# SYNTHESIS AND FUNCTIONALIZATION OF HYPERBRANCHED POLY(METHYL METHACRYLATE)

A Thesis

Presented to

The Graduate Faculty of the University of Akron

In Partial Fulfillment

Of the Requirement for the Degree

Master of Science

Chenying Zhao

August, 2019

SYNTHESIS AND FUNCTIONALIZATION OF HYPERBRANCHED

POLY(METHYL METHACRYLATE)

Chenying Zhao

Thesis

| | |
|---|---|
| Approved: | Accepted: |
| _____ | _____ |
| Advisor:<br>Coleen Pugh | Dean of the College<br>Dr. Ali Dhinojwala |
| _____ | _____ |
| Committee:<br>Dr. Chrys Wesdemiotis | Dean of Graduate School<br>Dr. Chand Midha |
| _____ | _____ |
| DepartmentChair<br>Dr. Tianbo Liu | Date |

## ABSTRACT

Hyperbranched polymers have unique physical and chemical properties that make them interesting to people in both academia and industry. One way to make hyperbranched polymers is to use self-condensing vinyl polymerization (SCVP).[1] Hyperbranched polymethacrylates can be prepared from methacrylate inimers (inimers are monomers that contain both initiation and polymerizable groups) by atom transfer radical polymerization (ATRP)[2] and self-condensing vinyl polymerization (SCVP).[3] The methyl methacrylate inimer was synthesized by reacting the carboxylic acid group of 2-bromo-3-hydroxy-2-methylpropionic acid with methacrylic acid and esterifying the alcohol group with methanol.[4] This methyl methacrylate inimer was then polymerized under atom transfer radical polymerization conditions.

Post-polymerization functionalization is often used to change and/or improve the properties of polymers. For hyperbranched polymers made by atom transfer radical polymerization, the halogen atoms (chlorine or bromine) remaining in the polymer backbone provide sites for post-polymerization functionalization. The halogen atoms in polymethacrylates are bonded to tertiary carbons, which are more hindered and less electrophilic than the halogen sites in hyperbranched polyacrylates, but are presumably more susceptible to cationic rearrangement. The hyperbranched poly(methyl methacrylate) is rearrangeable with heating and to give a primary bromine.

TABLE OF CONTENTS

LIST OF SCHEMES

LIST OF FIGURES

LIST OF TABLES

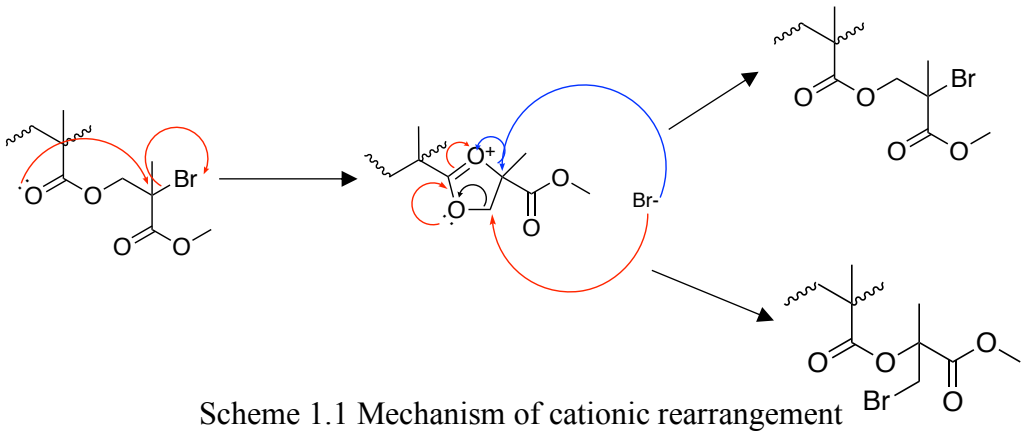
# CHAPTER I

## INTRODUCTION

Hyperbranched polymers have received much attention in both academic and industrial fields for their unique bulk properties such as enchanced solubility characteristics.[5] Hyperbranched polymers can be polymerized from $AB_n$ monomers,[6] self-condensing vinyl polymerization of an inimer,[7] self-condensing ring-opening polymerization of an inimer,[8, 9] and proton-transfer polymerization of an inimer.[3] In our previous work, we successfully produced hyperbranched polyacrylates using 3-hydroxyl-2-halopropionic acid with various ester groups[10-12] and some polymethacrylates with 2-bromo-3-hydroxyl-2-methyl propionic acid esterified with 1-butanol and 1-dodecanol.[4] Poly(methyl methacrylate) is a well-developed polymer material applied in multiple areas such as coatings, additives, light transmission and architectural structures. Compared to linear polymers, hyperbranched polymers have lower intrinsic viscosities at the same molecular weight and behave as non-Newtonian fluid. The hyperbranched poly(methyl methacrylate)s made in this thesis are truly architecture analogues of linear poly(methyl methacrylate)s. These hyperbranched poly(methyl methacrylate)s are prepared by polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate by atom transfer radical polymerization (ATRP). After

polymerization, the bromine atoms throughout in the polymer structure can be further reacted to introduce functional groups into the polymer.

Potential routes to functionalize the polymer are showing in Scheme 1.1. The bromine atom is a good leaving group but the carbon bonded to bromine is hindered by a methyl group. The hindrance introduced by the methyl group decreases the nucleophilic substitution accessibility but increase the possibility of rearrangement. The bromine in the polymer can regenerate a radical under atom transfer radical polymerization conditions and also be rearranged with heating to give a primary alkyl bromide. During the rearrangement, an dioxolenium intermediate would be produced.




Scheme 1.1 Mechanism of cationic rearrangement

# CHAPTER II

# LITERATURE REVIEW

## 2.1. Hyperbranched polymers

After years of development of polymers different, types of polymeric architectures were investigated. We could simply divide them into linear, branched, cyclic and crosslinked. Linear and crosslinked are the most usual types in our daily life. Branched polymers are more complicated and can be distinguished by more detailed structure features, such as stars,[13], combs,[14] dendrimers,[15] linear dendritic hybrids,[16] dendronized,[17] hypergrafted[18] and hyperbranched.[1] Hyperbranched polymers were first coined by Kim and Webster in 1988.[6] The properties of hyperbranched polymers are also similar to dendritic such as low viscosity, small shrinkage during phase transition from solution to solid, and low/no crystallization. But hyperbranched polymers were much easier in both polymerization and purification and provided engineers an alternative choice balancing price and properties. Therefore, hyperbranched polymers are highly valued in both academic and industrial areas. Compared to linear polymers, hyperbranched polymers show unique physical and chemical properties. The viscosity of hyperbranched polymers are lower than linear analogues in both molten and solution state.[19] Generally, the relationship between solution viscosity and

molecular weight can be analyzed by the Mark-Houwink-Sakurada equation. The $\kappa$ and $\alpha$ are constants to a certain solvent-polymer solution at a certain temperature.

$$[\eta] = \kappa M_w^{\alpha}$$ *Mark-Houwink-Sakurada Equation*

Chang and Fréchet defined the intrinsic viscosity as a function of the logarithm molar mass, they found that hyperbranched polymers exhibited a skewed gaussian distribution relationship and did not obey the Mark-Houwink-Sakurada relationship (shows in Figure 2.1). The slope of hyperbranched polymers was smaller than the slope for linear polymers and increased with increasing molecular weight. This phenomenon could be explained by entanglements in hyperbranched polymers and indicated the globular shape of hyperbranched polymers. The $\alpha$ was between 0.5 to 1 for a linear polymer and smaller than 0.5 when it comes to hyperbranched polymer.[5, 19]

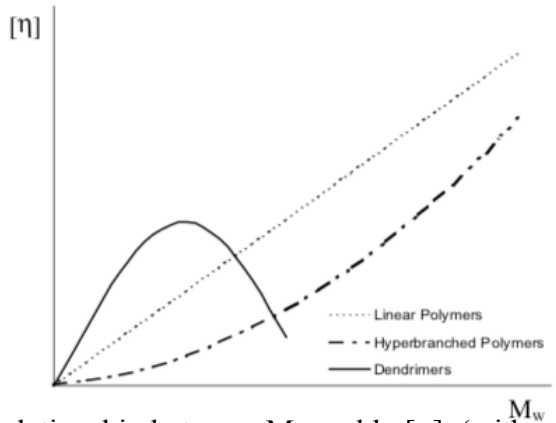



Figure 2.1 Relationship between $M_w$ and lg $[\eta]$. (with permission from ref. 5. Copyright 2004, Elsevier)

According to review by Dr. Smith,[20] hyperbranched polymers attracted people by their highly branched topological structures, numerous functional groups, one-pot synthetic procedures, especially in biology applications. Scientists and engineers already apply hyperbranched polymers into photoelectric materials, nanomaterials, coating, modifiers, sensors, adhesives et. al.[20]

2.2. Atom Transfer Radical Polymerization

Atom transfer radical polymerization is one of the most well-known approaches to realize living radical polymerization. An important features of living polymerizations is no irreversible terminations.[21] Conventional radical polymerizations present very limited control acting as bimolecular terminations due to the high reactivity of the radicals and slow initiation. [22]

The following equations show the propagating rate and bimolecular termination rate in a radical polymerization system. Those rates are closely related to propagating center concentration.

$R_p = k_p\,[M][M\cdot]$ Propagation rate.

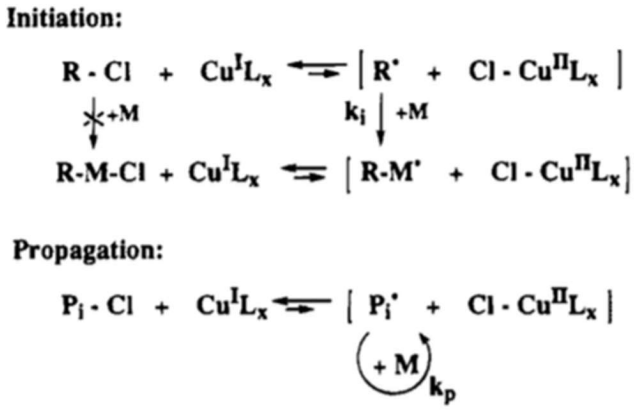
$R_{\,termination} = k_{ter}[M\cdot]^2$ Bimolecular Termination Rate.

The $k_{ter}$ for termination was much larger than $k_p$ . Consequently, irreversible terminations happens once propagating centers encounter each other. The termination rate is determined by the concentration of propagating radicals. The reduction of propagating centers causes more changes to termination than propagation since the propagation rate is 1st order and termination is 2nd in order to radical concentration. Decreasing the radicals' concentration slows down the propagation but the decreasing in terminations was more

obvious. In this way, the termination is ignorable comparing to propagation, and living radical polymerization is achieved.

For controlling radical polymerization, there are three main categories: nitroxide-mediated polymerization (NMP),[23] atom transfer radical polymerization (ATRP),[2] and reversible addition-fragmentation chain transfer polymerization (RAFT).[24] The method used in our work is atom transfer radical polymerization.

Classical atom transfer radical polymerizations systems contain: initiator, monomer, ligands, Cu(I)/Cu(II). As shown in Scheme 2.1, a reversible termination equilibrium is established in atom transfer radical polymerizations system.




Scheme 2.1 The ATRP mechanism. (with permission from ref. 2. 1995, American Chemical Society)

Atom transfer radical polymerization realized the control over propagating radicals (decrease the radical concentration) by the equilibrium (Scheme 2.1) between the propagating radicals and dormant species ($P_i$·Cl). The dormant species reacts with copper-ligand complex at lower oxidation state ($Cu^IL_x$), producing propagating radicals ($P_i$ ·) and

the deactivators ($Cl \cdot Cu^{II}L_x$). The deactivators reacted with propagating radicals in a reversible reaction and reformed the dormant species and activators. [2]

The propagation rate of ATRP is decided by the rate constant of polymerization, the concentration of monomer and the concentration of the propagating radicals, like all other radical polymerizations. Since the propagating radicals are not consumed during the propagation in ATRP systems, the concentration of propagating radicals depend on the concentration of the activators, deactivators, dormant species and the equilibrium constant of the reversible termination reaction according to the equation of propagating rate in ATRP system. [25]

$$Rp = k_p[M][P_i \cdot] = k_p K_{ATRP} \left( \frac{[P_i X]\left[\frac{Cu^I}{L_x}\right][M]}{[X - \frac{Cu^{II}}{L}]} \right)$$ propagating rate in ATRP system

This equilibrium was designed to decrease the concentration of the propagating radicals. The concentration of propagating radicals in ATRP system was low, because most of the growing chains are in dormant, favoring the deactivated state. As stated before, the uncontrollability of radical polymerization is derived from radicals' high reactivity and tendency to terminate. The equilibrium efficiently limited the concentration of propagating radicals in ATRP system and minimize irreversible terminations relative to propagation. Therefore, we presumed that irreversible termination was not detectable in this polymerization system and appeared to be a living polymerization.

