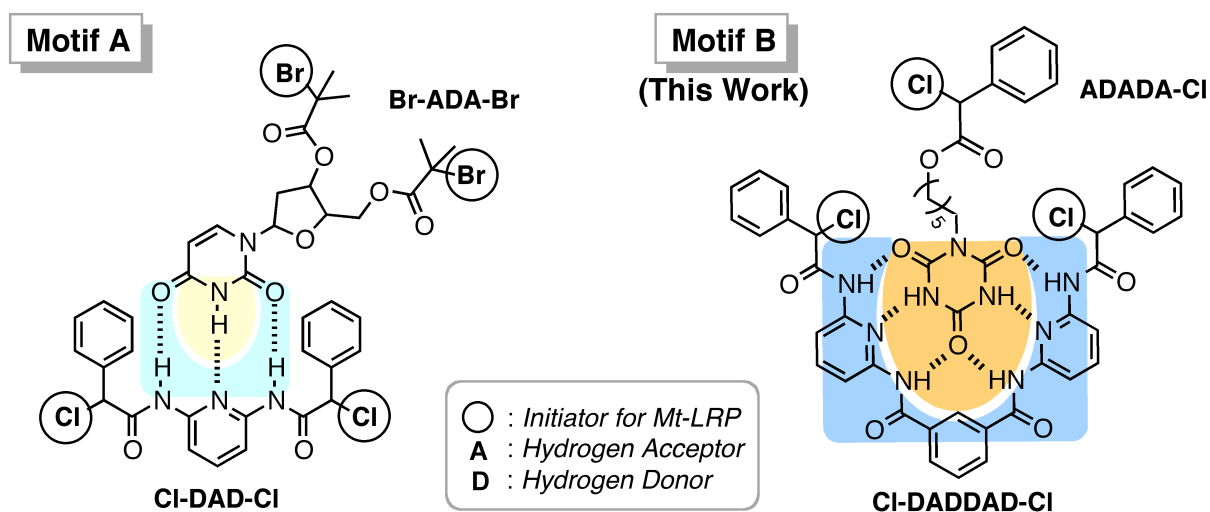


Scheme 1. Previous researches on interactions between polymers through introduction of dynamic interaction sites on the chains.

An interesting outcome of the central functionalization is to induce unprecedented microphase separation and self-assembly of block copolymers that carry complementarily interacting mid-chain central functionalities, particularly important in fabricating nano-scaled regular structures for advanced electronic materials.⁵ However, reported examples in this

line have been limited to selected polymers and, most seriously, the interactive sites therein are mostly placed randomly along the backbone. Precise introduction of interactive sites at specific positions would open the door to control block polymer self-assemblies in a more extensive and more unique fashion.

From these backgrounds, the author has focused on polymer-center positioning of “interactive sites” by the use of bi-headed functional initiating systems in metal-catalyzed living polymerization. In fact, the author has recently designed pairs of such bifunctional initiators that carry mutually complementary triple hydrogen-bonding sites [DAD and ADA: D = hydrogen donor; A = hydrogen acceptor; Scheme 2, Motif (A)].⁴ When mixed in non-polar solvents, the resultant pair of center-functionalized DAD- and ADA-homopolymers gave supramolecular X-shaped block copolymers. Combination of hydrophilic and hydrophobic polymer backbones, in turn, led to X-shaped amphiphilic block copolymers that formed unique and highly stable aggregates in aqueous solution.⁶ With association constant $K_{\text{ass}} \sim 10^2 \text{ M}^{-1}$, however, the three-point hydrogen-bonding interaction turned out not strong enough for stable self-assemblies under a wide range of conditions often required in materials applications.



Scheme 2. Designed initiators carrying complementary hydrogen bonding interaction sites for metal-catalyzed living radical polymerization [motif (A): 3-3 point interaction, motif (B): 6-5 point interaction].

This work is therefore set to introduce stronger and more directionally associable complementary hydrogen-bonding sites at the center of polymer chains. The author thus designed another motif of bifunctional initiator that embeds the so-called Hamilton receptor

[Scheme 2, Motif (B)].⁷ This recognition site consists of an array of six hydrogen-bonding points (DADDAD) complementary to the five-point array (ADADA) found in cyanuric acid, and their association constant ($K_{\text{ass}} \sim 10^4 \text{ M}^{-1}$) is much higher than with the three-point DAD-ADA motif previously examined by us.⁸

The author then examined metal-catalyzed living radical polymerization of these initiators and the central recognition of DADDAD-based polymer for ADADA-based molecule or polymer. The association power of the polymer was as high as that with the corresponding low molecular weight compound (i.e., the initiator), thereby strong enough for self-assemblies to be detected in SEC and NMR analyses. Similar reagents bearing complementary H-bonding sites have been reported for reversible addition fragmentation chain transfer (RAFT)⁹ and ring-opening metathesis polymerizations,¹⁰ and most of them aimed preparations of supramolecular block copolymers with the resultant chain-end associatable precursors; note that my interest is directed to functionalization at well-defined position (i.e., the chain center in this work), in addition to the formation of supramolecular complexes.

Experimental Section

Materials

Monomers (MMA and styrene: Aldrich; purity > 99 %) were dried overnight over calcium hydride and purified by distillation from calcium hydride before use. 2,6-Diaminopyridine (TCI; >98%), isophthaloyl dichloride (wako; >95%), 6-bromo-1-hexanol (Wako; >97%), cyanuric acid (TCI; >98%), 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, Wako; >97%), dicyclohexylcarbodiimide (DCC, Wako; >95%), 4-dimethylaminopyridine (Aldrich; 99%), triethylamine (Wako; 99%), thionyl chloride (Wako; >95%), 9-anthracenecarboxylic acid (TCI; >97%), $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (Cp^* : cyclopentadienyl, Aldrich), and α -chlorophenylacetylchloride (Aldrich; 90%) were used as received. Dichloromethane (Wako; dehydrated), dimethylformamide (Wako; dehydrated), and pyridine (Wako; dehydrated) were bubbled with dry argon for more than 15 min immediately before use. Toluene and THF (Kishida Kagaku; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use.

n-Monobutylamine (TCI; >98%) was degassed by reduced pressure before use. *n*-Octane and tetralin (internal standard for gas chromatography) were dried over calcium chloride and distilled from calcium hydride.

Synthesis of *N*-(6-aminopyridin-2-yl)-2-chloro-2-phenylacetamide (DADD–Cl, 1)

A mixture of 2,6-diaminopyridine (3.0 g, 27.5 mmol, 1.2 equiv), dehydrated THF (150 mL), and triethylamine (3.8 mL, 27.5 mmol, 1.2 equiv) were placed in an argon-filled 250-mL round-bottom flask. The solution was cooled to 0 °C, and *o*-chlorophenylacetyl chloride (3.6 mL, 22.9 mmol, 1.0 equiv) was slowly added under argon. The solution was then stirred for overnight at room temperature and filtered. The filtrated solution was evaporated to dryness, and the residue was dissolved in chloroform, followed by washing with NaHCO₃ saturated solution (100 mL; three times). The organic layer was dried over MgSO₄ for several hours, and the filtered solution was evaporated. Finally, the product was purified by silica-gel column chromatography (eluent: chloroform) and recrystallization with methylene chloride/hexane (DADD–Cl: 4.51 g, 75 % yield). ¹H NMR (DMSO-*d*₆, r.t.) δ (ppm): 10.40 (s, 1H), 7.56 (d, 2H), 7.38 (m, 4H), 7.15 (d, 1H), 6.19 (d, 1H), 5.91 (s, 1H), 5.86 (s, 2H).

Synthesis of *N*¹,*N*³-bis(6-(2-chloro-2-phenylacetamido)pyridin-2-yl)isophthalamide (Cl–DADDAD–Cl)

A mixture of DADD–Cl (**1**) (7.74 g, 29.6 mmol, 3.0 equiv), dehydrated THF (200 mL), and triethylamine (4.9 mL, 35.2 mmol, 3.6 equiv) were placed in an argon-filled 500-mL round-bottom flask. The solution was cooled to 0 °C, and the solution of isophthaloyl dichloride (2.0 g, 9.87 mmol, 1.0 equiv in 50 mL THF) was slowly added under argon atmosphere. The solution was allowed to reach room temperature and stirred for overnight. The reaction mixture was evaporated, dissolved with CH₂Cl₂, and washed with NaHCO₃ saturated solution (100 mL; three times). The organic layer was dried over MgSO₄ for several hours, and the filtered solution was evaporated, followed by silica gel chromatography with ethylacetate/hexane mixture eluent. Finally, the product was purified by recrystallization with dichloromethane and hexane mixture (Cl–DADDAD–Cl: 4.1 g, 63 % yield). ¹H NMR (CDCl₃, r.t.) δ (ppm): 8.78 (s, 2H), 8.56 (s, 2H), 8.49 (s, 1H), 8.18–8.05 (m, 4H), 7.91 (d, 2H), 7.76 (t, 2H), 7.64 (t, 1H), 7.56–7.31 (m, 10H), 5.53 (s, 2H).

Synthesis of 1-(6-hydroxyhexyl)-1,3,5-triazinane-2,4,6-trione (ADADA-OH, 2)¹¹

6-bromo-1-heanol (2.6 mL, 20 mmol, 1.0 equiv), cyanuric acid (13 g, 100 mmol, 5.0 equiv) and 100 mL of dry DMF were introduced in an argon-filled 150-mL round-bottom flask. 3.0 mL of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 20 mmol, 1.0 equiv) was added slowly under argon atmosphere and the reaction mixture was heated to 70 °C for 24 h. The mixture was evaporated to dryness, dissolved with MeOH, and filtered. The final product was purified by silica-gel column chromatography with CH₂Cl₂/CH₃OH (4/1) mixture eluent (ADADA-OH: 1.8 g, 39 % yield). ¹H NMR (DMSO-*d*₆, r.t.) δ (ppm): 11.20 (s, 2H), 4.33 (t, 1H), 3.61 (t, 2H), 3.36 (t, 2H), 1.71-1.18 (m, 8H).

Synthesis of 6-(2,4,6-trioxo-1,3,5-triazinan-1-yl)hexyl 2-chloro-2-phenylacetate (ADADA-Cl)

The mixture solution of DMAP (69.0 mg, 0.565 mmol, 0.13 equiv) and *o*-chlorophenylacetyl chloride (0.90 mL, 5.67 mmol, 1.3 equiv) in CH₂Cl₂ (10 mL) was added to ADADA-OH (3) (3.0 g, 13.1 mmol, 1.0 equiv) solution in dry DMF (15 mL). The mixture solution was cooled to 0 °C, and DCC (1.75 g, 8.50 mmol, 1.95 equiv) in CH₂Cl₂ (5 mL) was added slowly under argon atmosphere. The solution was allowed to reach room temperature and stirred for overnight. The mixture was filtered, evaporated to dryness, and purified by silica gel chromatography with CH₂Cl₂/CH₃OH (25/1) mixture eluent (ADADA-Cl: 0.48 g, 29 % yield). ¹H NMR (DMSO-*d*₆, r.t.) δ (ppm): 11.38 (s, 2H), 7.53-7.34 (m, 5H), 5.92 (s, 1H), 4.12 (m, 2H), 3.57 (t, 2H), 1.60-1.08 (m, 8H).

Synthesis of 6-bromohexylanthracene-9-carboxylate (Anthracene-Br, 3)¹²

Anthracene-9-carboxylic acid (1.11 g, 5 mmol), thionyl chloride (0.45 mL, 6.2 mmol), DMF (0.04 mL), and 10 mL of dry dichloromethane were introduced in an argon-filled 50-mL round-bottom flask. A mixture solution was stirred for 30 min at room temperature and then refluxed for another 4 h. The mixture was evaporated and obtained anthracene-9-carbonyl chloride was used without further purification. In another argon-filled 100-mL round-bottom flask, 6-bromo-1-heanol (6.54 mL, 50 mmol, 10 equiv) and 1 mL of dry pyridine were placed and anthracene-9-carbonyl chloride solution (dissolved in dry dichloromethane 30 mL) was added slowly under argon atmosphere. The solution was stirred for overnight at room temperature and then washed with brine solution for three

times. The organic layer was dried over MgSO_4 for several hours, and the filtered solution was evaporated. The product was purified by silica-gel column chromatography with dichloromethane as eluent and final product was obtained by silica gel chromatography with ethylacetate/hexane (1/9) mixture eluent (Anthracene-Br: 0.9 g, 47 % yield). ^1H NMR (CDCl_3 , r.t.) δ (ppm): 8.53 (s, 1H), 8.07-7.98 (m, 4H), 7.58-7.46 (m, 4H), 4.63 (t, 2H), 3.40 (m, 2H), 1.89-1.43 (m, 8H).

Synthesis of 6-(2,4,6-trioxo-1,3,5-triazinan-1-yl)hexylanthracene-9-carboxylate (ADADA-Ant)

Anthracene-Br (0.883 g, 2.29 mmol, 1.0 equiv), cyanuric acid (2.96 g, 22.9 mmol, 10.0 equiv) and 22 mL of dry DMF were introduced in an argon-filled 50-mL round-bottom flask. 0.69 mL of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 4.58 mmol, 2.0 equiv) was added slowly under argon atmosphere and the reaction mixture was heated to 70 °C for 24 h. The mixture was evaporated to dryness, dissolved with dichloromethane, and filtered. The product was purified by silica-gel column chromatography with $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (95/5) mixture eluent. Finally, the product was purified by precipitation in hexane (ADADA-Ant: 0.31 g, 35 % yield). ^1H NMR (CDCl_3 , r.t.) δ (ppm): 8.52 (s, 1H), 8.38 (s, 2H), 8.02 (m, 4H), 7.58-7.45 (m, 4H), 4.60 (t, 2H), 3.83 (t, 2H), 1.96-1.36 (m, 8H).

Polymerization Procedures

Polymerization was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. A typical procedure for styrene with Cl-DADDAD-Cl/ $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2/n\text{-BuNH}_2$ is given. In a round-bottom flask (50 mL) filled with argon was placed $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (9.6 mg, 0.012 mmol), toluene (0.05 mL), *n*-octane (0.37 mL), St (1.37 mL, 12.0 mmol), *n*-BuNH₂ solution (0.30 mL, 400 mM in toluene) and a solution of Cl-DADDAD-Cl (0.91 mL, 131.5 mM in THF) were sequentially added; the total volume was 3.00 mL. Immediately after mixing, aliquots (0.50–1.0 mL each) of the solution were injected into baked glass tubes, which were then sealed (except when a stopcock was used) and placed in an oil bath kept at 80 °C. In predominant intervals, the polymerization mixture was terminated by cooling to –78 °C in dry-ice-methanol. Monomer conversion was determined from residual monomer concentration measured by gas chromatography with *n*-octane (for MMA) or tetralin (for St) as an internal standard. The quenched solutions were evaporated to dryness to give the

products, which were subsequently dried overnight under vacuum at room temperature.