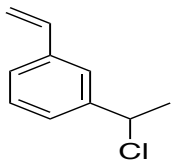
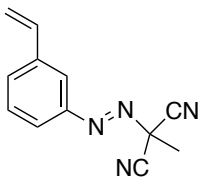
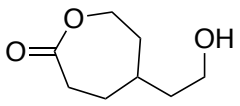
2.3. Synthesis of Hyperbranched Polymers

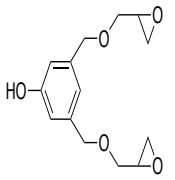
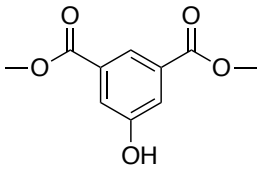
The synthetic methods of hyperbranched polymers can be divided into four categories: single-monomer methodology (SMM), double-monomer methodology (DMM),[26] couple-

monomer methodology (CMM)[27] and multi-component methodology (MCM).[28] For the single-monomer methodology, there are four approaches: Polycondensation of $AB_n$ monomers;[6] self-condensing vinyl polymerization of inimer (SCVP);[7] self-condensing ring-opening polymerization of inimer (SCROP)[8] and proton transfer polymerization of inimer (PTP).[3]

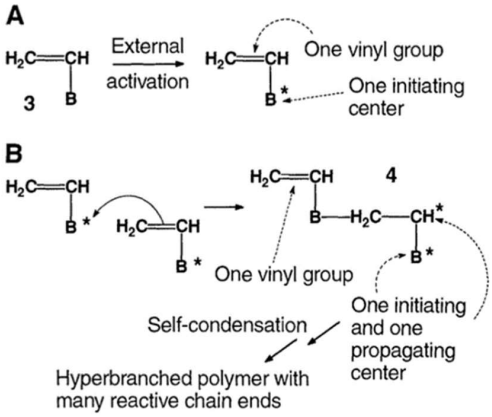
The polycondensation of $AB_n$ monomers to produce hyperbranched polymers was predicted by Flory in 1952.[29, 30] Various of hyperbranched polymers were synthesized after Flory's theories, including polyphenylenes,[6] polyesters,[31] poly(ether ketone)s,[32] and polyamides.[33] Furthermore, addition reactions can also involve in making hyperbranched polymers.

Aside from these step-growth polymerizations, chain-growth polymerizations were also developed in producing hyperbranched polymers, including self-condensing vinyl polymerization and self-condensing ring-opening polymerization. The monomer of self-condensing vinyl polymerization and self-condensing ring-opening polymerization shared a basic feature that the monomer included both polymerizable groups and initiation groups.

| Type | Monomer | Ref. | Monomer | Ref. |
|---|---|---|---|---|
| SCVP |  | 7 |  | [34] |
| SCROP |  | 9 |  | [35] |

| | | | | |
|---|---|---|---|---|
| PTP |  | 3 |  | 36 |

Nuyken et al.[37] reported that a branched structure were formed during the synthesis of $\alpha$-*tert*-butyl-$\omega$-[*p*-vinylphenyl]-terminated poly(2-methylpropene) macromonomers by using 4-chloromethylstyrene, triethylaluminium and water initiated d2-methylpropene. After that, using initiator-monomer to polymerize hyperbranched polymers in one-pot was reported by




Scheme 2.2 The self-condensing vinyl polymerization mechanism. (with permission from ref. 7. Copyright 1995, The American Association for the Advancement of Science)

Fréchet.[7]

Scheme 2.2 shows the scheme of self-condensing vinyl polymerization.[7] The monomer contains two functional groups: group A is the vinyl group and group B is the initiator. The

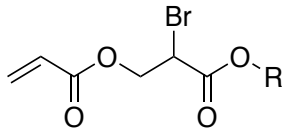
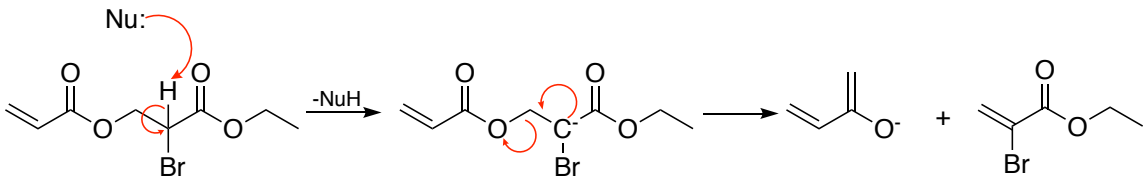


Figure 2.2 acrylate inimers

activated B group could initiate an A group on another monomer to generate a dimer. This dimer has a double bond, an initiation center and a propagating center. The initiation center and the propagating center may have the same reactivity. Consequently, the inimer is transformed to $AB_2$ type monomer and produce hyperbranched polymers.

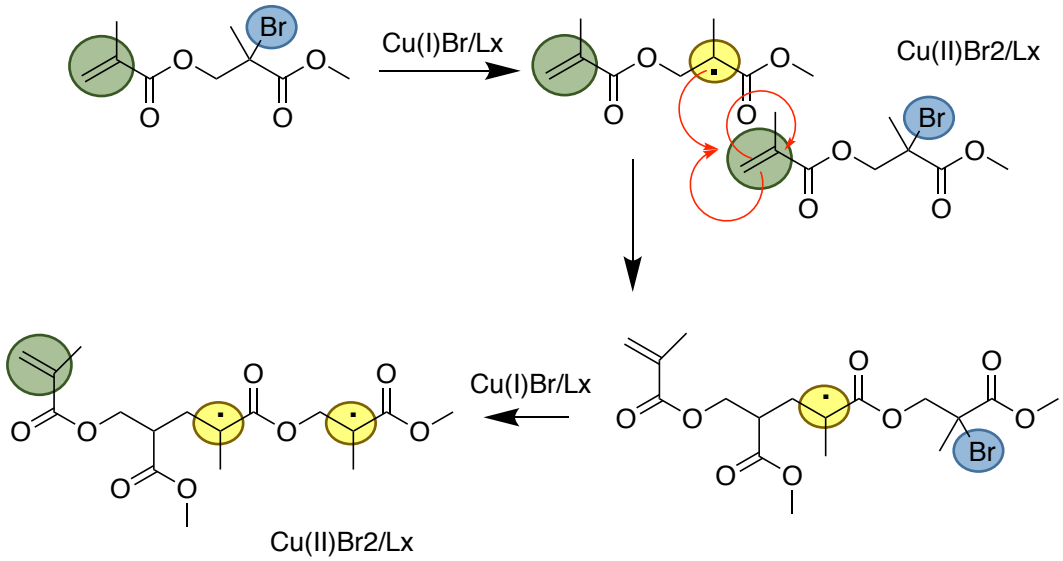
Atom transfer radical polymerization has been applied to produce hyperbranched polymers for years. If we introduce the halogenatecarbon into the ester group of acrylate/methacrylate, which could act as initiation group and polymerizes under ATRP mechanism. In our previous work,[10-12] a series of acrylate inimers were developed based on the 3-hydroxy-2-




Scheme 2.3 The $\beta$-elimination of butyl acrylate inimer with nucleophile.

bromopropionic acid structure. Figure 2.2 shows the structure of the acrylate inimers. R corresponds to different ester groups such as: alkyl groups, aromatic groups, sugars and et al. This monomer contained a vinyl bond, which was the polymerizable group and a brominate carbon as a pendent group, which could be activated and initiated a radical and propagation under atom transfer radical polymerization scheme. It was reported by previous students in our group that this kind of monomer had elimination problems in the presence of a basic ligand such as PMDETA.[11] After years of research, this elimination scheme was speculated and showed in in Scheme 2.3. We predicted that this elimination could be avoiding by substitute the hydrogen with a methyl group. As a consequence, the methacrylate inimers' structure was developed.

Liu developed the synthesis route of 2-methyl-3-hydroxyl-2-bromopropionic acid, which was flawlessly analogs to methacrylate monomers. And the radical from this type pendent group has familiar reactivity to linear methacrylate's radicals. The methacrylate inimers for hyperbranched poly(methacrylate)s were synthesized based on 2-methyl-3-hydroxyl-2-bromopropionic acid with various linear alkyl groups and polymerized under conventional ATRP conditions (polymerization scheme shows in Scheme 2.4) to produce hyperbranched poly(methacrylate).[4]

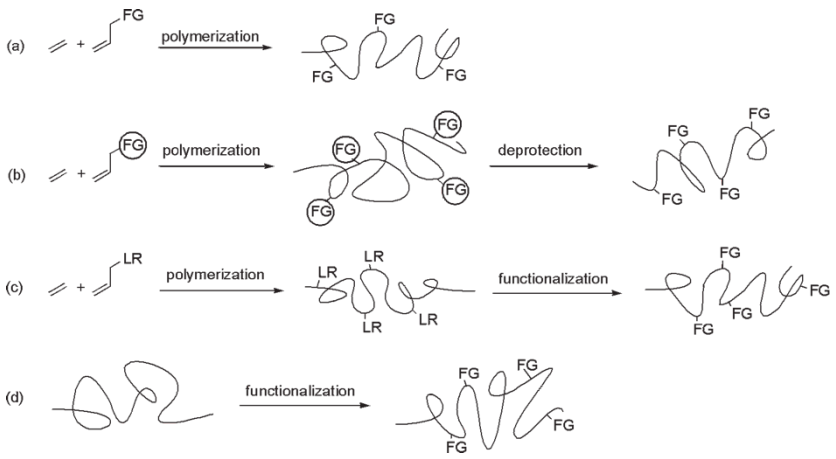



Scheme 2.4 The mechanism of methyl methacrylate inimer react under SCVP mechanism.

## 2.4. Introduce functional groups to polymers

To introduce functional groups to polymer, we could use functional monomers, functional initiators and post-polymerization.[38, 39] In the polymer backbone, the initiator only contributs very tiny amounts to the whole polymer chain and can't influence the properties of polymer chain. Consequently, end-capping is generally not considered as a methodology to functionalize polymer chains. There were various monomers with different functional

groups and it is easy to introduce these functional monomers into polymerizations. But these functional groups may introduced reactivity differences into the monomer, leading to composition variances in the copolymers or even making them not polymerizable. [40, 41] Post-polymerization was coined during transformation of natural rubber with sulfur. The advantage of post-polymerization is that the degree of polymerization can be maintained during the functionalization, but post-polymerization requires reaction sites on the polymer. Figure 2.3 shows four approaches provided by Boaen et al.[39] Approach (a) directly introduces functional groups by directly polymerizing functional monomers. Approaches (b), (c), and (d) introduce functional monomers and post-polymerizations. Approach (b)




Scheme 2.5 Four approaches to introduce functional groups into polymers. (with permission from ref. 39. Copyright 2005, Royal Society of Chemistry)

uses a protected monomer participates in the polymerization and then deprotects the target functional groups after polymerization. Approach (c) uses tolerant, latent reactivated monomers and subsequent functionalization is carried on the polymer. Apporach (d) is direct post-polymerization on an un-modified polymer.

Post-polymerization is a commonly used method to introduce functional groups in polymer chains. Mechanistically, substitutions, additions, eliminations and isomerization can be carried out on polymer chains (shown in Figure 2.4).[42] Addition reactions in post-polymerization generally are like their small molecule counterparts. Furthermore, additions of small molecules to polymer via radical chain reactions was also used in post-polymerization. Substitution reactions are the most important for post-polymerization

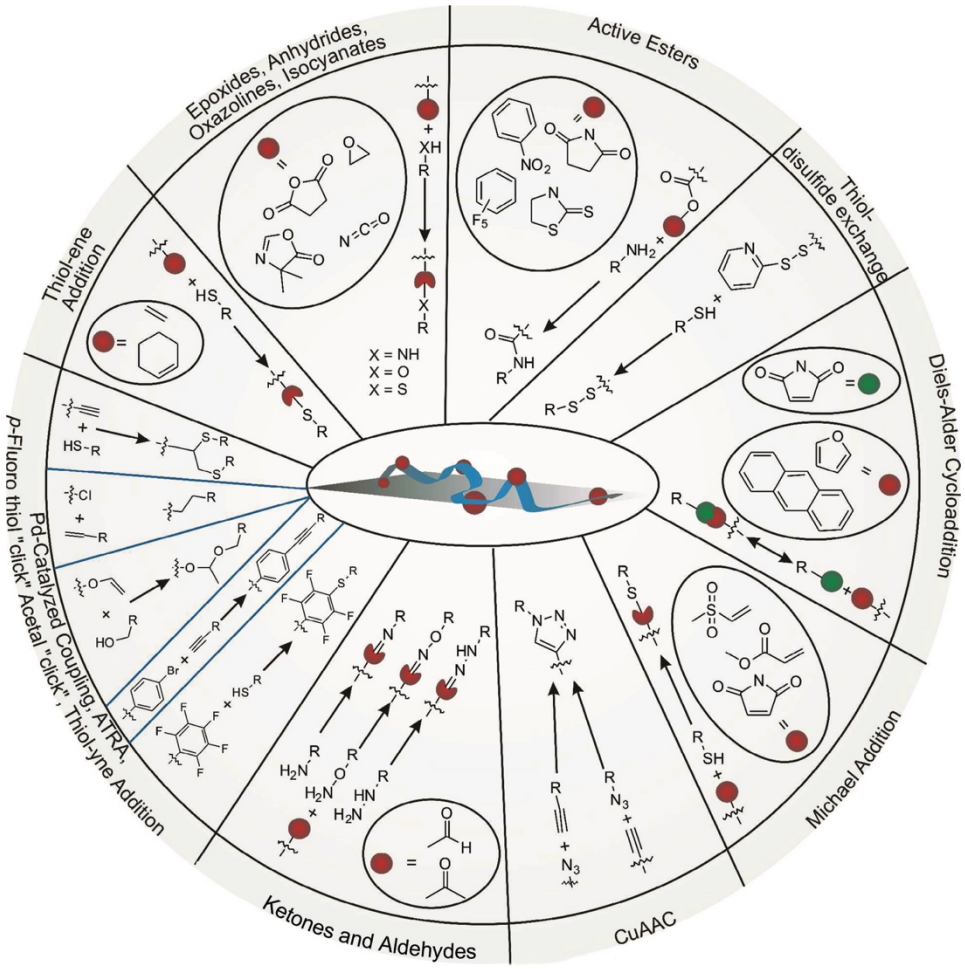



Figure 2.3 Main classes of reactions that can be used for the preparation of functionalized polymers via post-polymerization modification. (with permission from ref. 42. Copyright 2012, John Wiley and Sons)

because they can introduce various functional groups and involve many reaction types, including free radical substitutions, esterifications, amidations, hydrolysis, oxidations and reductions. Dehydrogenations and dehydrations can also happen on polymers and result in unsaturated or conjugated polymers as post-polymerization via eliminations. Although IUPAC does not regard isomerization as a modification approach, isomerization is worth being considered as a post-polymerization approach as it changes the configuration of the polymer chains. Theoretically, the isomerization will cause no change to the molecular weight of polymers.