SEC Evaluations of Complementary Interaction

The five kinds of CHCl_3 solutions were prepared with **PSt-DADDAD-PSt** (M_n , $NMR(DADDAD) = 5760$), ADADA-bearing molecule (**ADADA-Ant** or **ADADA-PMMA_1** (M_n , $NMR(ADADA) = 5690$), and the complementary equimolar mixtures for SEC analyses with UV (for **ADADA-Ant**) and RI detector (for **ADADA-PMMA_1**). Here, the concentration of each component (polymer or molecule) was set to 1.74 mM, which was 10 mg/mL for **PSt-DADDAD-PSt**, for all the solutions. For the complementary equimolar mixtures, the couples were blended in CHCl_3 , followed by overnight stirring at room temperature. The solutions with normal polymers for controlled experiments were also similarly prepared. See below for the SEC analyses.

^1H NMR Evaluations of Complementary Interaction

Stock solutions with DADDAD or ADADA-based molecules (initiator or polymer) were prepared in CDCl_3 with 40 mM (DADDAD) or 10 mM (ADADA), and the concentrations were calibrated through integration ratios with a standard solution (1,3,5-trimethoxybenzene, 503.074 mM in CCl_4) in ^1H NMR spectrum. With the accurate concentration values, a series of mixtures were prepared with various ratios $[[DADDAD]/[ADADA] = 0.5, 1, 2, 4, 8, 12, \text{ and } 16 \text{ molar ratio; } [ADADA] \text{ is constant (2 mM)}]$, followed by overnight stirring at room temperature before ^1H NMR measurement. An association constant (K_{ass}) was calculated with the peak shift values (see below).

Measurement

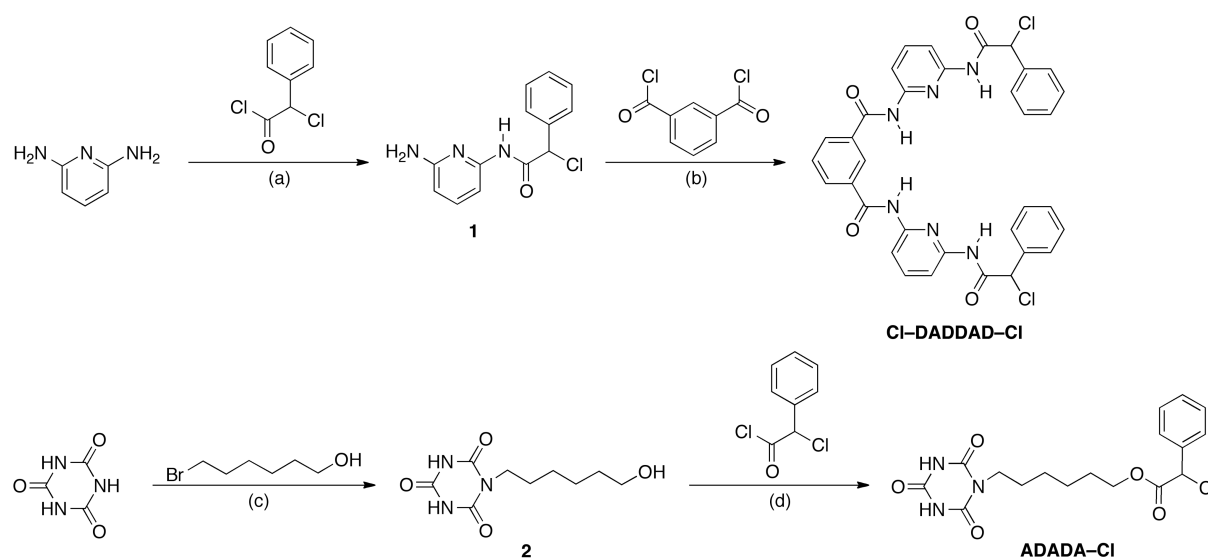
M_n and M_w/M_n of polymers were measured by size exclusion chromatography (SEC) in THF (at 40 °C) or CHCl_3 (at room temperature) as an eluent. For the THF-SEC, three polystyrene-gel columns [LF-404 (from Shodex); pore size, 3000 Å; 4.6 mm i.d. $\times$ 250 cm] were connected to a DU-H2000 pump, a 74S-RI refractive-index detector, and a 41-UV ultraviolet detector (all from Shodex) and flow rate was set to 0.3 mL/min. For the CHCl_3 -SEC, three polystyrene gel columns [K-805L (from Shodex); pore size 20–1000Å; 8.0 mm i.d. $\times$ 30 cm] were connected to a PU-980 pump and a 930-RI refractive-index detector, and a 970-UV ultraviolet detector set at 370 nm (all from Jasco) and flow rate was set to 1.0

mL/min. The columns were calibrated against 13 standard poly(MMA) (PMMA) samples (Polymer Laboratories; $M_n = 620\text{--}1,200,000$; $M_w/M_n = 1.06\text{--}1.22$) for obtained PMMA samples, and 13 standard polystyrene (PS) samples (Polymer Laboratories; $M_n = 500\text{--}3,840,000$; $M_w/M_n = 1.01\text{--}1.14$) for obtained PS samples, respectively. Polymer samples were purified by preparative SEC in CHCl_3 at room temperature on polystyrene gel preparative column [K-5002 (from Shodex); exclusion limit = 5×10^3 ; particle size = $15\text{ }\mu\text{m}$; $5.0\text{ cm i.d.} \times 30\text{ cm}$; flow rate = 10 mL/min] that were connected to a PU-2086 precision pump, a RI-2031 refractive-index detector, and UV-2075 ultraviolet detector (all from Jasco). ^1H NMR was recorded in CDCl_3 or $\text{DMSO-}d_6$ at room temperature on JEOL JNM-ECA500 spectrometer, operating at $500.16\text{ (}^1\text{H)}\text{ MHz}$. Ultraviolet–visible (UV/Vis) spectra were obtained from Shimadzu MultiSpec 1500 in H_2O at room temperature (optical path length = 1.0 cm).

Results and Discussion

1. Design of Hamilton Receptor-Based Bifunctional Initiator and Evaluation of Association Constant with the Complementary

As shown in Scheme 3, a Hamilton receptor-based bifunctional initiator (Cl-DADDAD-Cl) for metal-catalyzed living radical polymerization was prepared from 2,6-diaminopyridine, along with a complementary monofunctional initiator (ADADA-Cl) from cyanuric acid.



Scheme 3. Synthetic route to Cl-DADDAD-Cl and ADADA-Cl. Reagents and conditions: (a) Et₃N, THF, overnight, rt, (b) Et₃N, THF, overnight, rt, (c) DBU, DMF, 24 h, 70 °C, and (d) DMAP, DCC, DMF, CH₂Cl₂, overnight, rt.

The complementary interaction between Cl-DADDAD-Cl and ADADA-Cl initiators in CDCl₃ was examined by ¹H NMR spectroscopy, to determine the association constant (K_{ass}) (Figure 1): A series of mixtures at various mixing ratios were prepared ([Cl-DADDAD-Cl]/[ADADA-Cl] = 0.5, 1, 2, 4, 8, 12, and 16, see the Experimental Section), and the chemical shift of the NH proton in ADADA-Cl was examined. As the proportion of Cl-DADDAD-Cl was increased, the NH chemical shift dramatically shifted downfield: 13.05 ppm from 7.72 ppm for ADADA-Cl alone. From these changes, K_{ass} was estimated to be 7877.2 M⁻¹ (Table 1). As expected, the value was much higher than that ($K_{\text{ass}} = 83.3 \text{ M}^{-1}$) for my previous motif with the combination of DAD- and ADA-based initiators.

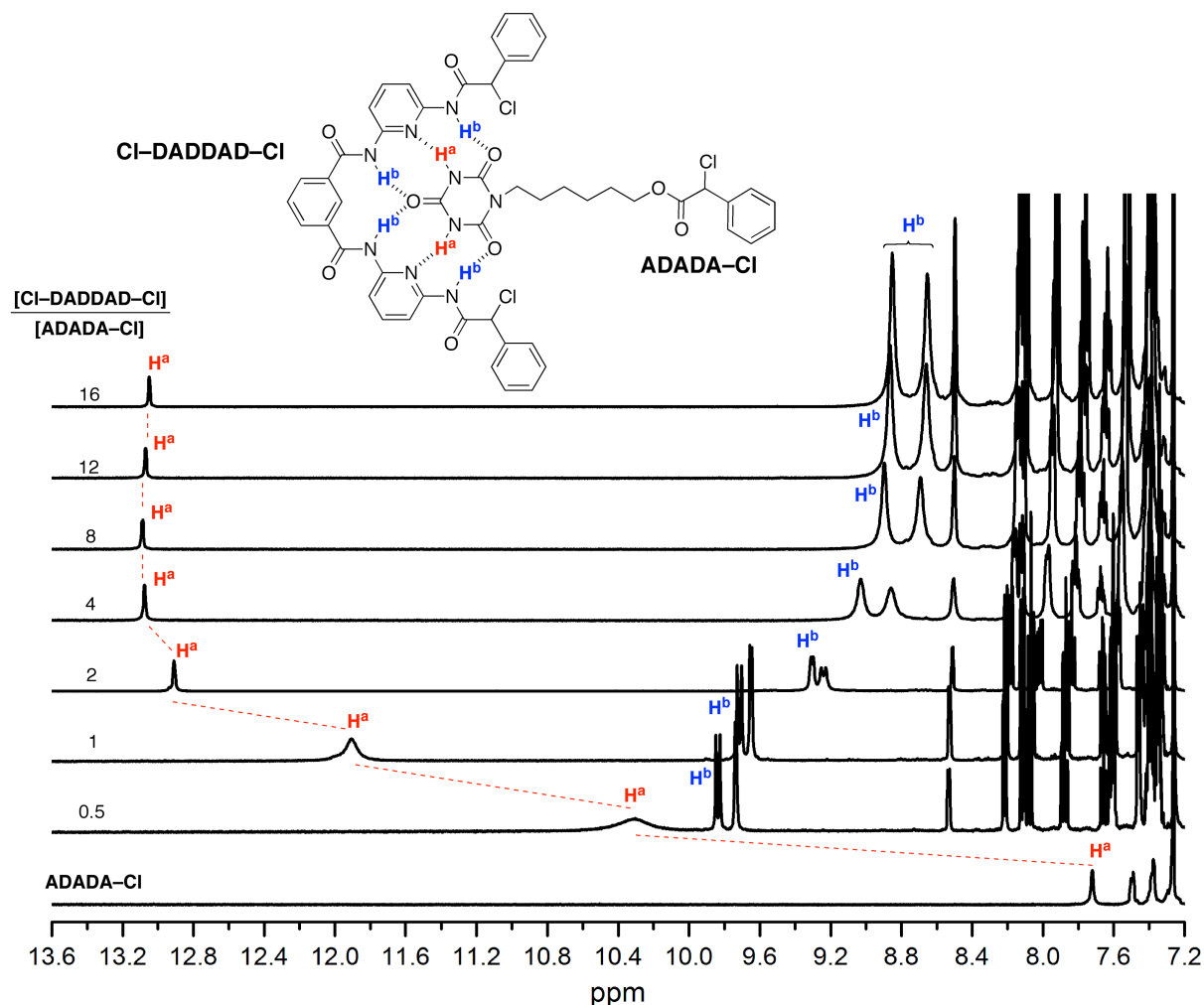


Figure 1. ^1H NMR spectra (CDCl_3 , room temperature) from 7.2 to 13.6 ppm of ADADA-Cl (bottom) and the mixtures with CI-DADDAD-Cl of various ratios ($[\text{CI-DADDAD-Cl}]/[\text{ADADA-Cl}] = 0.5, 1, 2, 4, 8, 12$, and 16) for calculation of K_{ass} : $[\text{ADADA-Cl}] = 2.0 \text{ mM}$ (constant); $[\text{CI-DADDAD-Cl}] = 0, 1, 2, 4, 8, 16, 24$, and 32 mM .

Table 1. Parameters for K_{ass} Calculation in This Work⁴

Combination	[ADADA] and [DADDAD]	δ_{mix} ppm	δ_{ADADA} ppm	δ_{∞} ppm
ADADA-Cl / CI-DADDAD-Cl ^a	$2.0 \times 10^{-3} \text{ mol/L}$	11.91	7.72	13.10^{b}
ADADA-PMMA / PSt-DADDAD-PSt ^a	$2.0 \times 10^{-3} \text{ mol/L}$	12.07	8.53	13.07^{b}

^asee Figure 1 for the interaction analyses by ^1H NMR ; ^bCalculated from curve fitting with third degree polynomial for plots with various mixing ratios.

2. Ru-Catalyzed Living Radical Polymerizations with Cl-DADDAD-Cl and ADADA-Cl

The designed initiators (Cl-DADDAD-Cl and ADADA-Cl) was combined with a ruthenium catalyst $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]$ in conjunction with an amine-based cocatalyst ($n\text{-BuNH}_2$) to polymerize common vinyl monomers [methyl methacrylate (MMA) and styrene (St)]. With Cl-DADDAD-Cl, for example, both monomers are smoothly consumed up to