For hyperbranched poly(methacrylate)s produced by ATRP, the bromine atom on the inimer plays two roles. The first role is as a pendent group that can be activated into the propagating radical for the self-condensing vinyl polymerization to produce hyperbranched polymers. The second role is the group with latent reactivity to incorporate the later post-polymerization. It is a functional group along the polymer and the end group.

In the publications from Coessens,[38, 43, 44] the accessibility of the nucleophilic substitution at the polymer end group (bromine or chlorine) produced by atom transfer radical polymerization was explored. Azide groups, amine groups (reduction of azide groups), acetate groups, phosphonium ion groups, hydroxyl groups (with *n*-butanolamine) were successfully substituted on the polyacrylate.[38] They also reported that the reactivity of poly(methyl methacrylate) was much lower than poly(methyl acrylate). Poly(methyl acrylate) reacted with 1.1 equivalents of sodium azide to reach conversion over 90% while for poly(methyl methacrylate), there was only about 40%.[38]

3-Hydroxyl-2-bromopropionic acid was used to synthesize hyperbranched poly(acrylates) and functionalized poly(lactic acid). To introduce functional groups into poly(lactic acid), we copolymerize lactic acid with 3-hydroxyl-2-bromopropionic acid, and the bromine introduced functional groups with latent reactivity to the polymer. The nucleophilic substitution reactions were successfully with sodium iodide and sodium azide on this copolymer.[45]

# CHAPTER III

# EXPERIMENTAL SECTION

## 3.1 Materials

Acetyl chloride (CAS 75-36-5, Tokyo Chemical Industrial, 98+%), D,L-alanine (CAS 302-72-7, Alfa Aesar, 99%), calcium oxide (CAS 1305-778-8, Honeywell, 96%), cupric sulfate pentahydrate (CAS 7758-99-8, Aldrich, 98+%), formaldehyde aqueous solution (CAS 50-00-0, Fisher, 37 wt%), hydrobromic acid aqueous solution (CAS 10035-10-6, EMD, 48%), magnesium sulfate (CAS 7487-88-9, Mallinckrodt, 98%), methacrylic anhydride (CAS 7760-93-0, Aldrich, 94%), N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA, CAS 3030-46-7, Fisher, 100%), phosphorus pentachloride (CAS 10026-10-6, STREM Chemical, 98%), polyethyleneimine branched (CAS 9002-98-6, Sigma Aldrich, $M_n$= 600 Da, $M_w$= 800 Da), potassium bromide (CAS 7760-93-0, Fisher, 98%), potassium carbonate (CAS 584-08-7，J.T.Baker, 99%), potassium hydroxide (CAS 1310-73-2, Fisher, 85%), sodium bicarbonate (CAS 144-55-8, J.T.Baker, 98%), sodium chloride (CAS 7647-14-5, Aldon, 98%), sodium nitrite (CAS 7632-00-0, Duda Disel, 99%), *p*-toluenesulfonic acid anhydride (CAS 104-14-4，) were used as recieved. Cuprous(I) bromide (CAS 7787-70-4, Alfa Aesar, 98%) was regenerated over acetic acid (CAS 64-19-7, Fisher, 100%) and

washed with methanol and diethyl ether till white, and dried under vacuum at room temperature.[46] Methanol (CAS 67-56-1, Fisher, 99%) was distilled from calcium oxide and stored over 4 Å molecular sieves. Triethylamine (CAS 121-44-8, J.T.Baker, 99%) was stirred over potassium hydroxide for 4 hours and distilled under nitrogen, and stored over potassium hydroxide. Reagent grade tetrahydrofuran (THF) was dried by distillation from purple sodium benzophenone ketyl under nitrogen. All other reactants and solvents were commercially available and used as received.

3.2 Techniques

NMR: $^{1}$H (300 MHz) and $^{13}$C (75 MHz) NMR spectra ($\delta$, ppm) were recorded on a Varian Mercury instrument. All the resonances were measured relative to residual solvent resonances.

GPC: Number-average ($M_n$) and weight average ($M_w$) molecular weights relative to linear polystyrene ($GPC_{PSt}$), and polydispersity (PDI=$M_w/M_n$) was determined by gel permeation chromatography (GPC) from calibration curve of log($M_n$) vs elution volume at 35 ℃ using THF as eluent (1.0 mL/min), a Phenogel guard column and set of 50 Å (Phenogel), 100 Å (Styragel), 500 Å (Styragel), $10^4$ Å (Styragel) and 2 linear (50-$10^6$ Å) Styragel 5 mm columns, a Waters 486 tunable UV/vis detector set at 254 nm, a Waters 410 differential refractometer and Millenium Empower 3 software. The samples were dissolved and filtered through a 0.45 $\mu m$ PTFE filter.

3.3 Synthesis of 2-amino-3-hydroxyl-2-methylpropionic acid

2-Amino-3-hydroxyl-2-methyl propionic acid was synthesized by the Alkabori reaction, published by Otani and Winitz.[47] This reaction reached 100% conversion in 60 minutes.

Potassium carbonate (31.1 g, 0.22 mol) was dissolved in DI water (1050 mL) a. This solution was stirred and heated to boil with heating mantle. D,L-alanine (10.0 g, 0.11 mol), 1M cupric sulfate (11.2 mL, 0.0112 mol) and 50 mL DI water were added at once into the system while refluxing. Heating to boiling again, 37% formaldehyde aqueous solution (33 mL, 0.42 mol) was added at once while refluxing. The blue solution was stirred at reflux with a water condenser for 60 minutes. After 60 minutes, the solution turned purple with red precipitates. The red precipitates were removed by filteration. The solution was neutralized with hydrobromic acid (50 mL, 48 % aqueous solutions, 0.22 mol) and the solution was concentrated by boiling off the solvent at 90℃ to 150 mL. $^{1}$H NMR (300 MHz, Deuterium Oxide) $\delta$ = 1.62 (s, C$H_3$), 3.83 (d, CH*H*OH, $^{2}$J = 12.4 Hz), 4.08 (d, C*H*HOH, $^{2}$J = 12.4 Hz).

3.4 Synthesis of 2-bromo-3-hydroxy-2-methylpropionic acid

2-Bromo-3-hydroxy-2-methylpropionic acid was synthesized from 2-methylserine by deaminohalogenation. This method was reported in the previous work of our group and resulted in 17-24% yield as follows. The concentrated solution of 2-amino-3-hydroxy-2-methyl propionic acid was transferred to a 250 mL 3-neck round bottom flask and potassium bromide (21.1g, 0.117 mol) was added at once. The solution was cooled to -15 ℃ aided by saturated calcium chloride solution and dry ice. The solution was acidified with hydrobromic acid (38mL, 48% aq, 0.33 mol,) at 0 ℃. Keep cooling down the solution with dry ice till -10 ℃ to -15 ℃. Sodium nitrite (19.5g, 0.282 mol) was added slowly over 45 minutes at -10 ℃ to -15 ℃. The ice bath was removed after finishing adding sodium nitrite. After stirring at room temperature for 17 hours, the brown solution was saturated

with sodium chloride, and then extracted with diethyl ether (50 mL × 10 = 500 mL). The organic layers were combined and washed with saturated sodium chloride aqueous solution (100 mL × 3 = 300 mL) and dried over magnesium sulfate. The solvent was evaporated at room temperature by open to air and got yellow transparent crystal. The crude product was recrystallized in dichloromethane (120 mL) at boiling to obtain 4.96 g (yield 24%) of 2-bromo-3-hydroxyl-2-methylpropionic acid as white crystals. $^{1}$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1.97 (s, C*H*$_3$), 3.85 (d, CH*H*OH, $^{2}$J = 12.1 Hz), 4.06 (d, CH*H*OH, $^{2}$J = 12.0 Hz).

3.5 Synthesis of 2-bromo-3-(methacryloyloxy)-2-methyl propanoic acid

2-Bromo-3-(methacryloyloxy)-2-methylpropanoic acid was synthesis by esterification of 2-bromo-3-hydroxyl-2-methylpropionic acid with methacrylic anhydride. To increase the reaction efficiency, we used methacrylic anhydride and *p*-toluenesulfonic acid. 2-Bromo-3-hydroxyl-2-methylpropionic acid (2.7408 g, 0.0150 mol), methacrylic anhydride (2.900 mL, 0.0195 mol) and *p*-toluenesulfonic acid (0.2152 g, 0.0011 mol) were added to a 50 mL round bottom flask at once and the system was stirred at room temperature for 20 hours. The mixtue became transparent, orange and viscous liquid after reaction. The reaction mixture was stirred with 30 mL saturated sodium chloride aqueous for 30 minutes and extracted with dichloromethane (10 mL × 3 = 30 mL). And the organic layer was washed with saturated sodium chloride aqueous (15 mL). The dichloromethane was evaporated at room temperature by open to air and produced white crystal. The crystal was recrystallized in boiling hexane (80 mL) and obtain 2.3598 g (yield 64%) target product as white crystals. $^{1}$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1.95 (s, *C*H$_3$C=), 1.97 (s, C*H*$_3$CBr), 4.51 (d, CH*H*OH, $^{2}$J

= 11.4 Hz), 4.64 (d, CH*H*OH, $^2$J = 11.4 Hz), 5.62 (s, CH$H_b$ = *trans* to $CO_2$), 6.13 (s, C$H_a$H = *cis* to $CO_2$).

3.6 Synthesis of 2-bromo-3-chloro-2-methyl-3-oxopropyl methacrylate

The carboxylic acid group was converted to an acid chloride to increase the reactivity of the 2-bromo-3-(methacryloyloxy)-2-methyl propanoic acid in the esterification. The chloroformylation reaction has a yield between 85% to 92% using the procedure as following. The reaction was carried in a round bottom flask. 2-Bromo-3-(methacryloyloxy)-2-methylpropanoic acid (3.1401 g, 0.0125 mol) and phosphorous pentachloride (3.4532 g, 0.0166mol) were added to the round bottom flask and stirred at room temperature for 1 to 4 hours. After reaction, it became bright yellow transparent liquid. The produced byproduct was removed by vacuum at room temperature and the product was distilled under vacuum (45-65 ℃/1 mm Hg) and the product 3.0245 g (yield 89.6%) was collected at 0 ℃ as transparent and colorless liquid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1. 94 (s, C$H_3$C=), 2.03 (s, *CH*$_3$CBr), 4.55 (d, CH*H*OH, $^2$J = 11.6 Hz), 4.69 (d, CH*H*OH, $^2$J = 11.6 Hz), 5.64 (s, CH$H_b$ = *trans* to $CO_2$), 6.12 (s, C$H_a$H = *cis* to $CO_2$),

3.7 Synthesis of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate

2-bromo-3-chloro-2-methyl-3-oxopropyl methacrylate was esterified with methanol in dry THF in the presence of triethylamine in 38% to 67% yield. Dry THF (40 mL) as the solvent and was added to a round bottom flask with dry triethylamine (2.00 mL, 0.0143 mol) and dry methanol (0.59 mL, 0.0146 mol). The 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate (3.0235 g, 0.0112 mol) was diluted with dry THF (10 mL) and added to an additional funnel. The 2-bromo-3-chloro-2-methyl-3-oxopropyl methacrylate solution was

added to the round bottom flask drop by drop over 20 minutes at 0℃ while stirring. After finishing adding the 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate, the reaction was carried out at room temperature for 17 hours. After the reaction, the triethylamonium chloride was removed by filtration and the solvent was removed by rotary evaporator. To remove the by-product 2-bromo-3-(methacryloyloxy)-2-methylpropanoic acid (preinimer), we used column chromatography with dichloromethane as eluent and the $Rf_1$= 0.84 $Rf_2$= 0.32 for the product and by-product. After the column, this reaction obtained 1.42 g (yield 47%) pure product as colorless transparent liquid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1.93 (s, C*H*$_3$CBr and *CH*$_3$C=), 4.48 (d, CH*H*OH, $^2$J = 12.8 Hz), 4.61 (d, CH*H*OH, $^2$J = 11.3 Hz), 5.60 (s, CH$H_b$ = *trans* to $CO_2$), 6.10 (s, C$H_a$H = *cis* to $CO_2$). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 18.32 (*C*H$_3$C=), 25.64 (*C*H$_3$CBr), 53.51 (*C*H$_3$O), 55.24 (*C*Br), 69.32 (*C*H$_2$), 126.62 (*C*H$_2$=), 153.68 (CH$_3$*C*=), 166.26 (methacrylate *C*=O), 170.09 (CBr*C*=O).