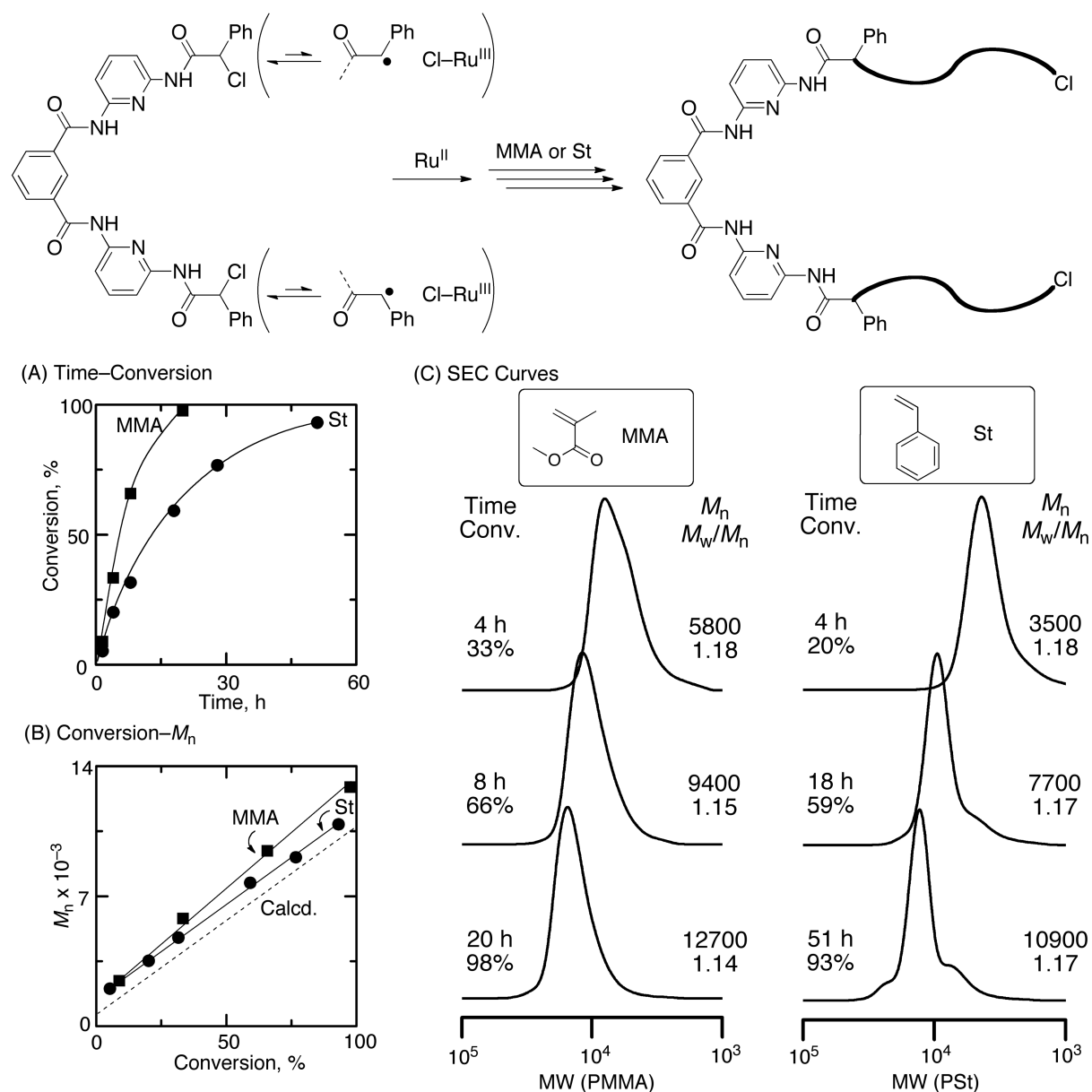


Figure 2. Time-conversion (A), conversion- M_n (B), and SEC curves (C) for polymerizations of MMA (■) and St (●) with Cl-DADDAD-Cl in conjunction with $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2/n\text{-BuNH}_2$ in toluene at 80 (MMA) or 100 °C (St): $[\text{Monomer}]_0 = 4000$ mM; $[\text{Cl-DADDAD-Cl}]_0 = 40$ mM; $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 4$ mM; $[n\text{-BuNH}_2]_0 = 40$ mM.

higher conversion [Figure 2 (A)]. The number-averaged molecular weights (M_n) increased in direct proportion to conversion [Figure 2 (B)], and the SEC curves of the obtained polymers shifted to higher molecular weight, while keeping narrow molecular weight distributions (MWDs). Unfortunately, an undesired small shoulder was observed for the poly(St) samples at higher conversion, but overall the two polymerizations were fairly controlled. Similarly, the polymerizations with ADADA-Cl were also controlled for both monomers (Figure 3).

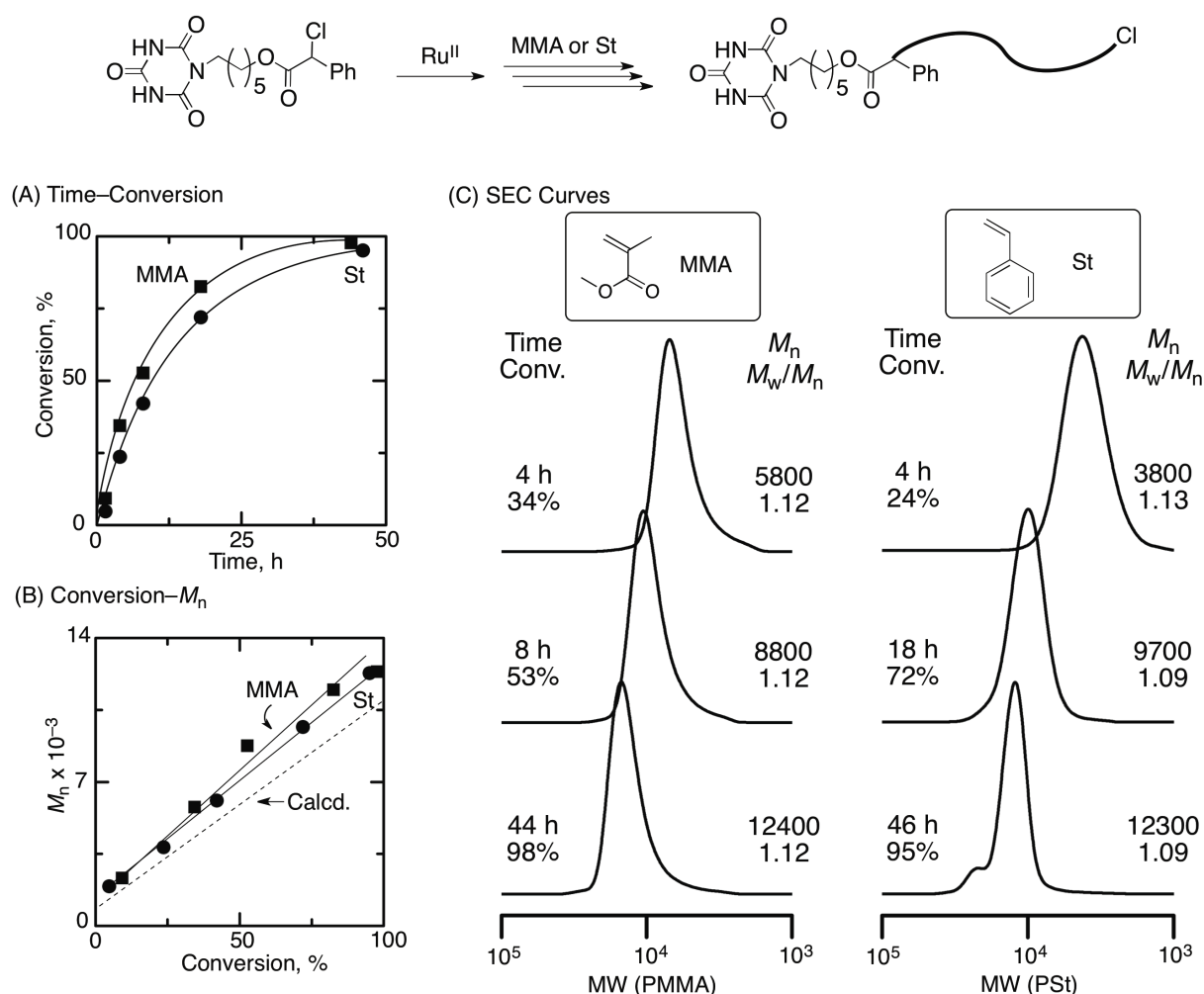


Figure 3. Time-conversion (A), conversion- M_n (B), and SEC curves (C) for polymerizations of MMA (■) and St (●) with ADADA-Cl in conjunction with $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2/n\text{-BuNH}_2$ in toluene at 80 (MMA) or 100 °C (St): $[\text{Monomer}]_0 = 4000$ mM; $[\text{ADADA-Cl}]_0 = 40$ mM; $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 4$ mM; $[n\text{-BuNH}_2]_0 = 40$ mM.

3. Structural Analysis of Poly(St) with Cl-DADDAD-Cl

Introduction of the Hamilton receptor in these polymers was analyzed by ^1H NMR spectroscopy. Figure 4 shows the ^1H NMR spectrum of poly(St) (PSt-DADDAD-PSt) obtained with Cl-DADDAD-Cl at 48 % conversion ($M_{n, \text{SEC}} = 8040$; $M_w/M_n = 1.09$; after removal of low molecular weight byproducts by fractional SEC). In addition to major peaks ($i-k$) from St repeating units, the spectrum showed minor peaks ($a-f$) from DADDAD in the initiator and the terminal methine peak (j') adjacent to Cl. The absence of peaks indicative of unreacted chlorides in Cl-DADDAD-Cl, namely, the methine peak between Cl and amide to appear at 5.5 ppm, indicate that living propagation indeed took place from both initiating sites.

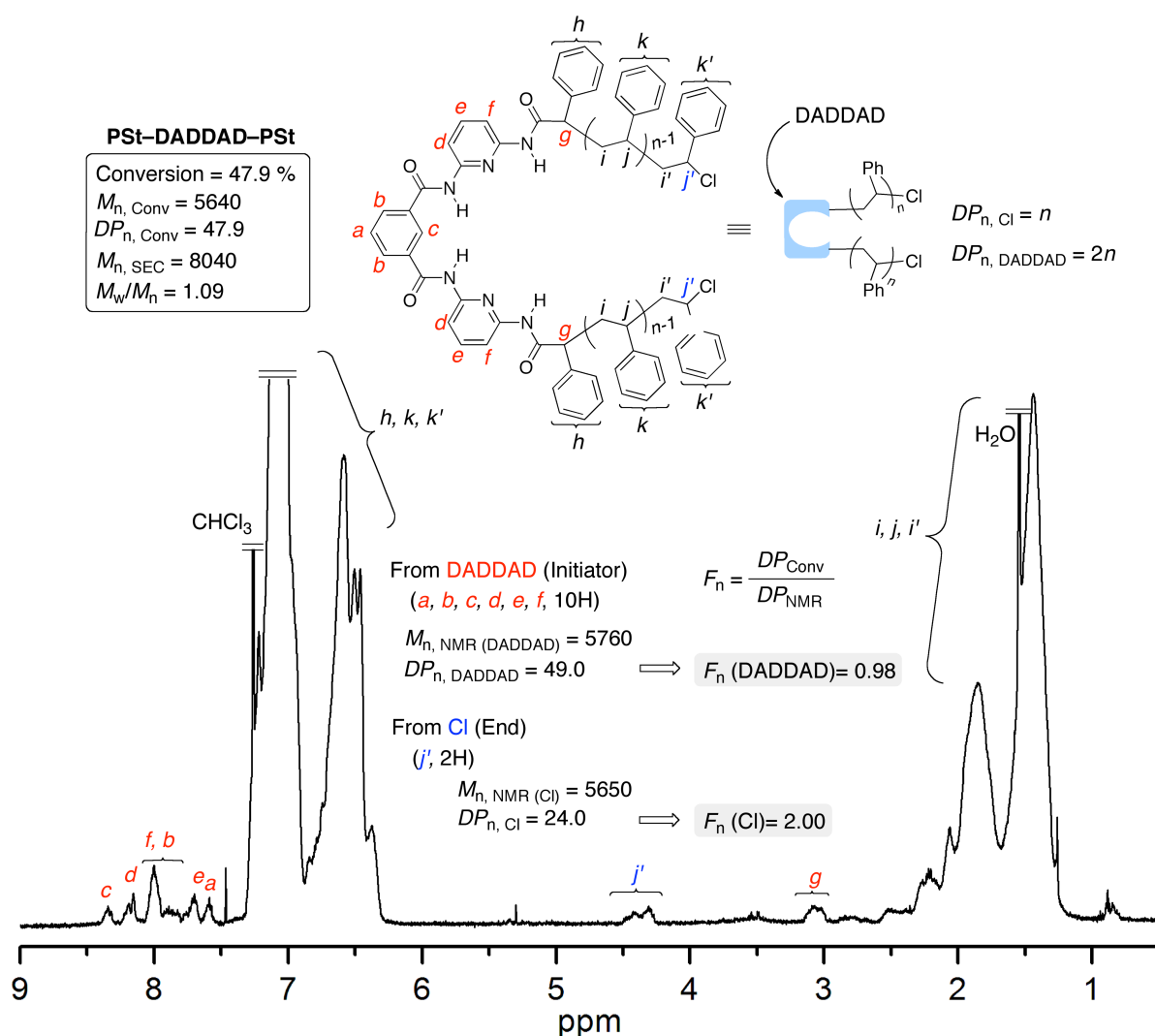


Figure 4. Structure analysis of PSt-DADDAD-PSt by ^1H NMR Spectra (CDCl_3 , room temperature).

Apparent M_n of the bi-headed polymers was thus estimated from the integration ratio of the DADDAD fragment and the Cl terminal to the backbone: $M_{n, \text{NMR (DADDAD)}} = 5760$; $M_{n, \text{NMR (Cl)}} = 5650$. These NMR-based values were close to M_n based on monomer conversion and monomer/initiator feed ratio ($M_{n, \text{conv}} = 5640$; $[M]_0/[I]_0 = 100$; conversion 47.9 %) but did differ from M_n by SEC ($M_{n, \text{SEC}} = 8040$; by polystyrene calibration). The difference ($M_{n, \text{SEC}} > M_{n, \text{conv}}$ or $M_{n, \text{NMR}}$) would be caused by difference in hydrodynamic volume between DADDAD-centered poly(St) and linear poly(St) standard samples.

From these data ($DP_{n, \text{Conv}}/DP_{n, \text{NMR}}$), the average numbers (functionalities) of –DADDAD– and –Cl units per chain were calculated, $F_n(\text{DADDAD}) = 0.98$ and $F_n(\text{Cl}) = 2.00$, respectively, and thus indicated that the hydrogen-bonding site was almost quantitatively introduced into the center of poly(St) backbone via a precisely controlled polymerization.

4. Molecular Recognition at the Chain Center of PSt–DADDAD–PSt

The multiple interactive site in PSt–DADDAD–PSt in fact specifically recognized organic compounds carrying an ADADA moiety, or a hydrogen bonding site complementary to DADDAD. For example, such an anthracene derivate (ADADA–Ant) was selectively captured by the polymer, as observed by SEC with UV detection at 370 nm (I_{max} for ADADA–Ant) as described below (Figure 5A); the anthracene alone gives a sharp SEC peak at $M_p = 700$ under these conditions.

Thus, under UV detection, an equimolar mixture of PSt–DADDAD–PSt ($M_p = 6800$; by SEC with refractive index detection) and ADADA–Ant in CHCl_3 gave a single SEC peak at $M_p = 3190$, in addition to a clearly weakened signal from free ADADA–Ant at $M_p = 700$. No such a peak was observed for free PSt–DADDAD–PSt, free ADADA–Ant, a non-functionalized PSt ($M_n = 5970$; $M_w/M_n = 1.02$; an SEC standard sample), nor its mixture with the anthracene, except for a very weak signal around $M_p = 6800$ found for the free PSt–DADDAD–PSt (the center unit appears weakly sensitive at 370 nm). All these observations demonstrate an efficient capture of ADADA–Ant by the complementary central unit in PSt–DADDAD–PSt. Note that such an interaction did not take place with standard PSt sample, excluding a possible π – π stacking interaction between the pendent aromatic rings in polystyrene and the anthracene's π –system or the ADADA unit.

5. Polymer Recognition of PSt–DADDAD–PSt at the Central Position

Next, my efforts were directed to the recognition of a polymer by the central unit in PSt–DADDAD–PSt. For this, complementary polymers (ADADA–PMMA) were prepared by the living polymerization of MMA with ADADA–Cl: ADADA–PMMA_1 ($M_{n, SEC} = 5480$; $M_{n, NMR} = 3610$; $M_w/M_n = 1.09$; Figure 5B) and ADADA–PMMA_2 ($M_{n, SEC} = 8800$; $M_{n, NMR} = 5690$; $M_w/M_n = 1.08$; $F_n(ADADA) = 1.14$). The anticipated polymer-polymer association via complementary DADDAD–ADADA interaction was analyzed in $CHCl_3$ by SEC now with an RI detector (Figure 5B).

For example, an equimolar mixture of PSt–DADDAD–PSt ($M_p = 6710$) and ADADA–PMMA_1 ($M_p = 5110$) led to a single unimodal peak at $M_{p, mix} = 7870$, which was clearly higher than those of the two component polymers. The result indicates that an apparent size of the PSt was uniformly increased in the presence of the partner polymer, most likely via their complementary hydrogen-bonding interaction. However, the observed molecular weight ($M_{p, mix} = 7870$) was considerably smaller than the sum of the two

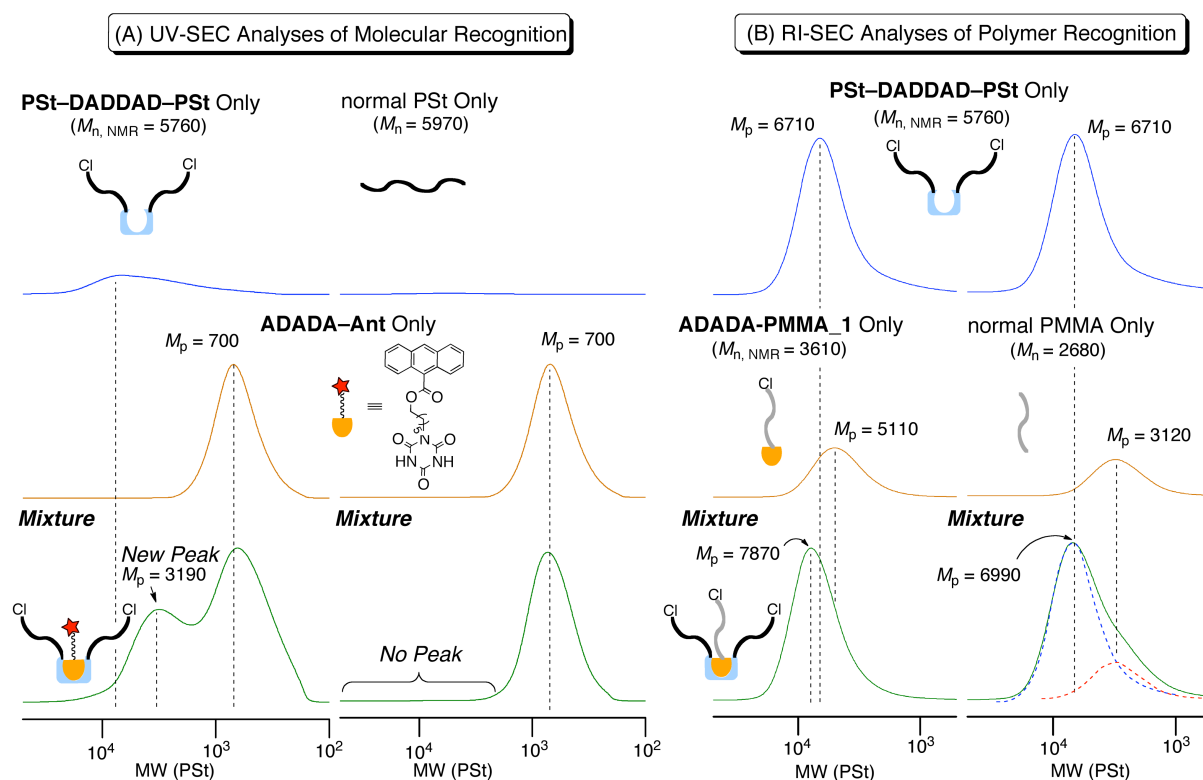


Figure 5. SEC analysis for (A) the molecular recognition of PSt–DADDAD–PSt with ADADA–Ant by UV-detector and (B) the polymer recognition of PSt–DADDAD–PSt with ADADA–PMMA_1 by RI-detector ($[PSt\text{--}DADDAD\text{--}PSt] = [ADADA]$, see the experimental section).

components (11820 = 6710 + 5110). This further suggests that the strong polymer-polymer interaction *at the center* of PSt-DADDAD-PSt may generate a polymer assembly that is clearly more compact in shape with a hydrodynamic volume expected from the sum of peak molecular weights of the linear component polymers.

6. Quantitative Analysis of Recognition Power of PSt-DADDAD-PSt with ^1H NMR

Finally, the complementary interaction between PSt-DADDAD-PSt and ADADA-PMMA was quantitatively evaluated to determine association constant K_{ass} , where a series of mixtures of the two components at varying molar ratios were analyzed in CDCl_3 at

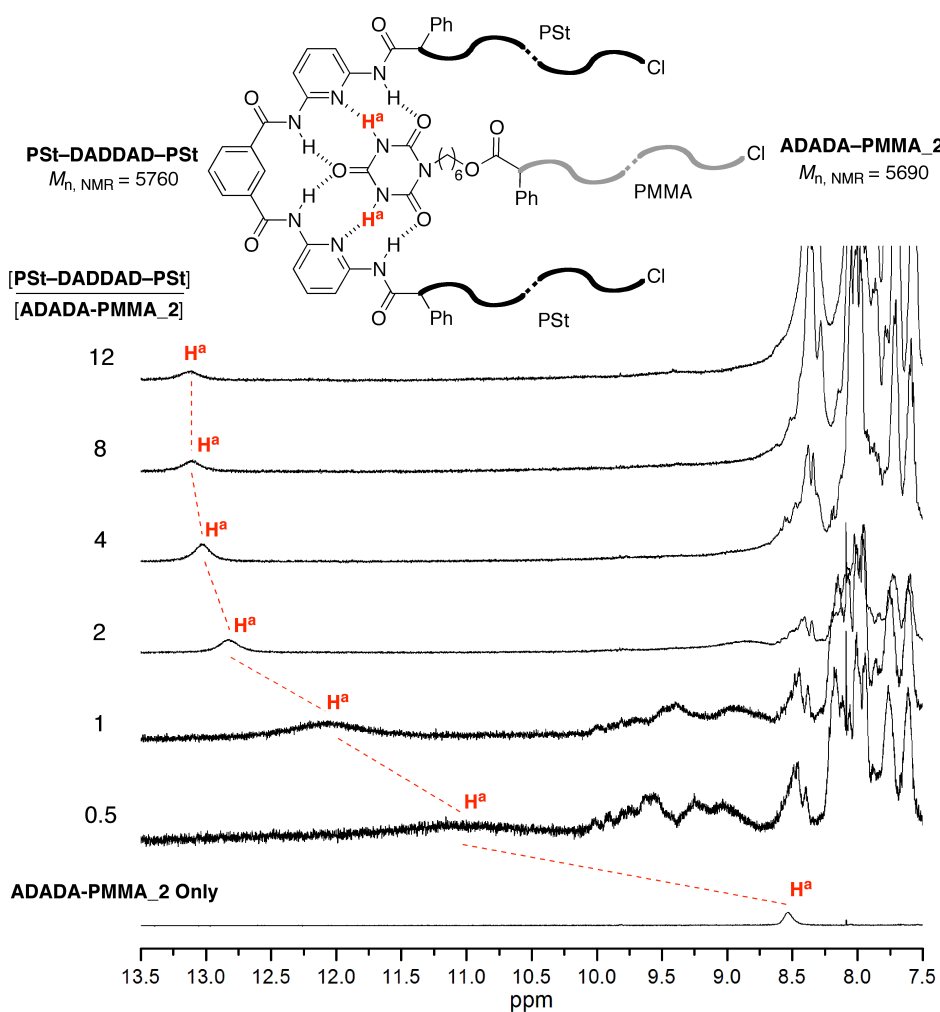


Figure 6. ^1H NMR spectra (CDCl_3 , room temperature) from 7.5 to 13.5 ppm of ADADA-PMMA_2 (bottom) and the mixtures with PSt-DADDAD-PSt of various ratios ($[\text{PSt-DADDAD-PSt}]/[\text{ADADA-PMMA}_2] = 0.5, 1, 2, 4, 8, \text{ and } 12$) for calculation of K_{ass} : $[\text{ADADA-PMMA}_2] = 2.0 \text{ mM}$ (constant); $[\text{PSt-DADDAD-PSt}] = 0, 1, 2, 4, 8, 16, \text{ and } 24 \text{ mM}$.

room temperature by ^1H NMR spectroscopy (Figure 6; with ADADA-PMMA_2). Similar to the analysis with ADADA-Cl, the NH proton signals of the PMMA consistently shifted downfield as the DADDAD polymer increased, to give $K_{\text{ass}} = 7968.5 \text{ M}^{-1}$ (Table 1). Importantly, this value is comparable to that between the complementary initiator pair (Cl-DADDAD-Cl and ADADA-Cl; $K_{\text{ass}} = 7877.2 \text{ M}^{-1}$), indicating the polymer-polymer interaction via the DADDAD-ADADA pair effectively works for chemically different polymers as with small molecules pairs, so strong and specific to overcome steric hindrance and the incompatibility between PSt and PMMA.

Conclusion

A bifunctional initiator for metal-catalyzed living radical polymerization was designed to bear “Hamilton receptor” of 6 complementary hydrogen-bonding points (Cl-DADDAD-Cl: D = hydrogen donor; A = hydrogen acceptor; Cl = initiator). The two initiating sites worked as the initiator for living polymerization to uniformly generate “controlled” vinyl polymer chains, indicating that the center of the resultant one chain was decollated with the receptor. Polystyrene is a non-polar carbon-based vinyl polymer, but the polymer from Cl-DADDAD-Cl (**PSt-DADDAD-PSt**) afforded to recognize the complementary molecule (**ADDAD-Ant**) and polymer (**ADDAD-PMMA**) at the center, which were characterized with SEC and ^1H NMR. Currently, the author is preparing polystyrene chains periodically carrying the receptor sites via radical coupling reaction of **PSt-DADDAD-PSt** as well as block copolymers carrying the receptor at the center, which are presented in the near future.

References and Notes

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$$\delta_{mix} = \delta_{ADADA} + \frac{(\delta_{\infty} - \delta_{ADADA}) \left(\left([ADADA] + [DADDAD] + \frac{1}{K_{ass}} \right) - \sqrt{\left([ADADA] + [DADDAD] + \frac{1}{K_{ass}} \right)^2 - 4[ADADA][DADDAD]} \right)}{2[ADADA]}$$

, where the experimental parameters are as follows,

[ADADA] and [DADDAD]: molar concentrations of ADADA- and DADDAD-functionalized compounds (i.e., initiators or polymers)

δ_{mix} : a chemical shift for NH proton of ADADA-functionalized compound for an equimolar mixture with DADDAD counterpart in ^1H NMR spectrum (H^a in Figure 1);

δ_{ADADA} : a chemical shift for NH proton of ADADA-functionalized compound;

K_{ass} : an association constant;

δ_{∞} : a saturated chemical shift for NH proton of ADADA-functionalized compound when an excess molar of DADDAD counterpart was mixed. The value was calculated from curve fitting with third degree polynomial for plots with various mixing ratios.

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Chapter 5

Periodic Introduction of Hamilton Receptors into Polystyrene Chain: Supramolecular Graft Copolymer with Regular Intervals

Abstract

The periodic programmed Hamilton receptor (-DADDAD-; D = hydrogen donor; A = hydrogen acceptor) in polymer backbone was designed from well-defined center-functional polystyrene with narrow molecular weight distribution (MWD) by chain extension. For the precision synthesis of precursor polymer, Hamilton receptor-based bifunctional initiator was employed and initiated ruthenium-catalyzed living radical polymerization of styrene to give well-controlled homopolymer with -DADDAD- units at the center position ($\text{PS}_{\text{DADDAD}}$). The chain extension of obtained precursor was achieved by ruthenium-catalyzed radical coupling polymerization; thereby -DADDAD- units were multiply introduced into polymer backbone with regular intervals $[(\text{PS}_{\text{DADDAD}})_n]$. Upon mixing in CDCl_3 , for example, a pair of "complementary" polymers, such as $(\text{PS}_{\text{DADDAD}})_n$ and $\text{PMMA}_{\text{ADADA}}$, formed supramolecular graft copolymer via complementary hydrogen bonds, where the terminal groups of guest polymers are connected to periodic positions in polymer backbone. Here, complementary association at the periodic positions demonstrated by ^1H NMR (association constant $\sim 10^4$) and UV SEC analysis. Moreover, the effect of well-defined positions for supramolecular self-assembly was examined by differential scanning calorimetry (DSC) compared with combination of randomly introduced Hamilton receptors (Not regular intervals between DADDAD motifs) in polymer backbone and $\text{PMMA}_{\text{ADADA}}$.

Introduction

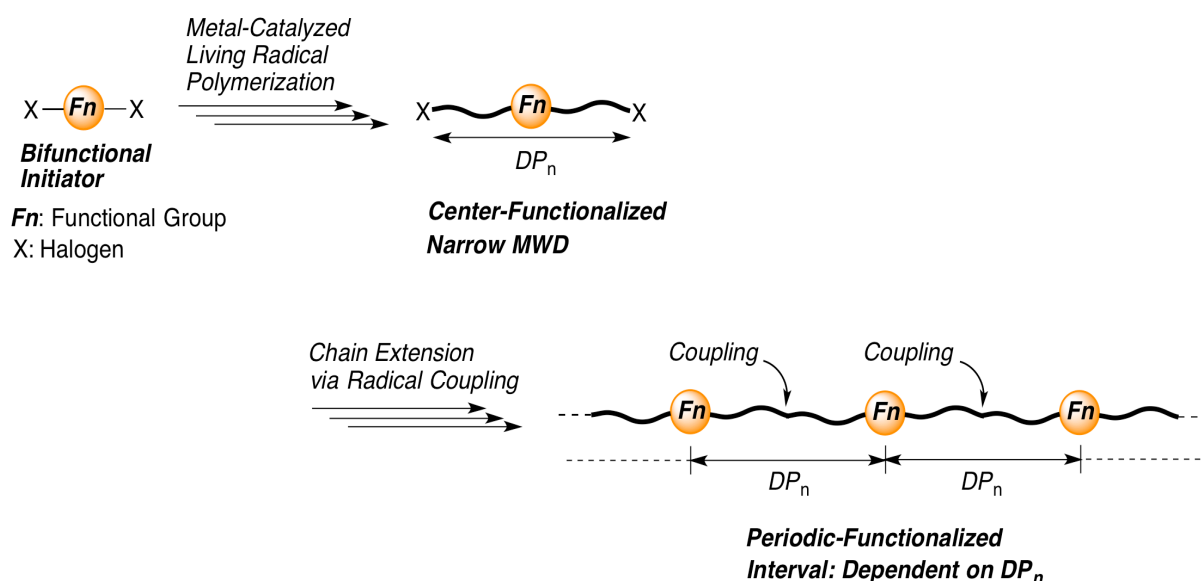
The beautiful double helix structure of DNA is induced by dynamic but selective interaction on the basis of complementary hydrogen bonds between two macromolecular chains. Herein it is crucial to array the four nucleobases giving two sets of complementary hydrogen bond interactions (i.e., adenine/thymine and guanine/cytosine) at well-defined position in chain. The non-covalent bond-based formation allows dissociation and re-association of the coupled strand, which is the origin of their functions such as replication and transcription. Hydrogen bond interaction also plays a key role in conformation of protein or catalysis of enzyme. Thus, it is noteworthy that hydrogen bond is well programmed in nature for the macromolecules to perform their functions.