3.8 Synthesis of methyl 2-bromo-3-hydroxy-2-methylpropanoate

The methyl 2-bromo-3-hydroxy-2-methylpropanoate was synthesis by reacting 2-bromo-3-hydroxy-2-methylpropionic acid with methanol catalyzed by hydrobromic acid at refluxing. 2-Bromo-3-hydroxy-2-methyl propionate (3.60 g, 0.0186 mol) and methanol (25 mL, 0.6180 mol) was added to a round bottom flask and stirred till dissolve. Then, 5 drops of hydrobromic acid was added to the solution. The esterification was carried at refluxing while stirring for 17 hours. The solvent was removed by rotary evaporator. After removing the solvent, we obtained a yellow oily liquid. The liquid was diluted with 50 mL dichloromethane and washed twice with saturated sodium bicarbonate solution (25 mL × 2 = 50 mL) and once with saturated sodium chloride solution (25 mL). The organic layer

was dried over magnesium sulfate. After removing the magnesium sulfate by filtration, the solvent was removed by rotary evaporator and the residue was distilled (65-80 ℃/1 mm Hg) to yield 1.8326 g (yield 50%) of methyl 2-bromo-3-hydroxy-2-methylpropionate as slightly yellow oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1.94 (C*H*$_3$CBr), 3.82 (C*H*$_3$OOC), 3.83 (CH*H*OH), 4.02 (CH*H*OH).

3.9 Synthesis of methyl 3-acetoxy-2-bromo-2-methylpropanoate

A solution of acetyl chloride (0.84 mL, 0.0118 mol) in dry diethyl ether (5mL) was added dropwise over 15 minutes via an additional funnel to the solution of methyl 2-bromo-3-hydroxy-2-methylpropionate (1.8326 g, 0.0093 mol) and triethylamine (1.72 mL, 0.0123 mol) in dry diethyl ether (30 mL) at 0 ℃. The reaction mixture was then stirred at room temperature for 17 hours. After the reaction, the mixture was filtered and poured in to ice water (50 mL) and then extracted the ice solution with diethyl ether (25 mL × 4 = 100 mL) and the organic layer was combined and dried over magnesium sulfate. After filtration, the solvent was removed by rotary evaporation and then distilled out (85-90 ℃/1 mm Hg) to yield 1.1075g (yield 49%) colorless transparent liquid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 1.92 (s, C*H*$_3$CBr), 2.08 (s, *CH*$_3$C=O), 4.42 (d, CH*H*OH, $^2$J = 11.3 Hz), 4.55 (d, CH*H*OH, $^2$J = 11.3 Hz). C NMR (75 MHz, $CDCl_3$) $\delta$= 20.80 (*C*H$_3$C=O), 25.47 (*C*H$_3$CBr), 53.55 (*C*H$_3$O), 55.09 (*C*Br), 69.04 (*C*H$_2$CBr), 170.09 (*C*=O).

3.10 ATRP of methyl 2-bromo-3-methacryloxy-2-methylpropionate with PMDETA as ligand in toluene

In a typical procedure, Cu(I)Br (0.0018 g, 0.012 mmol) was added to a dry Schlenk tube and evacuated at room temperature. The tube was refilled with nitrogen and then PMDETA

(0.0023 g, 0.013 mmol) and toluene (0.1 mL) were added under nitrogen. The mixture was stirring under nitrogen at room temperature for 5 minutes. Then, a solution of inimer (0.1445 g, 0.545 mmol), toluene (0.2 mL) and drops of DMF was added under nitrogen. The mixture was degassed by 5 freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes) cycles and the tube was refilled with nitrogen. The polymerization mixture was placed in a 90 ℃ oil bath and stirred for 24 hours. The reaction was quenched by immersing the tube in liquid nitrogen and exposing to air to thaw. Then, the reaction mixture was diluted with THF and passed through basic alumina, obtained colorless solution. The solution was concentrated by rotary evaporator to about 0.5 mL and added in 3 mL cold methanol, but no precipitation observed.

3.11 ATRP of methyl 2-bromo-3-methacryloxy-2-methylpropionate with PMDETA as ligand in dioxane

In a typical procedure, Cu(I)Br (0.0013 g, 0.009 mmol) was added to a dry Schlenk tube and evacuated at room temperature. The tube was refilled with nitrogen and then PMDETA (0.0021 g, 0.012 mmol) and dioxane (0.1 mL) were added under nitrogen. The mixture was stirred under nitrogen at room temperature for 5 minutes. Then, a solution of inimer (0.2003 g, 0.755 mmol), dioxane (0.1 mL) and drops of DMF were added under nitrogen. the mixture was degassed by 5 freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes) cycles and the tube was refilled with nitrogen. The polymerization mixture was placed in 80℃ oil bath and stirred for 24 hours. The reaction was quenched by immersing in liquid nitrogen and exposing to air to thaw. After the reaction, the mixture was diluted with THF and passed through basic alumina and obtained colorless solution. The solution was concentrated by

rotary evaporator to about 0.5 mL and added to in 5 mL cold methanol, but no precipitation obtained.

3.12 ATRP of methyl 2-bromo-3-methacryloxy-2-methylpropionate with PMDETA as lingand in THF

In a typical procedure, Cu(I)Br (0.0039 g, 0.027 mmol) was added to a dry Schlenk tube and evacuated at room temperature. The tube was refilled with nitrogen and then PMDETA (0.0048 g, 0.028 mmol) and THF (0.45 mL) were added under nitrogen. The mixture was stirred under nitrogen at room temperature for 5 minutes. Then, a solution of inimer (0.7164 g, 2.702 mmol), THF (0.45 mL) and drops of DMF were added under nitrogen. the mixture was degassed by 5 freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes) cycles and the tube was refilled with nitrogen. The polymerization mixture was placed in 50℃ oil bath stirring for 23 hours and quenched by immersing in liquid nitrogen. Then, the tube was exposed to air and thawed. The mixture was diluted with THF and passed through basic alumina as colorless solution. The solution was removed by rotary evaporator to about 0.3 mL and added to in 3 mL cold methanol directly, obtained 0.074 g product (yield 10%). $M_n$= 1,675 Da, $M_w$= 42,180 Da, PDI=20.91.

3.13 ATRP of methyl 2-bromo-3-methacryloxy-2-methylpropionate with PEI as ligand in dioxane

All of the ATRPs of methyl 2-bromo-3-methacryloxy-2-methylpropionate using polyethyleneimine as ligand in dioxane were carried out in the following procedure. The concentration (methyl 2-bromo-3-methyacryloxy-2-methylpropionate/dioxane= mmol/mL)

of the reaction was varyied from 0.8 mmol/mL to 3 mmol/mL. The following is an example of ATRP of the methyl inimer in dioxane with polyethyleneimine.

In a typical procedure, Cu(I)Br (0.0012 g, 0.008 mmol) was added to a Schlenk tube and evacuated at room temperature. After refilling the Schlenk tube with nitrogen, polyethyleneimine stock solution (3.0 $\mu$L, 400 mg/mL in toluene, 0.028 mmol) was added to the Schlenk tube under nitrogen and stirred for 5 minutes. Then, toluene was removed under vacuum. 2-Bromo-3-methacryloxy-2-methylpropionate (0.2437 g, 0.919 mmol), dioxane (0.3 mL) and drops of DMF were added to the Schlenk tube under nitrogen. After stirring at room temperature for 5 minutes, the mixture was degassed by 5 cycles of freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes) and then the Schlenk tube was refilled with nitrogen. the Schlenk tube was placed in 80 ℃ oil bath and stirred for 1 hour, got a brown insoluble gel. The mixture was diluted with THF, passed through basic alumina tip column to remove copper. The solvent was removed by rotary evaporation. The residue was dissolved in 0.5 mL THF and precipitated in 5 mL cold methanol to yield 0.024 g product (yield 9.8%) as white powder. $M_n$= 9,937 Da, $M_w$=41510 Da, PDI= 4.18.

3.14 ATRP of methyl 2-bromo-3-methacryloxy-2-methylpropionate with PEI as ligand in THF

All of the ATRPs of methyl 2-bromo-3-methacryloxy-2-methylpropionate using polyethyleneimine as ligand in THF were carried out in the following procedure. And the ratio of polyethyleneimine to Cu(I)Br was varied from 2 to 20. The following is an example of ATRP of the methyl inimer in THF with polyethyleneimine.

In a typical procedure, Cu(I)Br (0.0034 g, 0.025 mmol) was added to a Schlenk tube and evacuated at room temperature. After refilling the Schlenk tube with nitrogen, polyethyleneimine stock solution (30.6 $\mu$L, 300 mg/mL in THF, 0.25 mmol) was added into the Schlenk tube under nitrogen and stirred for 5 minutes. 2-Bromo-3-methacryloxy-2-methylpropionate (0.3280 g, 1.237 mmol), THF (1.55 mL) and drops of DMF were added to the Schlenk tube under nitrogen. After stirring at room temperature for 5 minutes, the mixture was degassed by 5 cycles of freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes) and then, the Schlenk tube was refilled with nitrogen. the reaction mixture was set in 50 ℃ oil bath for 5 hours. The reaction was quenched by immersing in liquid nitrogen and thawed to air. Dilute the mixture with THF and passed basic alumina tips column till solution was colorless. The solvent was removed by rotary evaporation. The residual was dissolved in 0.5 mL of THF and precipitated into 5 mL of cold methanol to obtain 99 mg (yield 30.2%) of product as white powder. $M_n$= 13,979 Da, $M_w$= 34,753 Da, PDI= 2.49.

3.15 Cationic rearrangement of hyperbranched poly(methyl methacrylate)

The precipitated hyperbranched poly(methyl methacrylate) (10 mg, 0.037 mmol) and nitromethane (0.2 mL) were added to a Schlenk tube. The Schlenk tube was sealed with a glass stopper aided with parafilm and a plastic clampa. The mixture was degassed by 5 cycles of freeze (5 minutes)-pump (15 minutes)-thaw (5 minutes). The Schlenk tube was refilled with nitrogen and set in 100 ℃ oil bath stirred for 48 hours. The reaction was quenched by immersing in liquid nitrogen and thawed to air. The mixture was diluted with THF and transferred to 20 mL vial. All solvent was removed by rotary evaporation. $^1$H NMR was used to characterize the mixture. Comparing to the $^1$H NMR spectrum before the

rearrangement, there were two new resonance shows up at 3.60 ppm 1.25 ppm, which matched the expectation that the new resonance moves to upfield.

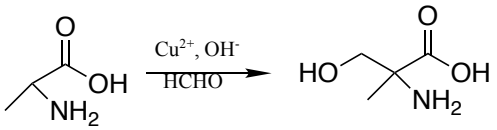
3.16 Nucleophilic substitution of the hyperbranched poly(methyl methacrylate) in acetone at room temperature

Hyperbranched poly(methyl methacrylate) (104 mg, 0.392 mmol, $M_n$= 14,028 Da, $M_w$= 34,154 Da, PDI= 2.43) and sodium iodide (0.5953 g, 3.397 mmol) were added to a round bottom flask at once. Added 1 mL of acetone to the round bottom flask as solvent. Alumina foil was used to cover the round bottom flask during the reaction. The reaction mixture was stirred at room temperature for 24 hours. After the reaction, acetone was removed by rotary evaporation and the residue was washed by cold methanol. 77.5 g yellow solid was obtained. The $^{1}$H NMR and $^{13}$C NMR shows no change before and after the reaction.

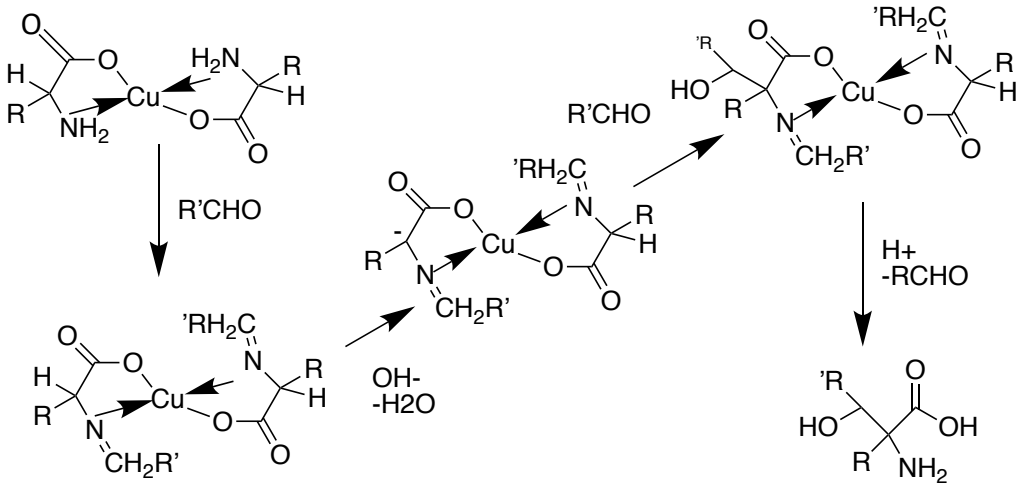
# CHAPTER IV

# RESULTS AND DISCUSSION

## 4.1. 2-Amino-3-hydroxy-2-methylpropionic acid




Scheme 4.1 Synthesis of 2-amino-3-hydroxy-2-methylpropionic acid.




Scheme 4.2 The mechanism of the Akabori reaction

2-Amino-3-hydroxy-2-methylpropionic acid was synthesized via an Akabori reaction[48] (scheme 4.1). The Akabori reaction was between the copper complex of an amino acid and carbonyl compound. The mechanism was shown in Scheme 4.2. The copper-amino acid complex stabilized the imine and increased the acidity of the $\alpha$-proton, which gave the base

a chance to abstract this proton and the carbanion group can react with a carbonyl group. In this reaction, we use formaldehyde rather than carboxy acid and resulted in hydroxymethylene group.