Even in some synthetic polymers, hydrogen bond interaction is important for the properties. The representative example is polyamide or nylon. The chain interacts with each other through the hydrogen bond in the repeating amide unit, and consequently the resin can be used as engineering plastic expressing high thermal and mechanical properties due to the hydrogen bond-based crystalline.¹ However, in most of synthetic polymers, chain-chain interaction is based on weaker interactions such as Van der Waals force or hydrophobic interaction without relying on stronger non-covalent bond such as hydrogen bond.

On the other hand, progress in living radical polymerization has allowed precision syntheses of end-functionalized polymers by using the corresponding initiator or terminator.² Furthermore, some multiple hydrogen-bonding groups with complementary association abilities have been developed through an array of hydrogen donors (D) and acceptors (A) for supramolecular chemistry with the self-assembled features.³ Thus, some studies have been conducted on an introduction of such complementary hydrogen bonding sites at chain terminal to construct supramolecular block copolymers.⁴ The interaction is dynamic but tight enough to induce phase separation like covalent bond-connected block copolymers and herein “terminal” interaction is ensured between two polymeric segments. However, there are a few examples on an introduction of such non-covalent bond at well-defined positions except for terminals.⁵

The author has designed bifunctional initiators ($X-Fn-X$: X = halogen or leaving group, Fn = functional group or hydrogen bonding site in this work) for metal-catalyzed living radical polymerization with complementary hydrogen bonding sites (Scheme 1).⁶ Such a bifunctional initiator in living polymerization could give polymers whose central

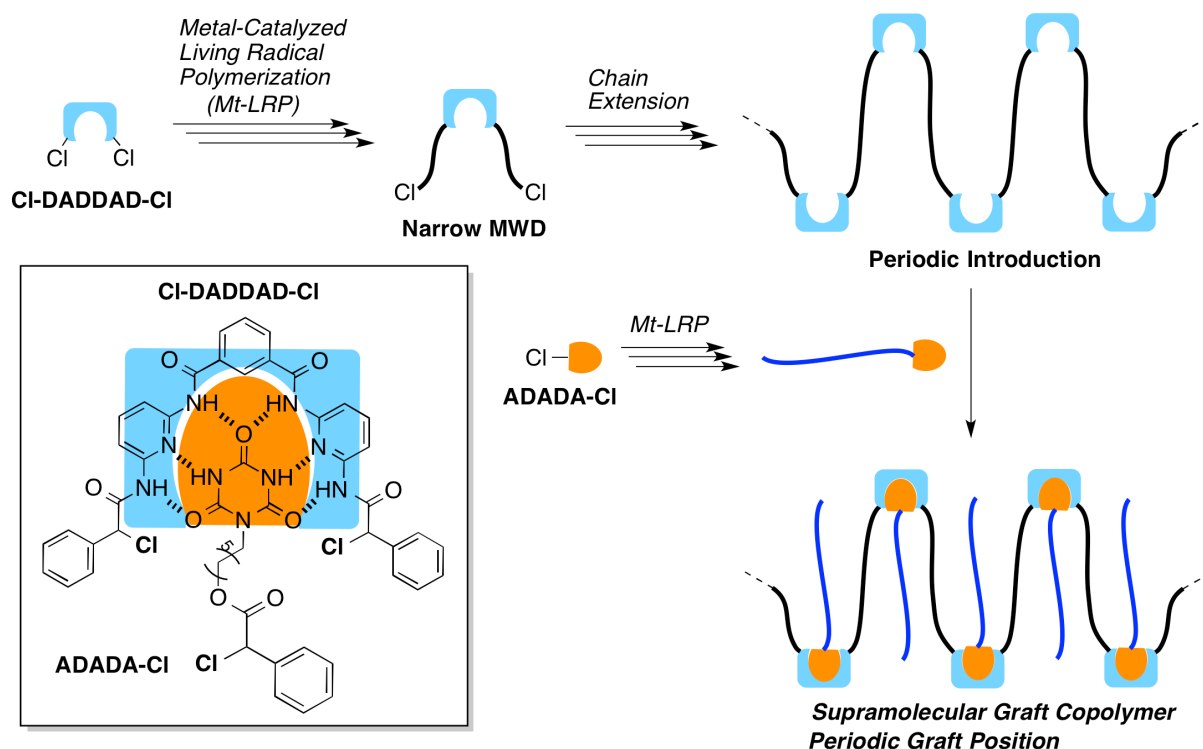
position is functionalized ($L\sim\sim\sim Fn\sim\sim\sim L$). In addition, chain extension reaction with the polymer from the bifunctional initiator would give longer polymer chains in which some Fn groups are periodically introduced at regular intervals, as the molecular weight distribution (MWD) of the starting polymer becomes narrow. Therefore, such bifunctional initiator with complementary hydrogen bonding sites would afford polymers that carry the interaction units at regular intervals almost equal to DP_n of the starting oligomer as well as on the central position.



Scheme 1. Periodically Functionalized Polymer Chains with Bifunctional Initiator for Metal-Catalyzed Living Radical Polymerization.

In my recent paper, the author has reported a bifunctional initiator for metal-catalyzed living radical polymerization carrying six hydrogen-bonding sites with the sequence of DADDAD (Figure 1: Cl-DADDAD-Cl).⁷ Herein two 2,6-diaminopyridine units are embedded via amide linkages called as Hamilton receptor between two C-Cl-based initiator sites and the DADDAD unit can complementarily interact with the five-point array (ADADA) in cyanuric acid-based initiator (ADADA-Cl) of high association constant ($K_{\text{ass}} = 7900 \text{ M}^{-1}$). The author has thus demonstrated that the center-functionalized polystyrene from Cl-DADDAD-Cl can be tightly associated with the end-functionalized poly(methyl methacrylate) (PMMA) from ADADA-Cl to give T-shaped supramolecular block copolymer. In this work, the author examined chain extension reaction of narrow MWD polystyrene (oligostyrene) carrying the receptor on the center to lead to unique polystyrene chains where some Hamilton receptors (DADDAD) are periodically embedded. Styryl radical tends to

incur coupling reaction rather than disproportionation without monomer, so generation of the radical species at higher concentration without monomer can be expected to promote the chain extension, as shown in my previous attempt (Chapter 3). Importantly, the main hydrocarbon-based structure can be maintained through the radical-radical coupling except the DADDAD units, and nevertheless the polystyrene chain is expected to interact with ADADA-functionalized PMMA giving periodically grafted supramolecular block copolymer.



Scheme 2. Structures of CI-DADDAD-Cl and ADADA-Cl and Supramolecular Graft Copolymer from the Initiators.

Experimental Section

Materials

Monomers (MMA and styrene: Aldrich; purity > 99 %) were dried overnight over calcium hydride and purified by distillation from calcium hydride before use. 2,6-Diaminopyridine (TCI; >98%), isophthaloyl dichloride (wako; >95%), 6-bromo-1-hexanol (Wako; >97%), cyanuric acid (TCI; >98%), 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, Wako; >97%), dicyclohexylcarbodiimide (DCC,

Wako; >95%), 4-dimethylaminopyridine (Aldrich; 99%), triethylamine (Wako; 99%), $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (Cp^* : cyclopentadienyl, Aldrich), and α -chlorophenylacetylchloride (Aldrich; 90%) were used as received. Dichloromethane (Wako; dehydrated), dimethylformamide (Wako; dehydrated), and pyridine (Wako; dehydrated) were bubbled with dry argon for more than 15 min immediately before use. Toluene and THF (Kishida Kagaku; purity 99.5%) was dried and purified by passing through purification columns (Solvent Dispensing System, Glass Contour) and bubbled with dry nitrogen for more than 15 min immediately before use. *n*-Monobutylamine (TCI; >98%) and 1,6-diaminohexane (1,6-DAH, TCI; >99%) was degassed by reduced pressure before use. *n*-Octane (internal standard for gas chromatography) was dried over calcium chloride and distilled from calcium hydride.

Synthesis of Complementary Hydrogen-Bonding Initiators

Cl-DADDAD-Cl (2,6-diamide pyridine-based dichloride of a *donor* (**D**) - *acceptor* (**A**) - *donor* (**D**) - *donor* (**D**) - *acceptor* (**A**) - *donor* (**D**) configuration) and ADADA-Cl (cyanurate-based chloride of an *acceptor* (**A**) - *donor* (**D**) - *acceptor* (**A**) - *donor* (**D**) - *acceptor* (**A**) configuration) were synthesized according to the literature.⁷

Polymerization Procedures

Polymerization was carried out by the syringe technique under dry argon in baked round bottom flask equipped with a three-way stopcock. A typical procedure for styrene (St) or methyl methacrylate (MMA) with initiator/ $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ /*n*-BuNH₂ is given. In a round-bottom flask (50 mL) filled with argon was placed $\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2$ (93.4 g, 0.117 mmol), toluene (0.34 mL), *n*-octane (3.63 mL), styrene (13.4 mL, 0.117 mol), *n*-BuNH₂ (2.93 mL, 400 mM in toluene) and a solution of Cl-DADDAD-Cl (9.00 mL, 130.3 mM in THF) were sequentially added; the total volume was 29.3 mL. Immediately after mixing, the solution was placed in an oil bath kept at 100 °C for 4 h. The polymerization mixture was terminated by cooling to -78 °C in dry ice-methanol. Monomer conversion was determined from residual monomer concentration measured by gas chromatography with *n*-octane as an internal standard (conversion = 14.0 %) from remained solution and the obtained polymer was purified by fractional SEC in CHCl₃ to remove low molecular weight oligomer and catalyst. The final product was dissolved in toluene and precipitated with MeOH. The obtained

polymer was filtered and dried overnight under vacuum at room temperature and measured with SEC ($M_n = 2770$, $M_w/M_n = 1.06$).

Chain Extension Procedure

The chain extension reaction was carried out by the syringe technique under dry argon in baked glass tubes equipped with a three-way stopcock or in sealed glass vials. A typical procedure for PS_{DADDAD} as macroinitiator (precursor) (M_n , NMR (Cl) = 2200) with Ru(Cp*)Cl(PPh₃)₂/1,6-DAH/P(*n*-Bu)₃/EtOH are given. In a round-bottom flask (50 mL) filled with argon was placed PS_{DADDAD} (0.319 g, 0.145 mmol), Ru(Cp*)Cl(PPh₃)₂ (34.7 mg, 0.044 mmol), toluene (1.56 mL), 1,6-DAH solution (0.58 mL, 500 mM in toluene), P(*n*-Bu)₃ solution (0.58 mL, 500 mM in toluene) and EtOH (0.91 mL) were sequentially added; the total volume was 3.63 mL. Immediately after mixing, the solution was placed in an oil bath kept at 100 °C for 104 h. The polymerization mixture was terminated by cooling to -78 °C in dryice-methanol. The quenched solution was evaporated and purified by fractional SEC in CHCl₃ to remove low molecular weight oligomer and catalyst. The final product was dissolved in toluene and precipitated with MeOH. The obtained polymer was filtered and dried overnight under vacuum at room temperature and measured with SEC ($M_n = 12500$, $M_w/M_n = 1.71$).

Measurement

M_n and M_w/M_n of polymers were measured by size exclusion chromatography (SEC) in THF (at 40 °C) or CHCl₃ (at room temperature) as an eluent. For the THF-SEC, three polystyrene-gel columns [LF-404 (from Shodex); pore size, 3000 Å; 4.6 mm i.d. × 250 cm] were connected to a DU-H2000 pump, a 74S-RI refractive-index detector, and a 41-UV ultraviolet detector (all from Shodex) and flow rate was set to 0.3 mL/min. For the CHCl₃-SEC, three polystyrene gel columns [K-805L (from Shodex); pore size 20–1000 Å; 8.0 mm i.d. × 30 cm] were connected to a PU-980 pump and a 930-RI refractive-index detector, and a 970-UV ultraviolet detector set at 250 nm (all from Jasco) and flow rate was set to 1.0 mL/min. The columns were calibrated against 13 standard poly(MMA) (PMMA) samples (Polymer Laboratories; $M_n = 620$ –1,200,000; $M_w/M_n = 1.06$ –1.22) for obtained PMMA samples, and 13 standard polystyrene (PS) samples (Polymer Laboratories; $M_n = 500$ –3,840,000; $M_w/M_n = 1.01$ –1.14) for obtained PS samples, respectively. The chain

extended PSt–DADDAD–PSt (Multiple DADDAD–PSt) was used as standard (0.5 mg/mL) and the other samples were prepared by same molar concentration with multiple DADDAD–PSt. Polymer samples were purified by preparative SEC in CHCl₃ at room temperature on polystyrene gel preparative column [K-5002 (from Shodex); exclusion limit = 5×10^3 ; particle size = 15 μ m; 5.0 cm i.d. $\times$ 30 cm; flow rate = 10 mL/min] that were connected to a PU-2086 precision pump, a RI-2031 refractive-index detector, and UV-2075 ultraviolet detector (all from Jasco). ¹H NMR was recorded in CDCl₃ at room temperature on JEOL JNM-ECA500 spectrometer, operating at 500.16 (¹H) MHz. Differential scanning calorimetry (DSC) was performed on polymer samples under a dry nitrogen flow at heating or cooling rate of 5 °C/min on a DSCQ200 calorimeter (TA Instruments) equipped with a RCS 90 electric machine. All polymer samples were prepared by film casting in CHCl₃ from same stock solutions (10 mg/mL for poly(St) and 20 mg/mL for poly(MMA)).

Results and Discussion

1. Precise Syntheses of Polystyrene Precursor from Cl–DADDAD–Cl

For syntheses of polystyrene precursors in chain extension, styrene was polymerized via metal-catalyzed living radical polymerization with Cl–DADDAD–Cl as an initiator under 100 mer condition ($[\text{St}]_0/[\text{Cl–DADDAD–Cl}]_0 = 100$), in conjunction with ruthenium catalyst $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]$ and amine cocatalyst ($n\text{-BuNH}_2$). For periodic incorporation of the DADDAD site in polystyrene chain via the chain extension, the polystyrene precursor is required to show very narrow molecular weight distribution and quantitative functionality of Cl on both ends as well as the DADDAD site on the center.