The synthesis of 2-amino-3-hydroxy-2-methyl propionic acid in this thesis followed the experiments published by Otani and Winitz.[47] The reaction reached 100% conversion in 60 minutes according to the $^1$H NMR. Figure 4.1 is the $^1$H NMR of the reaction aliquot, we

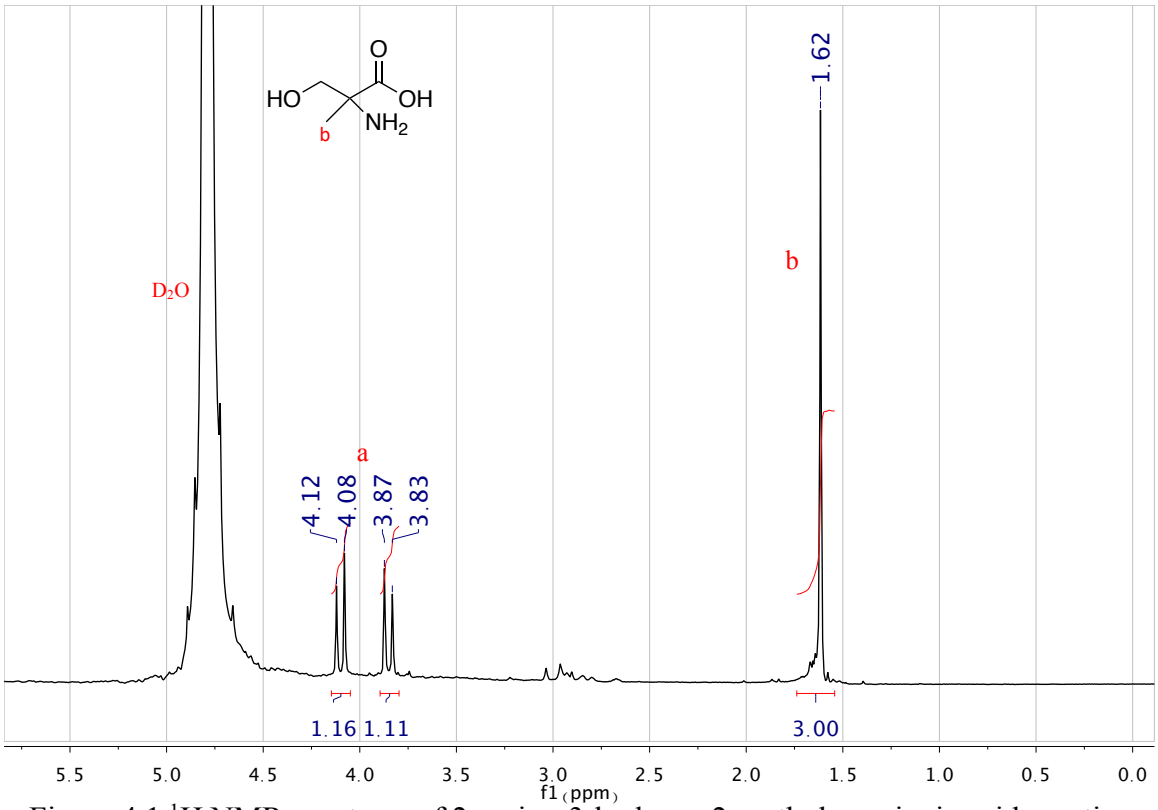


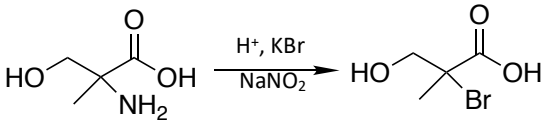

Figure 4.1 $^1$H NMR spectrum of 2-amino-3-hydroxy-2-methyl propionic acid-reaction (aliquot)

can saw that the resonance of the methine group in alanine completely disappeared at 3.84 ppm. For 2-amino-3-hydroxy-2-methyl propionic acid, the singlet resonance at 1.62 ppm was most likely the methyl group without adjacent proton. The hydrogens of the methylene group were attached to a chiral center and were inequivalent; they were therefore split by

each other and appeared as a doublet of doublets at 3.85 ppm and 4.10 ppm. If we compared the integral of those protons and set the integral of resonance at 1.62 ppm as 3.00, the integral of the resonance at 3.85 ppm and 4.10 ppm were 1.16 and 1.11, which matched the expectation of the proton integrals of this molecule. The reactant used in this reaction was a racemic mixture, and the reaction was not stereoselective. Therefore, the product was a racemic mixture. The hydroxyl group and carbonyl group were not detectable in the $^{1}H$ NMR spectrum due to the proton exchange.

4.2. 2-Bromo-3-hydroxy-2-methylpropionic acid

This halohydrin was the key intermediate of the methyacrylate inimer for hyperbranched




Scheme 4.3 Synthesis of 2-bromo-3-hydroxy-2-methylpropionic acid.

poly(methacrylate). Generally, halohydrin was synthesized by hydrohalogenation of olefins, which gave to the mixture of regioisomers and were hard to separate.[49] We used a deaminohalogenation reaction to synthesize the bromohydrin (scheme 4.3) which could be purified easily. A diazonium ion intermediate was formed during this reaction and underwent nucleophilic substitution to give to an alkyl bromide and nitrogen. Figure 4.2 was the $^{1}$H NMR spectrum of 2-bromo-3-hydroxy-2-methylpropionic acid. The chemically

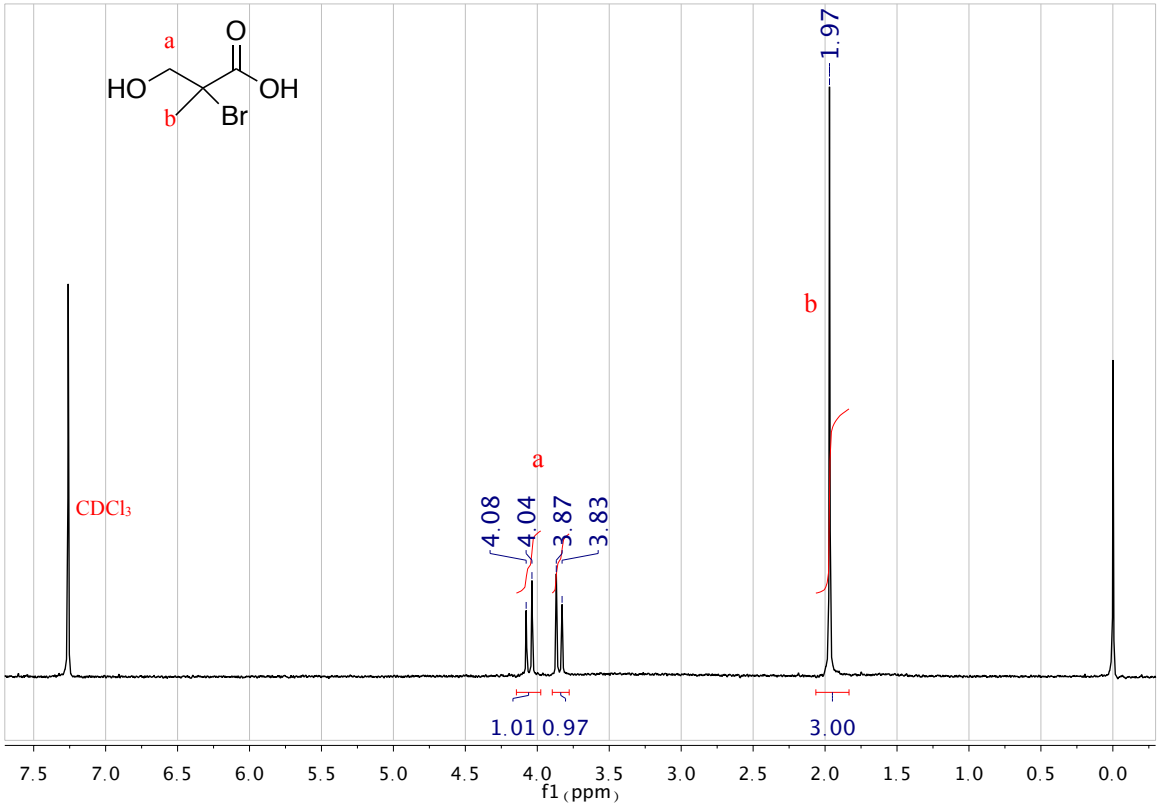
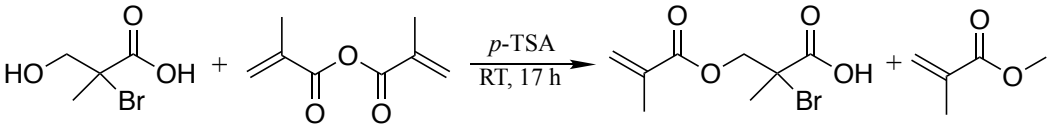



Figure 4.2 $^{1}$H NMR spectrum of 2-bromo-3-hydroxy-2-methylpropionic acid.

inequivalent hydrogens of the methylene group appeared as a doublet of doublets showed at 3.85 ppm and 4.06 ppm which were moving from 3.85 ppm and 4.10 ppm. The methyl group resonanted at 1.97 ppm. The proton integrals were 3.00 at 1.97 ppm, 0.97 at 3.85 ppm and 1.01 at 4.06 ppm. Those integrals matched the proton existence in 2-bromo-3-hydroxy-2-methylpropionic acid.

4.3. 2-Bromo-3-(methacryloyloxy)-2-methyl propanoic acid




Scheme 4.4 Synthesis of 2-bromo-3-(methacryloyloxy)-2-methylpropionic acid.

2-Bromo-3-hydroxy-2-methylpropionic acid was reacted with methacrylic anhydride catalyzed by *p*-toluenesulfonic acid to make the precursor of inimers (Scheme 4.4). Methacrylic acid also was also produced in this reaction. Methacrylic acid was removed by extracting the reaction mixture with water. The precursor was purified by recrystallizing from boiling hexanes and yielded white crystals. Figure 4.4 showed the $^{1}$H NMR spectrum of 2-bromo-3-(methacryloyloxy)-2-methylpropanoic acid. We can saw that the two methyl groups on the methacrylate and bromohydrin were both singlets and overlapped. The methyl group of the bromohydrin resonated at 1.97 ppm and the methyl group of the methacrylate part resonated at 1.95 ppm. The two hydrogen at the methylene group of the bromohydrin were still chemically inequivalent and resonated as a doublet of doublets at 4.51 and 4.63 ppm. The *cis* hydrogen to the methyl group had a resonance at 6.13 ppm and the *trans* hydrogen to the methyl group at 5.62 ppm.

The integrals of those protons fit the protons distribution in 2-bromo-3-(methacryloyloxy)-2-methylpropionic acid which indicated that the target molecule was made.

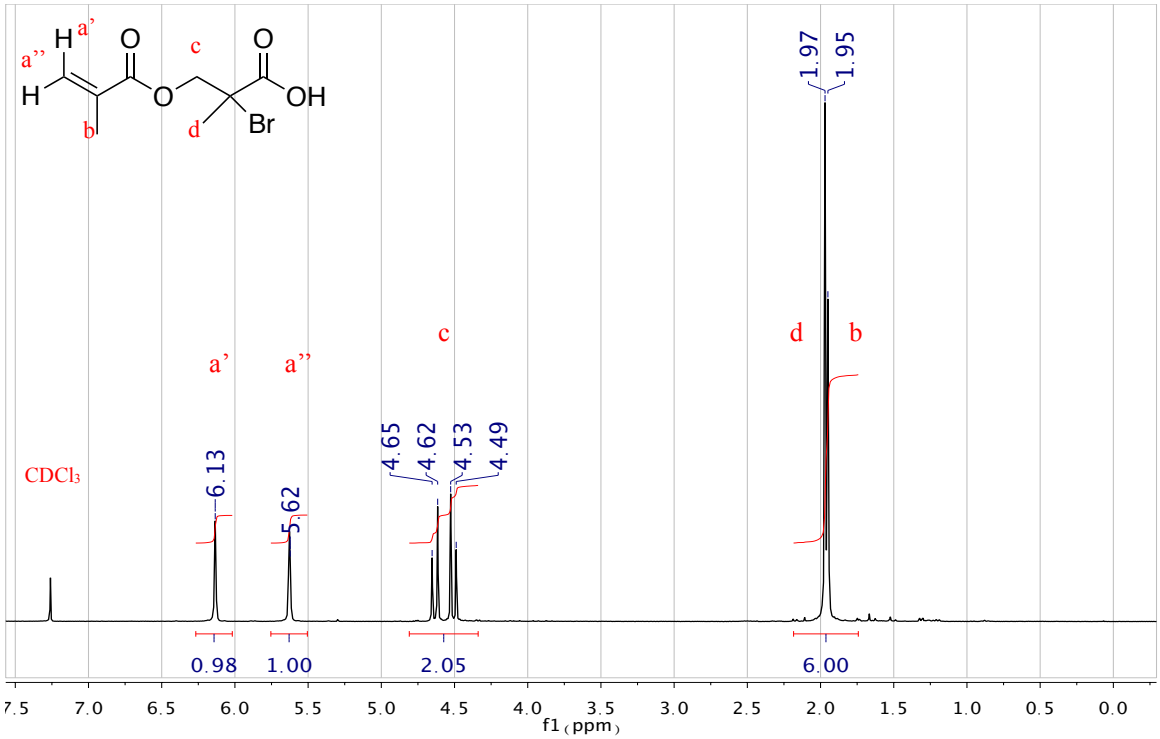
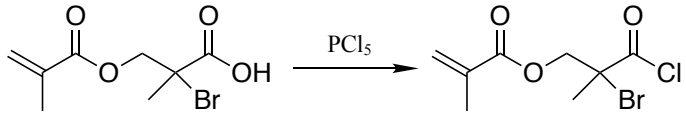



Figure 4.3 $^{1}$H NMR spectrum of 2-bromo-3-(methacryloyloxy)-2-methyl propionic acid.

4.4. 2-Bromo-3-chloro-2-methyl-3-oxopropyl methacrylate




Scheme 4.5 Synthesis of 2-bromo-3-chloro-2-methyl-3-oxopropyl methacrylate.

To increase the reactivity of the precursor inimer with different alcohols, the precursor was reacted with phosphorous pentachloride to give a highly reactive acyl chloride. The acyl chloride was purified by vacuum distillation. Compared to 2-bromo-3-(methacryloyloxy)-2-methypropionic acid, the chemical shifts of the product were insignificant. The methyl group on the bromohydrin shifted from 1.97 ppm to 2.03 ppm due to the acyl chloride structure and all other resonances were slightly moved to downfield.

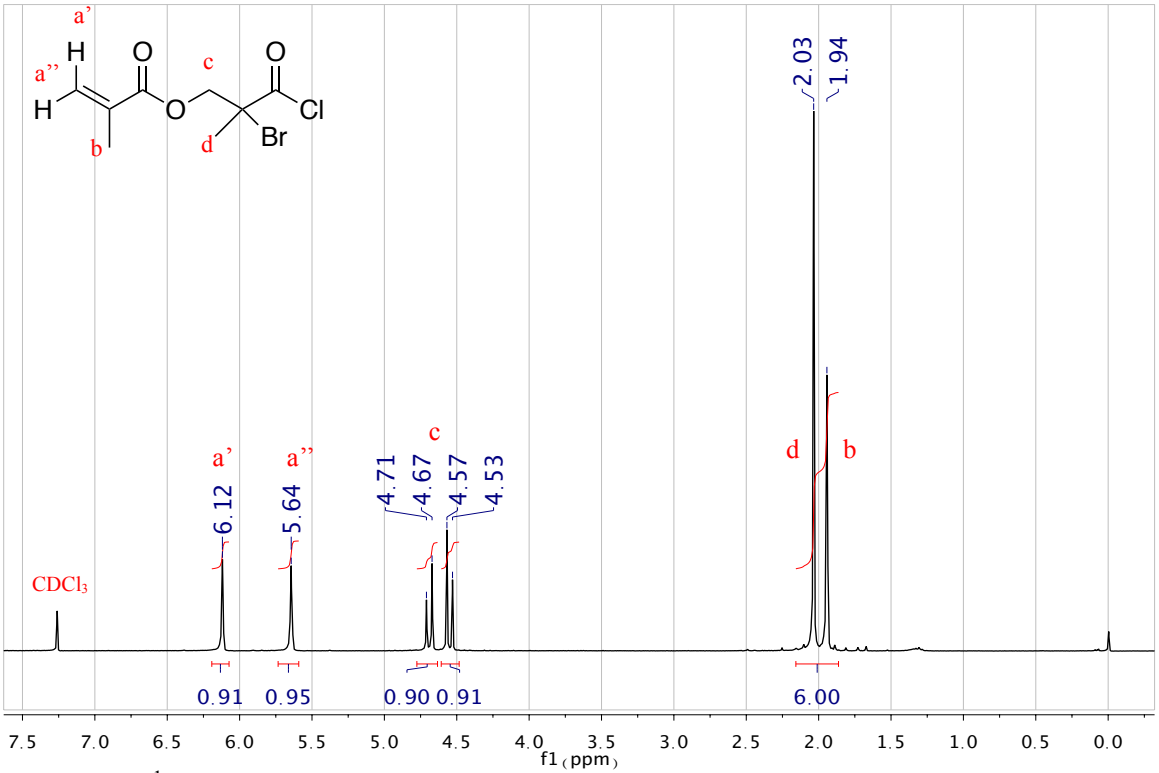
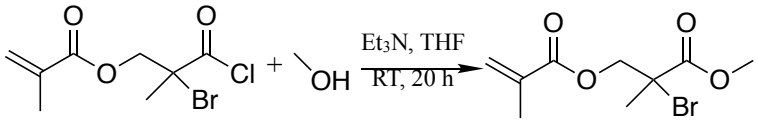



Figure 4.4. $^{1}$H NMR spectrum of 2-bromo-3-chloro-2-methyl-3-oxopropyl methacrylate.

4.5. Synthesis of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate




Scheme 4.6 Synthesis of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate.

The 2-bromo-3-methyoxy-2-methyl-3-oxopropyl methacrylate was the inimer used to make hyperbranched poly(methyl methacrylate). As shown in Scheme 4.6, the 2-bromo-3-chloro-2-methy-3-oxopropyl methacrylate was reacted with methanol with the existence of triethylamine in THF. 2-Bromo-3-(methacryloyloxy)-2-methylpropionic acid was produced as side product in this reaction, and could be removed by gel chromatography using dichloromethane as eluent. The $^{1}$H NMR and $^{13}$C NMR spectrum of the 2-bromo-3-methyoxy-2-methyl-3-oxopropyl methacrylate were shown in Figure 4.5 and Figure 4.6. In the $^{1}$H NMR spectrum, the hydrogens attached to the double bond resonated at 6.10 ppm and 5.60 ppm (The hydrogen *cis* to the methyl group was at the downfield). The resonance of the methylene in bromohydrin part moved upfield to 4.48 ppm and 4.60 ppm. The methyl groups of the bromohydrin part and methacrylate part are completely overlapped into one resonance at 1.94 ppm. If we integrated the hydrogen at the methoxy group at 3.80 ppm as 3.00, the integral of the resonance at 1.93 ppm was about 6. The integrals of the resonances at 4.48 to 4.60 were about one. The integrals of the hydrogens on the double bonds also matched our expectation. Those resonances and integrals imply that this $^{1}$H NMR spectrum was for our methyl methacrylate inimer.

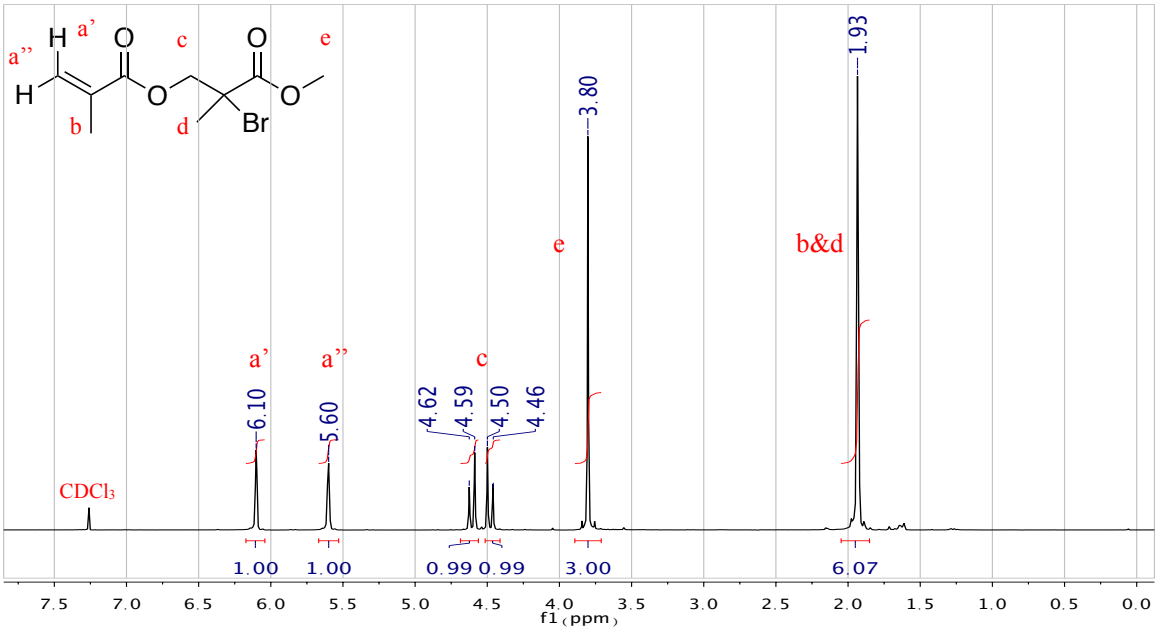



Figure 4.5 $^{1}$H NMR spectrum of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate.

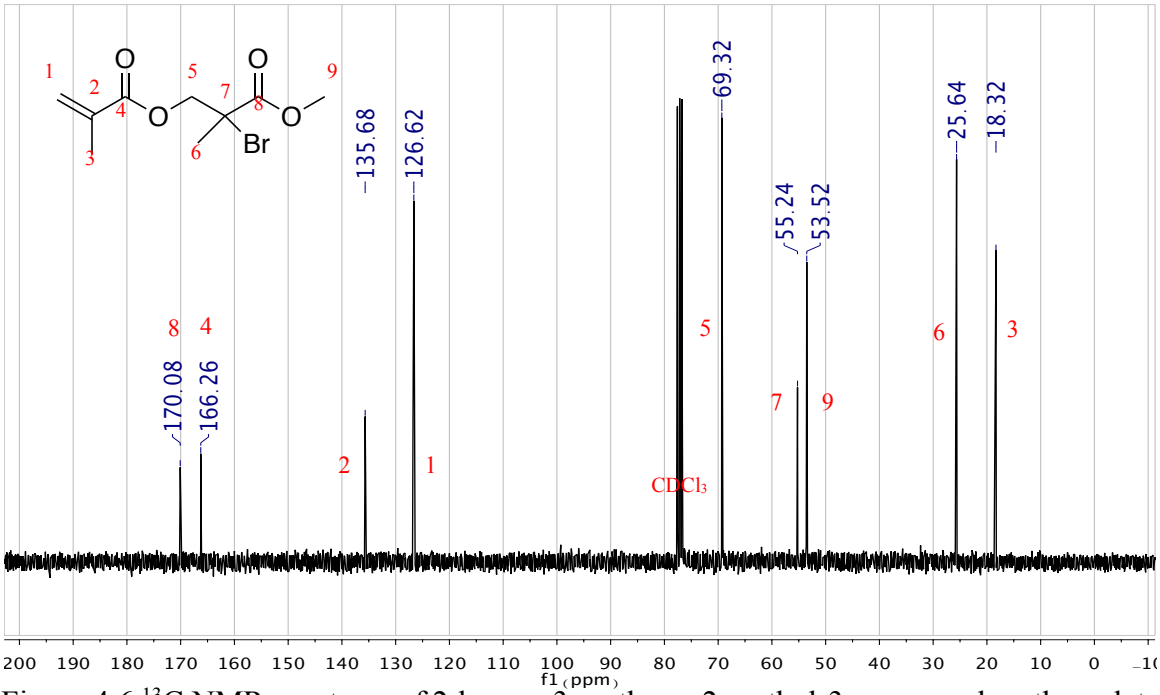
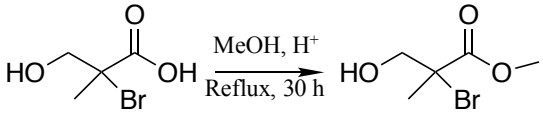



Figure 4.6 $^{13}$C NMR spectrum of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate.

In the $^{13}$C NMR spectrum, the resonances at 170 ppm and 167 ppm were assigned to the two carbonyl groups of the inimer, and the resonance at downfield belongs to the carbonyl

group of the methacrylate. The carbons of the double bond resonated at 135 ppm and 126 ppm. The methylene group resonated at 70 ppm and the halogenated carbon resonated at 58 ppm. The resonance of the methoxy group was at 54 ppm, and the methyl groups were upfield at 26 ppm and 19 ppm.

4.6. Methyl 2-bromo-3-hydroxy-2-methylpropanoate.




Scheme 4.7 Synthesis of 2-bromo-3-hydroxy-2-methylpropanoate.

In the esterification of 2-bromo-3-hydroxy-2-methyl propanoate, Methanol was not only the reactant but also the solvent (Scheme 4.7). The reaction was catalyzed by hydrobromic acid and was carried out at reflux for 20 hours. The product was purified by distilling under

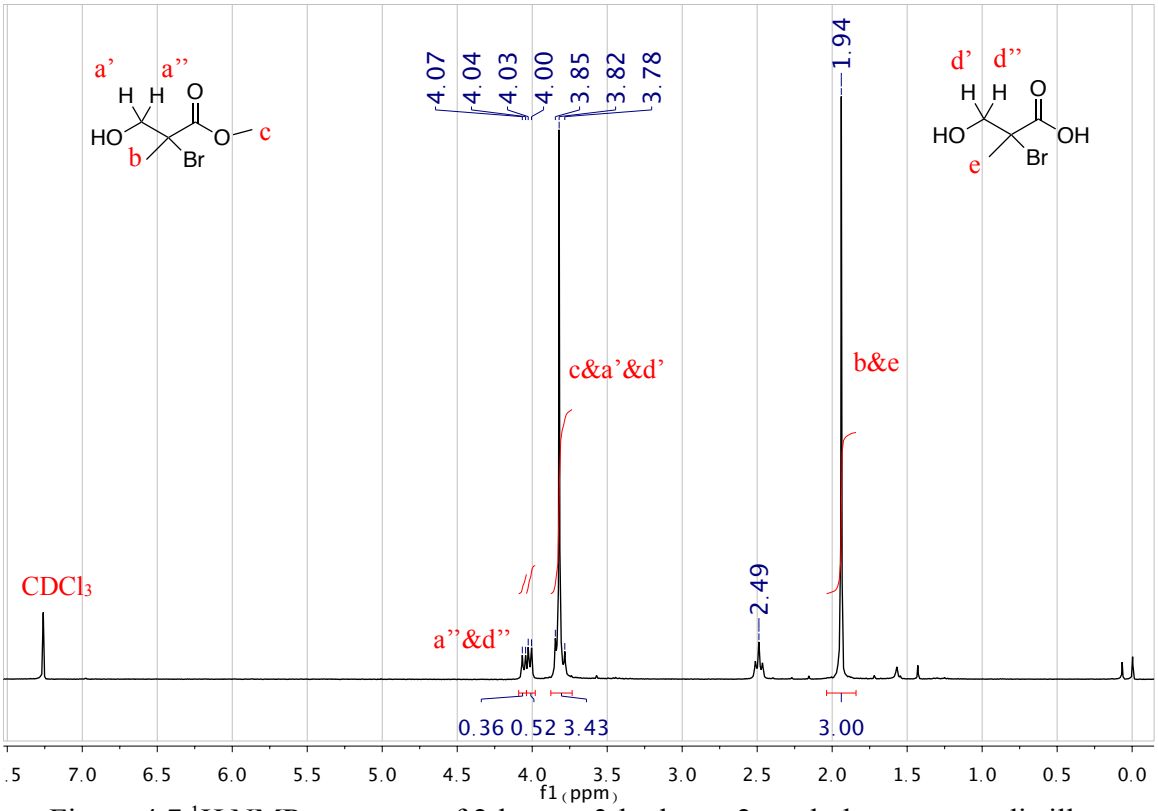
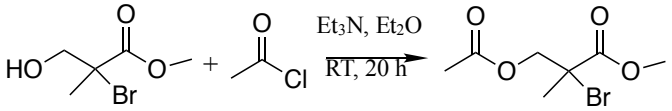