To ensure quantitative Cl capping, the polymerization for the precursor preparation was quenched at lower conversions (14% and 48%). Figure 1 (A) and (B) show SEC curves of the obtained polystyrenes ($\text{PS}_{\text{DADDAD}3\text{k}}$ and $\text{PS}_{\text{DADDAD}8\text{k}}$) (the samples were purified after purification with preparative SEC in chloroform). The narrow molecular weight distributions ($M_w/M_n = 1.06$ and 1.09) indicated that the polymerizations were well controlled. Higher number-averaged molecular weights (M_n s) than calculated values from the injection ratio and conversion are likely due to higher excluded chain volume of the DADDAD-functionalized polystyrene chains than that of standard polymers for SEC calibration.

The structures were further analyzed with ^1H NMR. As shown in Figure 2A for $\text{PS}_{\text{DADDAD}3\text{k}}$, besides main peaks from protons of polystyrene (c and d), minor peaks from the DADDAD unit were clearly observed around 8 ppm (a). Furthermore, peaks from a methylene group neighboring to amide and phenyl in the DADDAD unit (b) and another methylene neighboring to terminal Cl (e) were also observed. Number-averaged degrees of polymerization (DP_n s) were calculated with integration ratios of the main peaks to the minor from DADDAD and Cl ($DP_{n, \text{DADDAD}}$ and $DP_{n, \text{Cl}}$, respectively), and thus functionalities of DADDAD and Cl ($F_{n, \text{DADDAD}}$ and $F_{n, \text{Cl}}$) were estimated from the ratio with the actual $DP_{n, \text{Conv}}$ that is calculated from conversion (14%) and injection ratio ($[\text{styrene}]_0/[\text{Cl–DADDAD–Cl}]_0 = 100$): $F_{n, \text{DADDAD}} = DP_{n, \text{Conv}}/DP_{n, \text{DADDAD}} = 1.06$; $F_{n, \text{Cl}} = DP_{n, \text{Conv}}/DP_{n, \text{Cl}} = 1.88$ (Entry 1 in Table 1). Similarly, the functionalities for $\text{PS}_{\text{DADDAD}8\text{k}}$ were also estimated (see Entry 2). These data certainly supported that the two samples of the polystyrene precursor almost quantitatively carry the Hamilton receptor and Cl at the both terminals.

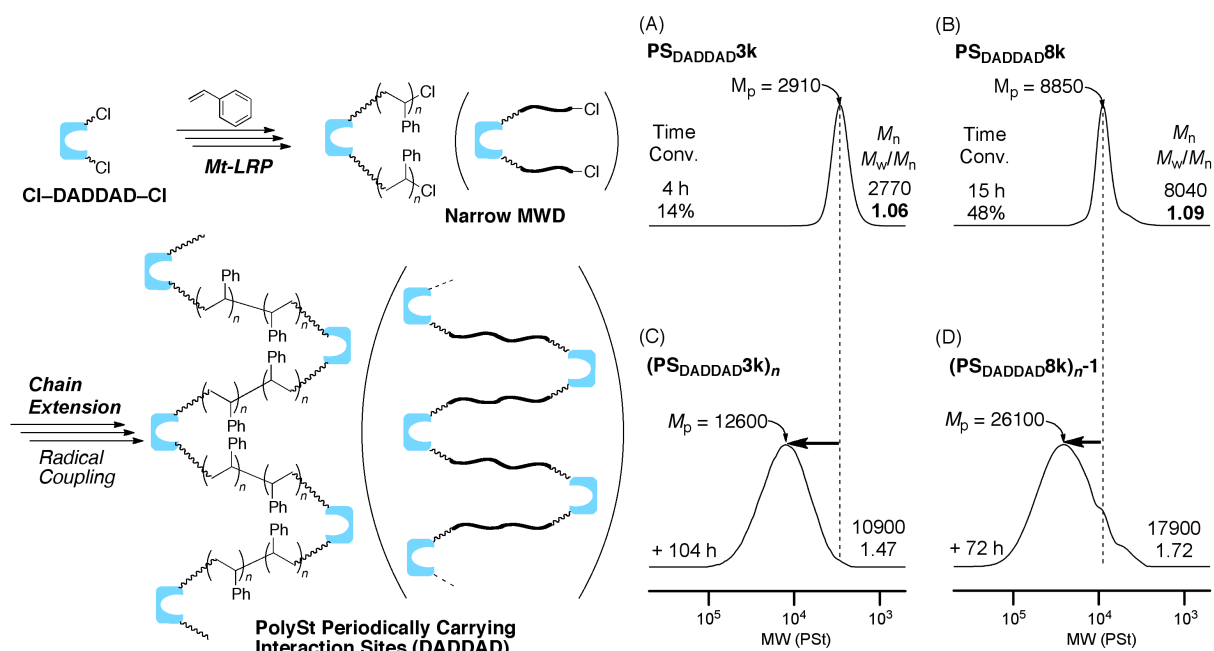


Figure 1. SEC curves of (A) $\text{PS}_{\text{DADDAD}3\text{k}}$ and (B) $\text{PS}_{\text{DADDAD}8\text{k}}$ by living radical polymerization with Cl-DADDAD-Cl and periodically programmed hydrogen bonding sites into (C) $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ and (D) $(\text{PS}_{\text{DADDAD}8\text{k}})_{n-1}$ by chain extension. Polymerization: $[\text{St}]_0 = 4.0 \text{ M}$; $[\text{Cl-DADDAD-Cl}] = 40 \text{ mM}$; $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 4.0 \text{ mM}$; $[\text{n-BuNH}_2]_0 = 40 \text{ mM}$ in toluene at 100°C . Chain extension reaction: $[\text{PS}_{\text{DADDAD}}] = 40 \text{ mM}$; $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 12.0 \text{ mM}$; $[\text{NH}_2-(\text{CH}_2)_6-\text{NH}_2]_0 = 80 \text{ mM}$; $[\text{P}(\text{n-Bu})_3]_0 = 80 \text{ mM}$ in toluene/EtOH = 3/1 v/v % at 100°C .

Table 1. Samples of -DADDAD- or ADADA-Functionalized Polymers in This Work^a

Sample Code	$DP_{n, \text{Conv}}^{\text{d}}$	$DP_{n, \text{Init}}^{\text{e}}$	$DP_{n, \text{Cl}}^{\text{e}}$	$F_{n, \text{Init}}^{\text{f}}$	$F_{n, \text{Cl}}^{\text{f}}$	$M_{n, \text{SEC}}^{\text{g}}$	M_w/M_n^{g}
$\text{PS}_{\text{DADDAD}3\text{k}}^{\text{b}}$	14.0	13.2	7.43	1.06	1.88	2770	1.06
$\text{PS}_{\text{DADDAD}8\text{k}}^{\text{b}}$	47.9	49.0	24.0	0.98	2.00	8040	1.09

^aAll polymer samples were purified by preparative SEC in CHCl_3 or precipitated in MeOH to remove low molecular weight residues. ^b $[\text{St}]_0 = 4.0 \text{ M}$, $[\text{Cl-DADDAD-Cl}]_0 = 40 \text{ mM}$, $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 4.0 \text{ mM}$, $[\text{n-BuNH}_2]_0 = 40 \text{ mM}$ in toluene at 100°C for 4 h or 15 h.

^c $[\text{MMA}]_0 = 4.0 \text{ M}$, $[\text{ADADA-Cl}]_0 = 40 \text{ mM}$, $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 4.0 \text{ mM}$, $[\text{n-BuNH}_2]_0 = 40 \text{ mM}$ in toluene at 80°C . ^dMeasured by gas chromatography with *n*-octane as an internal standard. ^eCalculated with ^1H NMR. ^fDetermined by $DP_{n, \text{Conv}}/DP_{n, \text{motif}}$ or $DP_{n, \text{Conv}}/DP_{n, \text{Cl}}$.

^gMeasured by size-exclusion chromatography calibrated with PMMA or PS standards in THF.

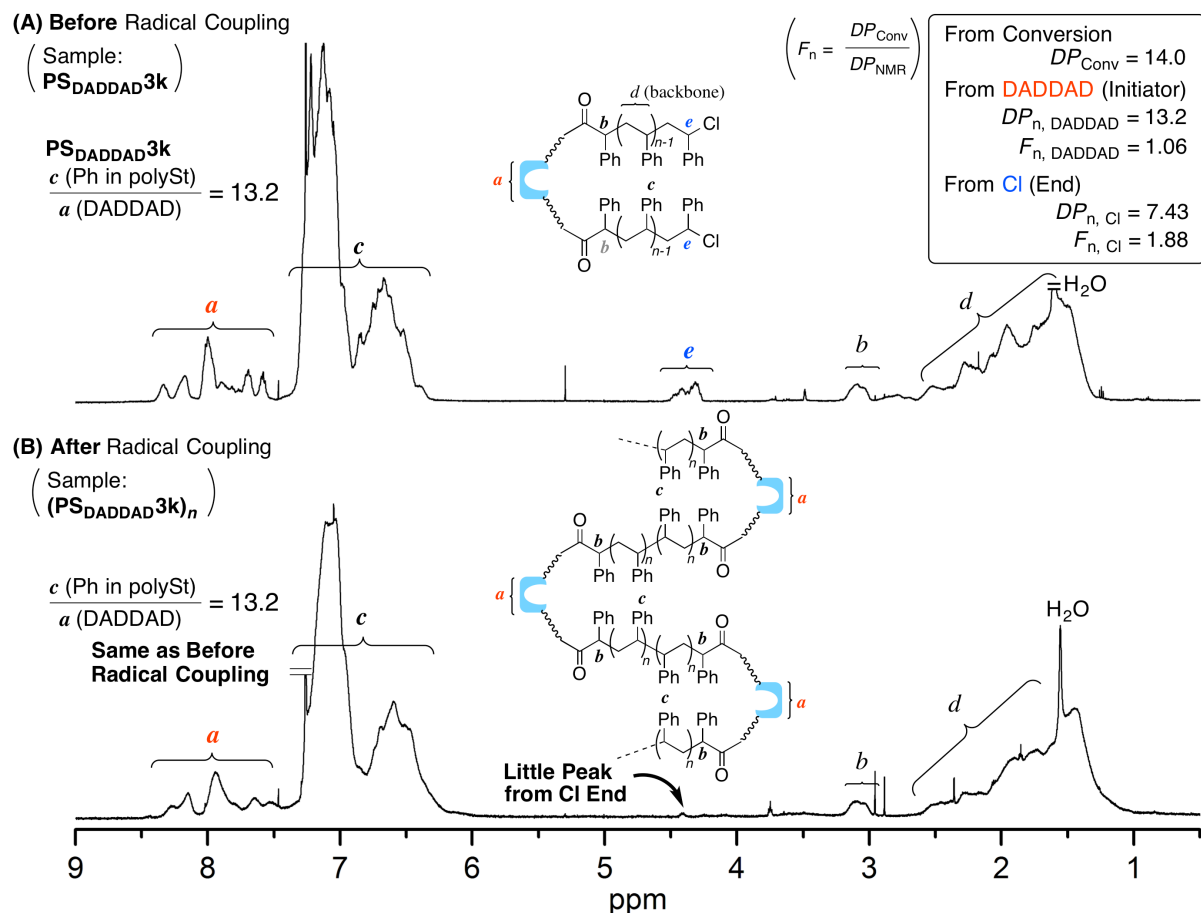


Figure 2. Structure analysis of (A) $\text{PS}_{\text{DADDAD}3\text{k}}$ as precursor and (B) $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ by ^1H NMR spectra (CDCl_3 , room temperature).

2. Radical-Radical Coupling Reaction of $\text{PS}_{\text{DADDAD}}$

Chain extension via radical-radical coupling was performed with the polystyrene samples ($\text{PS}_{\text{DADDAD}3\text{k}}$ and $\text{PS}_{\text{DADDAD}8\text{k}}$) as the precursors. The author has recently reported ruthenium-catalyzed radical coupling reaction with similar bifunctional polystyrene (Chapter 3), and then the same condition was applied in this work. In addition to ruthenium catalyst (RuCp^*), diamine-based cocatalyst [$\text{NH}_2-(\text{CH}_2)_6-\text{NH}_2$], higher basic ligand [$\text{P}(n\text{-Bu})_3$], and ethanol were combined for the radical-radical coupling reaction. After several days on heating, SEC curves of the product were clearly shifted to higher molecular weight and the MWDs were broader, indicating polycondensation occurred via the radical-radical coupling between chains [Figure 1 (C) and (D) and Entry 1 and 2 in Table 2] (the reaction with $\text{PS}_{\text{DADDAD}8\text{k}}$ was twice carried out for sample preparation).

Table 2. Samples of Chain Extended Polymers in This Work^{a, b}

Entry	Sample Code	$M_{n, SEC}^c$	M_w/M_n^c	M_p^c	$M_{p, (precursor)}^c$	M_n , Repeating Chain ^d	N DADDAD ^e
1	(PS _{DADDAD3k}) _n	10910	1.47	12600	2910	2130	5.92
2	(PS _{DADDAD8k}) _{n-1}	17900	1.72	26100	8850	5580	4.68
3	(PS _{DADDAD8k}) _{n-2}	16200	1.61	20960	8850	5580	3.76

^aAll polymer samples were purified by preparative SEC in CHCl₃ to remove low molecular weight residues. ^b[Macroinitiator]₀ = 40 mM, [Ru(Cp*)Cl(PPh₃)₂]₀ = 12 mM, [NH₂-(CH₂)₆-NH₂]₀ = 80 mM, [P(*n*-Bu)₃]₀ = 80 mM in toluene at 100 °C for more than 69 h.

^cMeasured by size-exclusion chromatography calibrated with PMMA or PS standards in THF.

^dCalculated with ¹H NMR of precursors. ^eDetermined by M_p/M_n , Repeating Chain.

¹H NMR spectrum of the product (PS_{DADDAD3k})_n was quite similar to that of the precursor (PS_{DADDAD3k}) except for disappearance of peak from Cl-end groups around 4.5 ppm. Importantly, there was no change in ratio of peak integration from polystyrene main peak to that from the DADDAD unit, although the molecular weight was apparently increased from the SEC analysis. These results indicated that the objective chain extension was successfully achieved, and the interval molecular weight or length between the Hamilton receptor in the resultant polystyrene chain was supposed to be same as that of the precursor. The averaged numbers of the receptor were roughly estimated as 4.3 for (PS_{DADDAD3k})_n and 2.9 for (PS_{DADDAD8k})_{n-1} from the peak top molecular weights [M_p for (PS_{DADDAD})_n/ M_p for PS_{DADDAD}].