Figure 4.7 $^{1}$H NMR spectrum of 2-bromo-3-hydroxy-2-methylpropanoate distillate.

vacuum. Figure 4.7 was the $^{1}H$ NMR of the distillate. The $^{1}H$ NMR spectrum indicated remained unreacted 2-bromo-3-hydroxy-2-methyl propanoate. The $^{1}H$ NMR of methyl 2-bromo-3-hydroxy-2-methylpropanoate showed the resonances of methoxy and methylene of the bromohydrin are overlapped at 3.78 ppm to 3.85 ppm. The methyl group resonated upfield at 1.94 ppm. The remained 2-bromo-3-hydroxy-2-methylpropionic acid had resonances overlapping with methyl 2-bromo-3-hydroxy-2-methylpopanoate at 1.94 ppm and 3.78 to 3.85 ppm. But the resonances of 2-bromo-3-hydroxy-2-methylpropanoate at 4.04 ppm and 4.07 ppm, which were slightly overlapping with the resonances of our target molecule, provided that there was unreacted reactant remained.

4.7. Methyl 3-acetoxy-2-bromo-2-methylpropanoate

Methyl 3-acetoxy-2-bromo-2-methylpropanoate was the model compound of the




Scheme 4.8 Synthesis of methyl 3-acetoxy-2-bromo-2-methylpropanoate

hyperbranched poly(methyl methacrylate) to help explore the reactivity in post-polymerization. The reaction was carried between methyl 2-bromo-3-hydroxy-2-methylpropionic acid and acetyl chloride in the presence of triethylamine in diethyl ether. The product was purified by extraction and vacuum distillation. As shown in Figure 4.8, the acetoxy protons resonated at 2.05 ppm and the methyl group of the bromohydrin resonated at 1.92 ppm. The doublet of doublets of the methylene group moved downfield to 4.43 ppm and 4.55 ppm. The methoxy group was similar to the inimer with a resonance

at 3.81 ppm. The integrals approximately matched the hydrogen distribution of methyl 3-acetoxy-2-bromo-2-methylpropanoate.

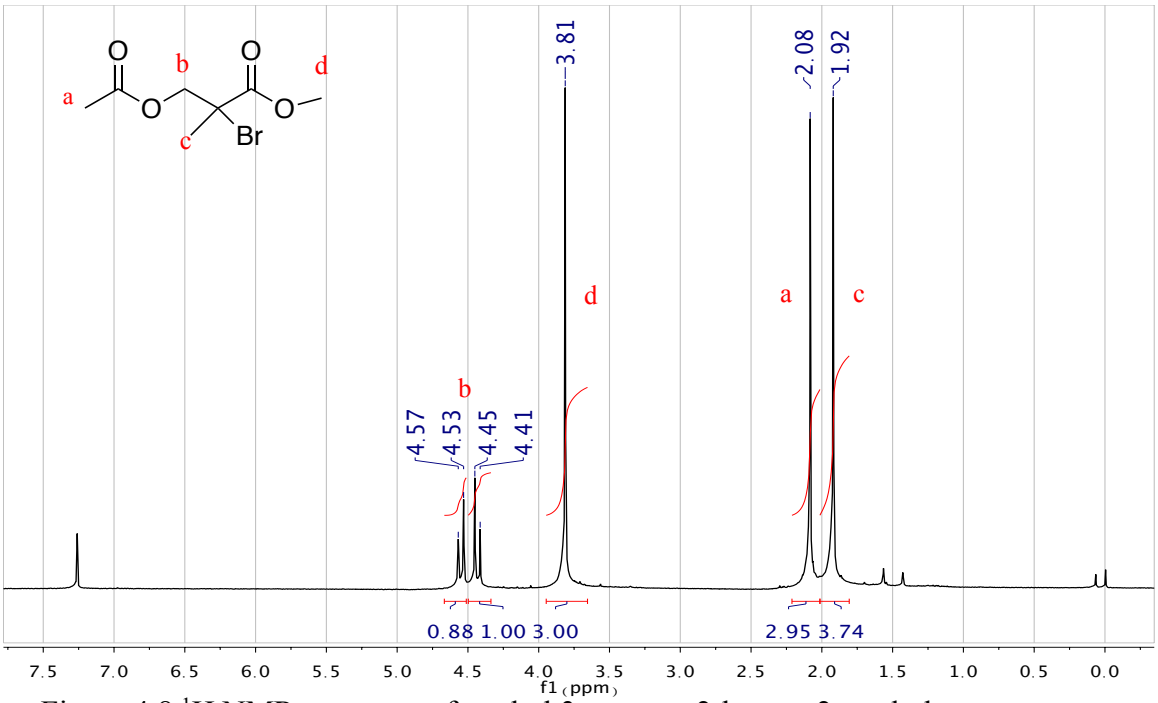



Figure 4.8 $^{1}$H NMR spectrum of methyl 3-acetoxy-2-bromo-2-methylpropanoate.

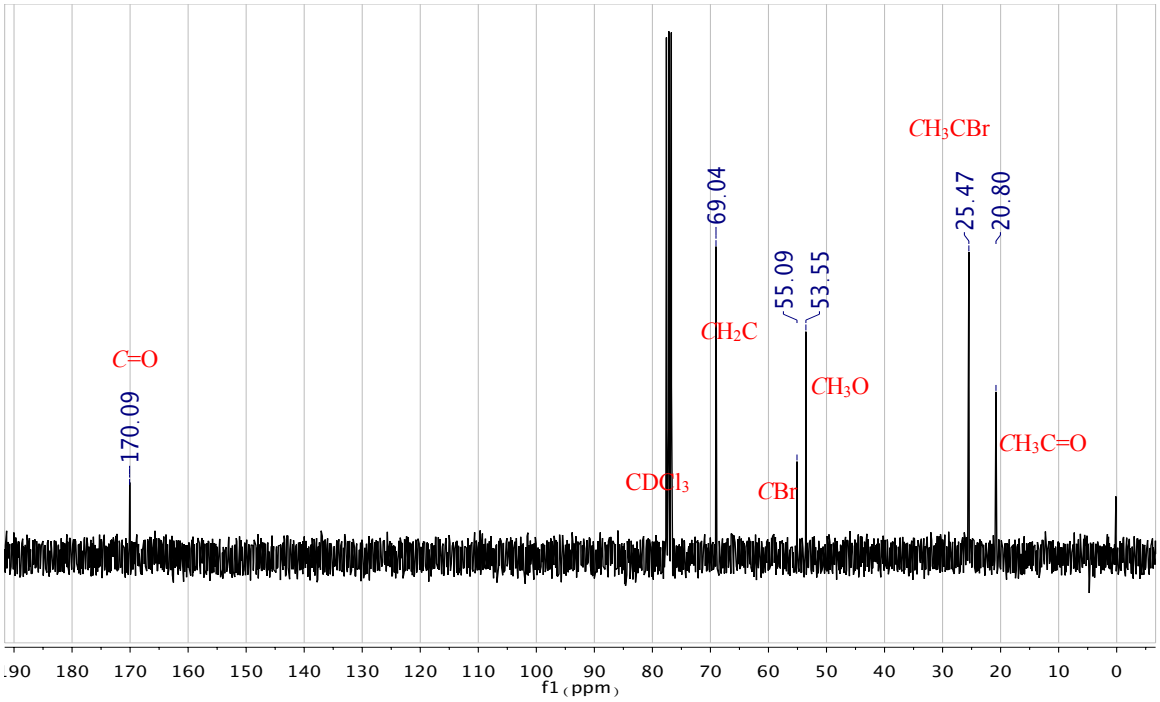
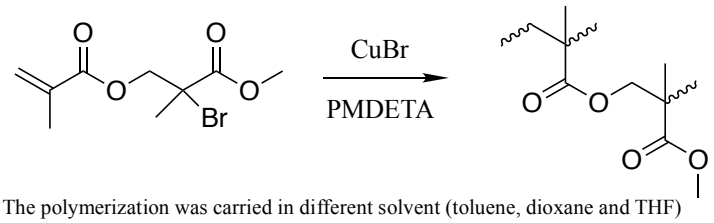



Figure 4.9 $^{13}$C NMR spectrum of methyl 3-acetoxy-2-bromo-2-methylpropanoate

4.8. Polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate using PMDETA as ligand




The polymerization was carried in different solvent (toluene, dioxane and THF)

Scheme 4.9 polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate via ATRP with PMDETA

Table 4.1 Polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate with PMDETA

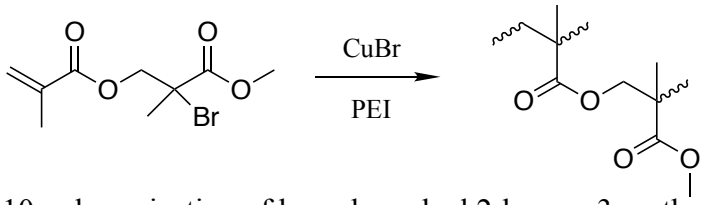
| entry | [Inimer]/[Cu(I)Br] | Solvent | Concentration (mmol/mL) | Temp (°C) | Time (h) | Conversion (%) | Yield (%) | Comments |
|---|---|---|---|---|---|---|---|---|
| 1 | 49 | toluene | 1.9 | 90 | 14 | - | - | Ref. 4 |
| 2 | 49 | toluene | 2.6 | 90 | 88 | 53 | - | |
| 3 | 51 | toluene | 1.8 | 100 | 120 | - | - | |
| 4 | 46 | dioxane | 0.9 | 80 | 18 | 40 | - | |
| 5 | 99 | THF | 3 | 50 | 35 | 25 | 10 | |

Several attempts were made to polymerize the 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate via ATRP using PMDETA as ligand (Scheme 4.9). The polymerization was carried out in different solvents at different temperatures (Table 4.1). Table 4.1 listed the attempts made with PMDETA. The polymerizations carried out using PMDETA as ligand didn't reach conversion over 60%. And no polymer was obtained after precipitation in cold methanol. Those indicated that the polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate was not efficient.

Figure 4.10 was the $^{1}$H NMR spectrums of the aliquot taken from polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate in dioxane with PMDETA at 80 ℃ at 0 hour and 18 hours, and the aliquot of the polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate in toluene with PMDETA at 100℃ after 120 hours. The $^{1}$H NMR shows conversion for those polymerizations while no polymer was yielded. It indicated that some side reactions happened and leaded to no product. According to the $^{1}$H NMR spectrums taken from the aliquots of the polymerization in dioxane with PMDETA at different temperature, we could find that some unknown resonances resonated at the area 3.7 ppm to 4.2 ppm and close to the hydrogen on the double bond. Similar resonances also resonated in the $^{1}$H NMR spectrum of the polymerization in toluene. Compared with the reaction at 80℃ in dioxane, the reaction at 100℃ in toluene had more unknown resonances at the same area in $^{1}$H NMR spectrums, which indicated that there were temperature-related side reactions happened in this system. Another attempt made with PMDETA was carried out in THF at 50 ℃ (entry 5, Table 4.1). No side reaction was observed in this reaction. But the polymerization was not ideal as tiny polymer yielded in low conversion (about 27%

in 72 hours). This data indicated that the polymerization of methyl 2-bromo-3-methacryloxy-2-methylpropionate was not efficient with PMDETA as ligand via ATRP condition.

4.9 Polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate using polyethyleneimine(PEI) as ligand




Scheme 4.10 polymerization of hyperbranched 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate via ATRP using PEI as ligand.

Table 4.2 Polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate with PEI.

Δ indicates the polymer has problem with removing Cu(I)

| entry | [Inimer]/[Cu(I)Br] | [Ligand]/[Cu(I)Br] | Solvent | Concentration (mmol/mL) | Temp (℃) | Time (h) | Conversion (%) | Yield (%) | Comments |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 109 | 33 | Dioxane | 3.06 | 80 | 20 | - | 38 | Cross link |
| 2 | 115 | 12 | Dioxane | 0.8 | 80 | 20 | 69 | 10 | Δ |
| 3 | 121 | 12 | THF | 0.8 | 50 | 20 | 65 | 30 | Δ |
| 4 | 50 | 10 | THF | 0.8 | 55 | 5 | 92 | 42 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 5 | 56 | 6 | THF | 0.8 | 55 | 21 | 50 | 42 |
| 6 | 48 | 5 | THF | 0.8 | 55 | 21 | 27 | 33 |
| 7 | 46 | 2 | THF | 0.8 | 55 | 45 | 25 | - |

Since the polymerization with PMDETA was not efficient, we move to a more active ligand, branched polyethyleneimine (Scheme 4.10). The reaction was carried out in different solvent, with different [ligand]/Cu(I)Br] ratio and different inimer concentration. The conversion was calculated by compared the integral of the double bond of methacrylate at 6.10 ppm and 5.60 ppm before and after reaction, DMF was used as internal standard.