3. Interaction of (PS_{DADDAD})_n with ADADA-Functionalized Polymer

The complementary interaction of the chain-extended polystyrene (PS_{DADDAD8k})_{n-1} with the complementary site (ADADA)-terminated PMMA (PMMA_{ADADA9k}; $M_{n, SEC}$ = 8800, $M_{n, NMR}$ = 5690, M_w/M_n = 1.08) was examined with ¹H NMR and the association constant K_{ass} was estimated.⁸ A series of mixtures of the two polymers at varying molar ratios were prepared from same stock solutions and the solutions were analyzed at room temperature by ¹H NMR spectroscopy (Figure 3; a series of mixtures of (PS_{DADDAD8k})_{n-1} with PMMA_{ADADA9k}; ([PS_{DADDAD8k})_{n-1}]/[PMMA_{ADADA9k}] = 0.5, 1, 2, 4, 8, and 12). As increasing the molar ratio of (PS_{DADDAD8k})_{n-1}, the peak from NH group of PMMA_{ADADA9k}

significantly shifted to downfield from 8.51 ppm to 12.17 ppm. From these changes, K_{ass} was estimated to be 10275 M^{-1} (Table 3), which was clearly higher than the precursor pair ($\text{PS}_{\text{DADDAD}8\text{k}}$ with $\text{PMMA}_{\text{ADADA}9\text{k}}$; $K_{\text{ass}} = 7968.5 \text{ M}^{-1}$) and initiator pair (Cl-DADDAD-Cl

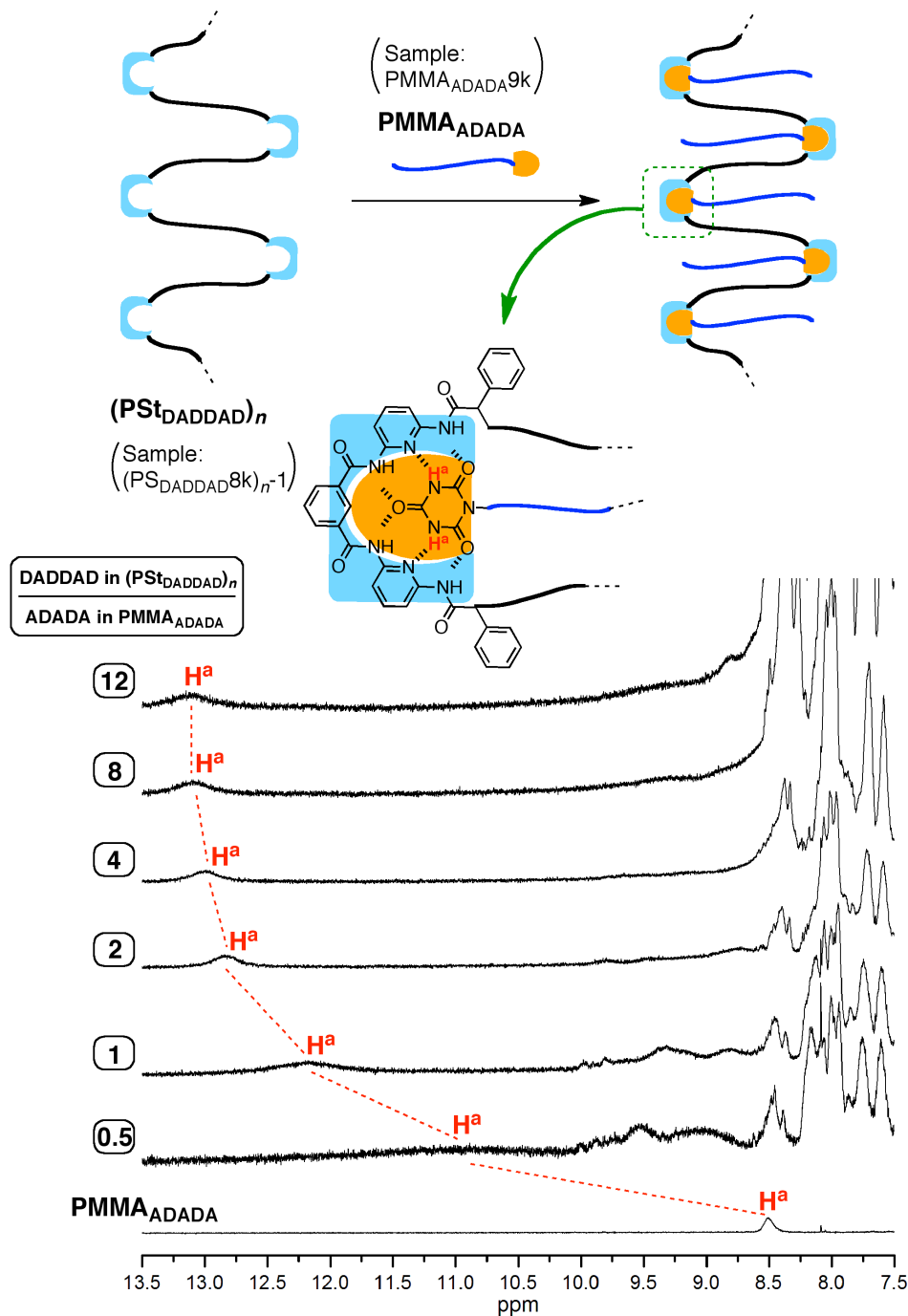


Figure 3. ^1H NMR spectra (CDCl_3 , room temperature) from 7.5 to 13.5 ppm of $\text{PMMA}_{\text{ADADA}9\text{k}}$ (bottom) and the mixtures with $(\text{PSt}_{\text{DADDAD}8\text{k}})_{n-1}$ of various ratios ($[(\text{PSt}_{\text{DADDAD}8\text{k}})_{n-1}]/[\text{PMMA}_{\text{ADADA}9\text{k}}] = 0.5, 1, 2, 4, 8$, and 12) for calculation of K_{ass} : $[\text{PMMA}_{\text{ADADA}9\text{k}}] = 2.0 \text{ mM}$ (constant); $[(\text{PSt}_{\text{DADDAD}8\text{k}})_{n-1}] = 0, 1, 2, 4, 8, 16$, and 24 mM .

with ADADA-Cl; $K_{\text{ass}} = 7877.2 \text{ M}^{-1}$).⁷ Importantly, herein, the local concentration of –DADDAD– units in complementary interaction system may increase by multiply introduced hydrogen bonding sites in same polymer chain thus, steric hindrance and the incompatibility between PSt and PMMA would overcome by strong and specific complementary interaction.

Table 3. Parameters for K_{ass} Calculation in This Work

Combination	[ADADA] and [DADDAD]	δ_{mix} / ppm	δ_{ADADA} / ppm	δ_{∞} / ppm
(PS _{DADDAD} 8k) _n -1 and PMMA _{ADADA} 9k ^a	$2.0 \times 10^{-3} \text{ mol/L}$	12.17	8.51	13.07 ^b

^asee Figure 3 for the interaction analyses by ¹H NMR ; ^bCalculated from curve fitting with third degree polynomial for plots with various mixing ratios.

The interaction was further examined with SEC analyses. Next, my effort was directed to the periodic recognitions of chain extended poly(St) with complementary associatable different polymer pair (PMMA_{ADADA}12k; $M_{\text{n, SEC}} = 11900$, $M_{\text{n, NMR}} = 9140$, $M_{\text{w}}/M_{\text{n}} = 1.12$). For SEC analysis, poly(St) can be specifically detected with UV detector in which the wavelength was set at 250 nm while poly(MMA) is inactive with UV detector. Thus, the peak shift of (PS_{DADDAD})_n with PMMA_{ADADA}12k should be considered as a one of the evidence for periodic complementary hydrogen bonding interaction.

The results with a combination of ADADA-free PMMA (normal PMMA: $M_{\text{n}} = 10260$, $M_{\text{w}}/M_{\text{n}} = 1.04$; an SEC standard sample) with (PS_{DADDAD}8k)_n-2 are described (Figure 4 right). The equimolar mixed solution in CHCl₃ was prepared and injected into SEC in CHCl₃ as an eluent where a UV detector at 250 nm was equipped. The normal PMMA is almost inactive for the wavelength, whereas the (PS_{DADDAD}8k)_n is absorbable to give peaks ($M_{\text{p}} = 11410$). From the equimolar mixture, no peak shifts appeared in the range of high MW and similar peaks were seen to that only for (PS_{DADDAD}8k)_n. Thus, although it is rather reasonable, the normal PMMA was found to be incapable of recognizing DADDAD units in poly(St). On the other hand, an equimolar mixture of (PS_{DADDAD}8k)_n-2 and PMMA_{ADADA}12k ($M_{\text{p}} = 10590$; almost inactive for the UV detector) led to a single unimodal peak at $M_{\text{p, mix}} = 14000$, which was clearly higher than (PS_{DADDAD}8k)_n (Figure 4 left). These results indicate that an apparent size of the chain extended poly(St) was uniformly increased in the presence of the complementary polymer pair, most likely via their complementary hydrogen-bonding

interaction. The combinations of $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ pairs were similarly analyzed with $(\text{PS}_{\text{DADDAD}8\text{k}})_n$ sets. As expected, although the peak shift of the $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ ($M_p = 2320$) and ADADA-free PMMA combination was not observed, the equimolar complementary pair of $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ and $\text{PMMA}_{\text{ADADA}12\text{k}}$ was shown at $M_{p, \text{mix}} = 3430$, which was also uniformly shifted to higher molecular weight. However, the peak shift of $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ pair is less significant than $(\text{PS}_{\text{DADDAD}8\text{k}})_n$ pair, even both combination indicate that $(\text{PS}_{\text{DADDAD}})_n$ certainly recognized with $\text{PMMA}_{\text{ADADA}}$. These results seem to be affected by spacer length between recognition sites (DADDAD units) in polymer chain. The short spacer length of $(\text{PS}_{\text{DADDAD}3\text{k}})_n$ would not provide enough space between component polymers to overcome steric hindrance and repulsion of different polymer chains. Moreover, the obtained molecular weight for the mixtures of $(\text{PS}_{\text{DADDAD}})_n$ and $\text{PMMA}_{\text{ADADA}}$ were quite lower than ideal values ($M_{p, \text{mix}} = M_{p, A} + M_{p, B}$). The possible is that the hydrogen-bonded polymer is collapsed and regenerated passing through the SEC column due to dynamic association and dissociation of hydrogen bonds during SEC analysis. Another possibility is that the strong polymer-polymer interaction at the regular positions of $(\text{PS}_{\text{DADDAD}})_n$ may

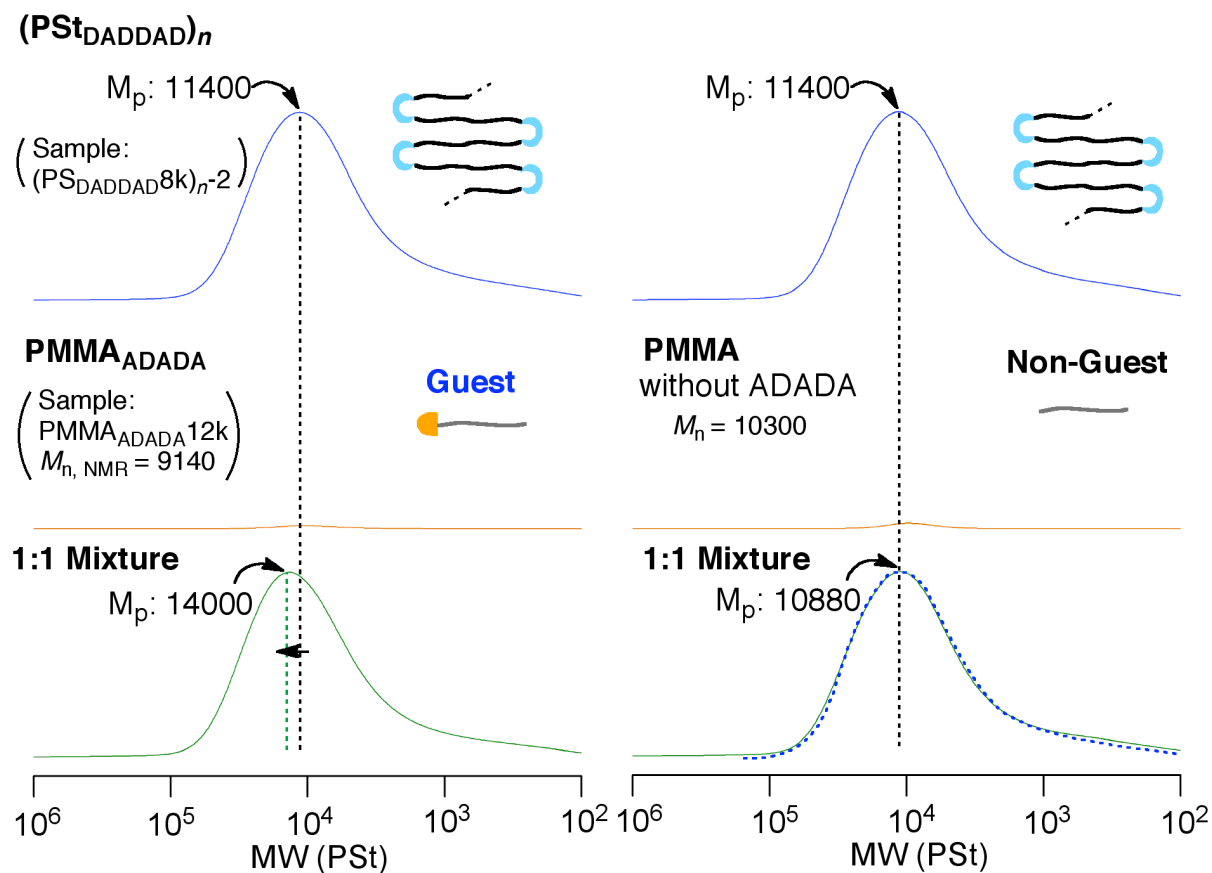


Figure 4. UV-SEC analysis for the polymer recognition of (A) with short spacer and (B) with long spacer between hydrogen bonding motifs.

generate a polymer assembly with complementary polymer pair that is clearly more compact in shape with a hydrodynamic volume expected from the sum of molecular weights of the linear polymers. Nevertheless, polymer recognition at the precisely controlled periodic positions was well confirmed.

4. Importance of Well-Defined Positions for Recognition Sites

To demonstrate the effect of well-defined positions of recognition sites in polymer chain, the author designed specific poly(St) carrying randomly introduced DADDAD motifs into polymer chain (Not regular intervals between DADDAD motifs) and prepared by chain extension of precursor mixture for $\text{PS}_{\text{DADDAD}3\text{k}}$ and $\text{PS}_{\text{DADDAD}8\text{k}}$ (Figure 5). As a result, The SEC curve of obtained $(\text{PS}_{\text{DADDAD}3\text{k}-r-\text{PS}_{\text{DADDAD}8\text{k}})_n$ clearly shifted to higher molecular weight and the MWD was also broader, indicating chain extension via radical coupling polymerization was successfully achieved between mixed polymer chains ($M_{n, \text{SEC}} = 12300$,

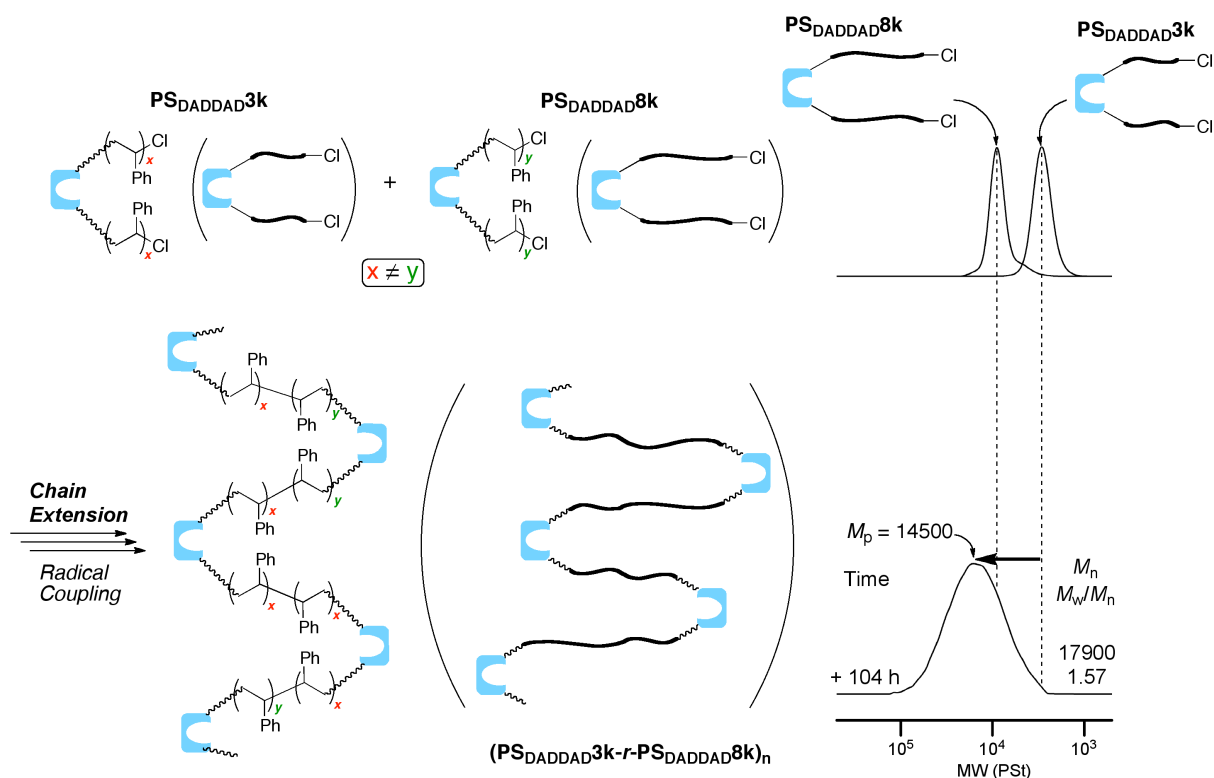


Figure 5. SEC curves of obtained randomly programmed hydrogen bonding sites into $(\text{PS}_{\text{DADDAD}3\text{k}-r-\text{PS}_{\text{DADDAD}8\text{k}})_n$ (bottom) via chain extension of $\text{PS}_{\text{DADDAD}3\text{k}}$ and $\text{PS}_{\text{DADDAD}8\text{k}}$ mixture (top). Chain extension reaction: $[\text{PS}_{\text{DADDAD}3\text{k}} + \text{PS}_{\text{DADDAD}8\text{k}}] = 40 \text{ mM}$; $[\text{Ru}(\text{Cp}^*)\text{Cl}(\text{PPh}_3)_2]_0 = 12.0 \text{ mM}$; $[\text{NH}_2-(\text{CH}_2)_6-\text{NH}_2]_0 = 80 \text{ mM}$; $[\text{P}(n\text{-Bu})_3]_0 = 80 \text{ mM}$ in toluene/EtOH = 3/1 v/v % at 100°C .

$M_w/M_n = 1.57$, $M_{n, \text{Repeating chain}} = 3180$).

The author then evaluated the position effect of interactive sites in $(\text{PS}_{\text{DADDAD}})_n$ by differential scanning calorimetry (DSC). All polymer samples were casted in chloroform for sever days and the casted films of equimolar mixtures were also prepared from same stock solutions (see Experimental Section). First of all, the thermal properties of homopolymers were analyzed by DSC and showed clear glass transition temperatures (Figure 6A). Herein, the $(\text{PS}_{\text{DADDAD}3\text{k-r-PS}_{\text{DADDAD}8\text{k}})_n$ gives higher T_g than $(\text{PS}_{\text{DADDAD}8\text{k}})_{n-2}$ even it has lower molecular weight. This phenomena should depend on a spacer length between rigid DADDAD groups ($M_{n, \text{Repeating chain}}$) thus, Hamilton receptor group derive higher T_g in polymer chain $((\text{PS}_{\text{DADDAD}3\text{k-r-PS}_{\text{DADDAD}8\text{k}})_n, M_{n, \text{Repeating chain}} = 3180; (\text{PS}_{\text{DADDAD}8\text{k}})_{n-2}, M_{n, \text{Repeating chain}} = 5580)$.

Next, the mixtures of $(\text{PS}_{\text{DADDAD}})_n$ with $\text{PMMA}_{\text{ADADA}}$ were also examined and normal PMMA (normal PMMA: $M_n = 10260$, $M_w/M_n = 1.04$) was employed to compare with complementary pairs. For the mixture of $(\text{PS}_{\text{DADDAD}8\text{k}})_{n-2}$ and $\text{PMMA}_{\text{ADADA}12\text{k}}$, the T_g of PMMA was obviously decreased from 102.2 °C to 88.3 °C ($\Delta T_{g, \text{PMMA-ADADA}} \approx 14$ °C) and the T_g of chain extended PSt was surprisingly increased to 161.4 °C ($\Delta T_{g, (\text{PS-DADDAD}8\text{k})_n} \approx 50$ °C) while the mixture of $(\text{PS}_{\text{DADDAD}8\text{k}})_{n-2}$ and normal PMMA showed similar T_g comparing with homopolymers ($T_{g, \text{mix}} = 109.4$ °C). On the other hands, non-regular interaction pair of $(\text{PS}_{\text{DADDAD}3\text{k-r-PS}_{\text{DADDAD}8\text{k}})_n$ ($T_{g, \text{mix}} = 103.5$ °C) and its non-recognition pair ($T_{g, \text{mix}} = 114.5$ °C) indicated vicinal T_g values between homo polymer components. In other words, the

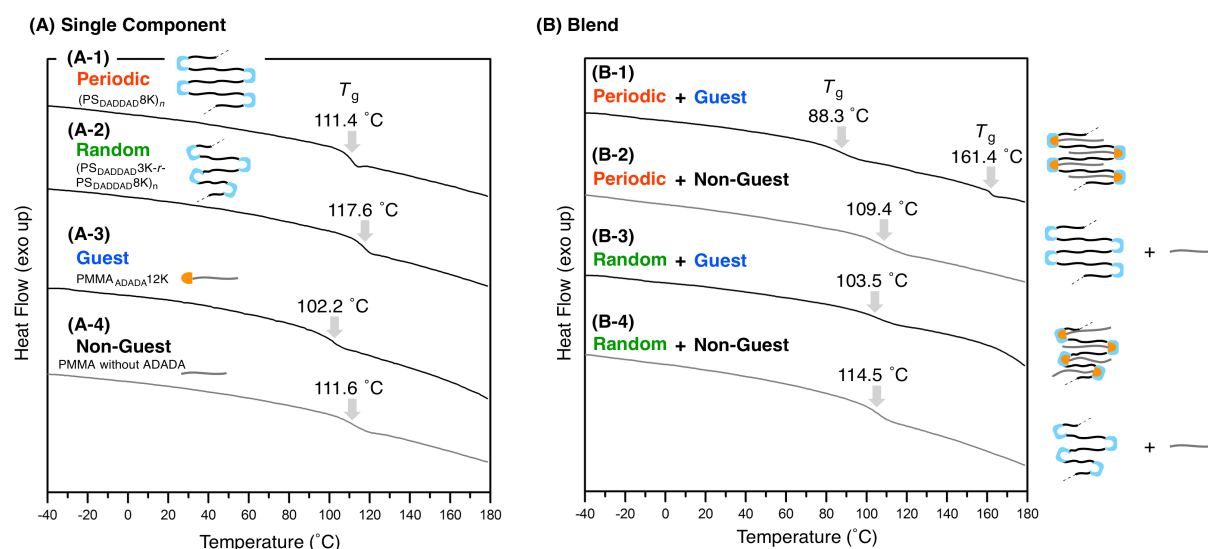


Figure 6. DSC thermograms of glass transition temperatures for (A) single component (homopolymers) and (B) their blends for periodic complementary hydrogen bonding interactions (heating and cooling rate: 5 °C/min).

variations of T_g for the complementary hydrogen bonding interaction at the random positions and non-interaction between polymers (with normal PMMA) showed similar thermal behavior thus the complementary hydrogen bonding interactions at the regular positions (well-defined positions) should influence to thermal property of polymer mixture. These results are likely due to array of PMMA, which was well separated by complementary interaction at the periodic positions indicating the thermal property of supramolecular polymer depends on interaction positions.

Conclusion

A chain extended poly(St) carrying periodically introduced Hamilton receptors (-DADDAD-) onto polymer chain was successfully synthesized by radical coupling polymerization from precisely controlled center-functional precursor (PS_{DADDAD}) with narrow MWD under the combination of Ru(Cp*) in conjunction with P(*n*-Bu)₃, EtOH, and 1,6-DAH. From this product, the author has demonstrated the supramolecular graft copolymer with regular intervals, which was comprised of complementary hydrogen bonds at the periodic programmed positions in the polymer backbone with complementary polymer pair (PMMA_{ADADA}). The complementary polymer-polymer recognitions at periodic programmed positions were characterized with SEC and ¹H NMR analysis in CDCl₃ revealed that the association constant of polymer pair, where it was much higher than initiator pair (Cl-DADDAD-cl and ADADA-Cl) and precursor pair (PS_{DADDAD} and PMMA_{ADADA}). The DSC analysis supported importance of periodic positions (well-controlled interactive sites) for supramolecular self-assembly compared with randomly introduced Hamilton receptors. Currently, the author is studying the phase separation of supramolecular graft copolymer with strong association, which will be presented in the near future.

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- (8) (a) Fielding, L. *Tetrahedron* **2000**, 56, 6151-6170. (b) Thordarson, P. *Chem. Soc. Rev.* **2011**, 40, 1305-1323. (c) Mathematical model chosen to determine K_{ass} : The data were fitted to the following equation to provide K_{a} :

$$\delta_{\text{mix}} = \delta_{\text{ADADA}} + \frac{(\delta_{\infty} - \delta_{\text{ADADA}}) \left[\left([\text{ADADA}] + [\text{DADDAD}] + \frac{1}{K_{\text{ass}}} \right) - \sqrt{\left([\text{ADADA}] + [\text{DADDAD}] + \frac{1}{K_{\text{ass}}} \right)^2 - 4[\text{ADADA}][\text{DADDAD}]} \right]}{2[\text{ADADA}]}$$

, where the experimental parameters are as follows,

[ADADA] and [DADDAD]: molar concentrations of ADADA- and DADDAD-functionalized compounds (i.e., initiators or polymers)

δ_{mix} : a chemical shift for NH proton of ADADA-functionalized compound for an equimolar mixture with DADDAD counterpart in ^1H NMR spectrum (H^a in Figure 3);

δ_{ADADA} : a chemical shift for NH proton of ADADA-functionalized compound;

K_{ass} : an association constant;

δ_{∞} : a saturated chemical shift for NH proton of ADADA-functionalized compound when an excess molar of DADDAD counterpart was mixed. The value was calculated from curve fitting with third degree polynomial for plots with various mixing ratios.

LIST OF PUBLICATIONS

Chapter 1

“Supramolecular X-Shaped Homo and Block Polymers by Mid-Segment Complementary Hydrogen-Bonds: Design of Bifunctional Initiators with Interactive Sites for Metal-Catalyzed Living Radical Polymerization”

Sang-Ho Lee, Makoto Ouchi, Mitsuo Sawamoto

Macromolecules, **2012**, 45, 3702-3710.

Chapter 2

“Chain Center-Functionalized Amphiphilic Block Polymers: Complementary Hydrogen Bond Self-Assembly in Aqueous Solution”

Sang-Ho Lee, Makoto Ouchi, Mitsuo Sawamoto

J. Polym. Sci., Part A: Polym. Chem., **2013**, 51, 4498-4504.

Chapter 3

“Chain Extension of Center-Functionalized Polystyrene via Radical-Radical Coupling: Periodic Introduction of Complementary Interaction Site on Polymer Chain”

Sang-Ho Lee, Makoto Ouchi, Mitsuo Sawamoto

to be submitted.

Chapter 4

“Functionalization at the Central Position of Vinyl Polymer Chains: Highly Associable Multipoint Hydrogen Bonds for Complementary Self-Assemblies”

Sang-Ho Lee, Makoto Ouchi, Mitsuo Sawamoto

Macromol. Rapid Commun., **2014**, 35, 431-436.

Chapter 5

“Periodic Introduction of Hamilton Receptors into Polystyrene Chain: Supramolecular Graft Copolymer with Regular Intervals”

Sang-Ho Lee, Makoto Ouchi, Mitsuo Sawamoto

to be submitted.

ACKNOWLEDGMENTS

This thesis presents the studies which were carried out from 2010 to 2014 at the Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University under the direction of Professor Mitsuo Sawamoto and Associate Professor Makoto Ouchi.

Fist of all, the author would like to express his sincere gratitude to Professor Mitsuo Sawamoto for his continuous guidance and encouragement throughout the course of this work. He is also grateful to Associate Professor Makoto Ouchi and Assistant Professor Takaya Terashima for their helpful suggestion and stimulating discussion.

The author acknowledges his appreciation to Professor Shinzaburo Ito and Professor Yoshiki Chujo for careful reviewing of this thesis and fruitful comment.

The author sincerely thanks the members of the Korea Institute of Science and Technology (KIST), particularly Dr. Kyung-Youl Baek, his previous supervisor, for hid discussion and kind advice about the way of life in Japan and Ms. Hyun-Ji Kim for her technical support in cryo-TEM analysis.

Sincere thanks should go to all the members of Sawamoto Laboratory for their constant suggestion and heartfelt friendship, particularly Dr. Yusuke Hibi and Mr. Yuta Koda for their discussion and help in experiments. The author is also obliged to Ms. Miro Takayama for her assistance during the author's campus life.

I am very grateful for financial support by the Grant-in-Aid for the Global COE Program, "International Center for Integrated Research and Advanced Education in Materials Science", the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan (2010-2014).

Finally, the author wishes to express his deep appreciation to his parents, Soong-Je Lee and Keum-Jua Choi, his aunt Jin-Hee Lee, his sister Ju-Hyun Lee, and his all family for their constant care and affectionate encouragement.

April 2014



Sang-Ho Lee