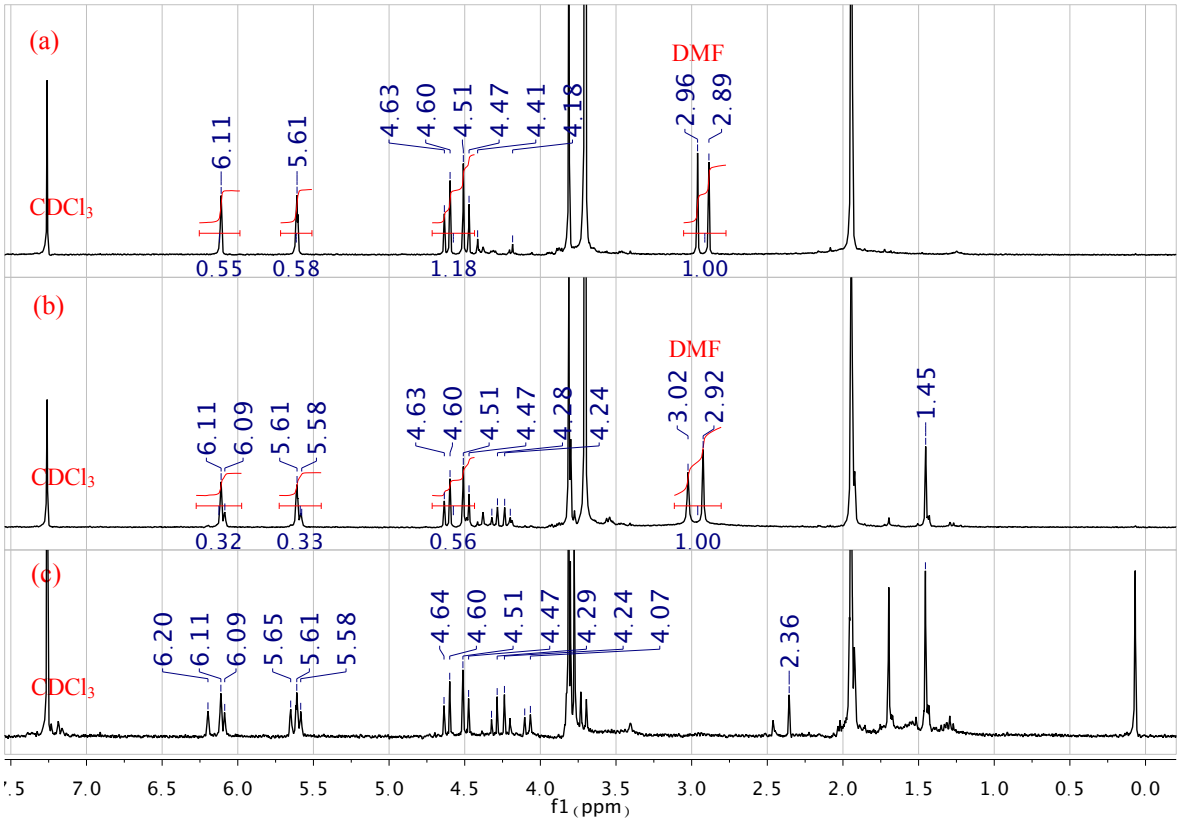



Figure 4.10 (a) $^{1}$H NMR spectrum of the aliquot taken from the polymerization of inimers in dioxane with PMDETA at 80 ℃ 0 h; (b) $^{1}$H NMR spectrum of the aliquot taken from the polymerization of inimers in dioxane with PMDETA at 80 ℃ 18 h; (c) $^{1}$H NMR spectrum

Table 4.2 showed results from different polymerization with polyethyleneimine as ligand with different [ligand]/[Cu(I)Br] ratio in different solvent at different temperature. We can see that the polymerization worked well with high [ligand]/[Cu(I)Br] ratio (table 4.2, entry 1) but the product was crosslinked. The gelation was avoided by decreasing the reaction concentration. 0.8 mmol/mL inimer in THF was a proper concentration which can allow the polymerization have high conversion without the gelation.

Another issue also stood out that the high conversion hyperbranched poly(methyl methacrylate) had problem with removing the cupper (Table 4.2, entry 2, 3). The copper compound was tried to be removed with basic alumina and extraction (the reaction mixture was diluted with chloroform and then extract with saturated ammonium chloride aqueous /methanol 1:1 v/v solution until the aqueous phase was colorless), and both failed to get transparent and colorless solution. For the Table 4.2 entry 4, the copper compounds were successfully removed by using both basic alumina and acidic alumina. As the [ligand]/[Cu(I)Br] ratio decreasing, the reaction rate and the difficulty in remove cupper compounds also decreased. Compared with [ligand]/[Cu(I)Br] equaled to 6, the ratio equaled to 10 worked better which gave a conversion over 70% in 5 hours. And [ligand]/[Cu(I)Br] =10 also decreased the difficulties in removing cupper comparing with the case that the ratio was 12. The GPC data was shown in table 4.3, we can see that for 50% conversion sample ( Table 4.3, entry 1), the molecule weight is about 3.5 kDa, while when the conversion increase to 74% (Table 4.3, entry 2), the molecule weight is over 16.83 kDa, which is four times than 50% conversion sample. It indicated that the molecule weight of

hyperbranched polymer were not linear to the conversion. And to make high molecule weight hyperbranched polymers, we should try to reach high conversion.

Table 4.3 the GPC data of hyperbranched poly(methyl methacrylate) polymerized in THF using PEI as ligand, at 55 ℃, 0.8 mmol/mL

| entry | [Inimer]/[Cu(I)Br] | [Ligand]/[Cu(I)Br] | Conversion (%) | Yield (%) | | $M_n$ ($10^{-3}$ Da) | $M_w$($10^{-3}$ Da ) | PDI |
|---|---|---|---|---|---|---|---|---|
| 1 | 56 | 6 | 50 | 42 | RI | 3.41 | 6.11 | 1.79 |
| | | | | | UV | 3.38 | 6.11 | 1.81 |
| 2 | 49 | 10 | 77 | 30 | RI | 16.83 | 37.14 | 2.20 |
| | | | | | UV | 13.98 | 34.74 | 2.24 |
| 3 | 51 | 10 | 92 | 42 | RI | 12.24 | 35.28 | 2.88 |
| | | | | | UV | 10.75 | 34.45 | 3.20 |
| 4 | 51 | 10 | 68 | 33 | RI | 22.61 | 48.54 | 2.14 |
| | | | | | UV | 20.87 | 46.76 | 2.24 |
| 5 | 50 | 10 | 74 | 38 | RI | 16.98 | 54.44 | 3.20 |
| | | | | | UV | 15.24 | 52.64 | 3.45 |

According to the data in Table 4.3, we concluded that 10 equivalents of ligands to Cu(I)Br

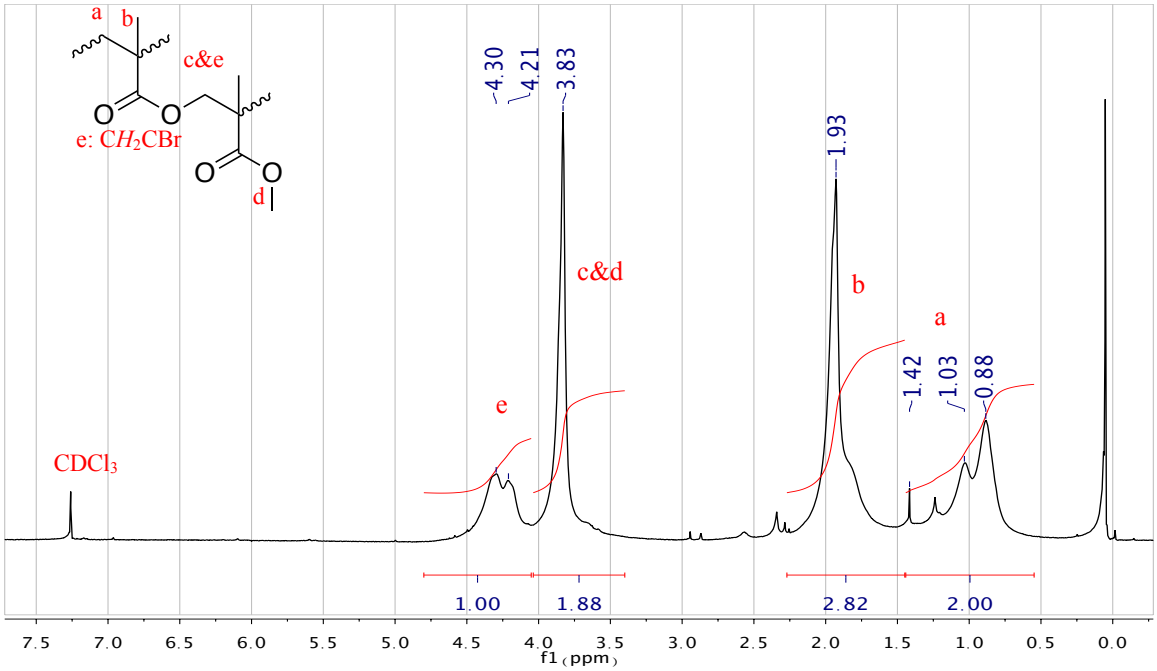



Figure 4.11 $^{1}$H NMR spectrum of hyperbranched poly(methyl methacrylate) produced by ATRP from 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate

was comparably the proper polymerization condition for polymerization of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate via ATRP using polyethyleneimine as ligand. Figure 4.10 and Figure 4.11 are the $^{1}$H NMR and $^{13}$C NMR spectrum of the hyperbranched poly(methyl methacrylate). The hyperbranched poly(methyl methacrylate) had resonance in the area of 4.00 ppm to 4.50 ppm, which belonged to the methylene group that was connected to an unreacted initiating site. The methoxy group resonated at 3.83 ppm as a comparably sharp signal. The methylene group on the polymer backbone resonated in the area of 0.75 ppm to 1.45 ppm. The methyl group directly connected to the polymer backbone resonated in the area of 1.45 ppm to 2.30 ppm. In the $^{13}$C NMR spectrum, the resonance at 167 ppm for the carboxy group of the methacrylate disappeared, and the

methylene group's signal at 70 ppm is insignificant. The brominated carbon and the methoxy still resonated at the same area. The resonance of the methyl group of the methacrylate at 18.32 ppm disappeared and a new resonance resonated at 45 ppm which possibly belonged to the methylene group on the polymer backbone.

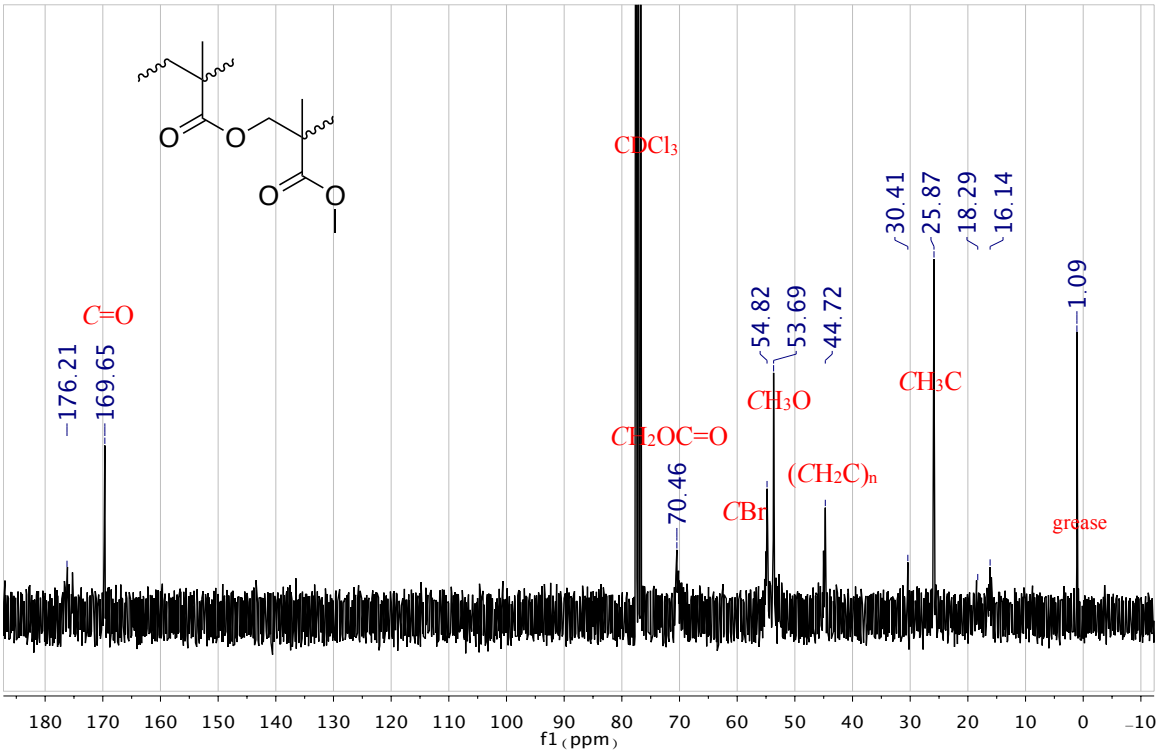
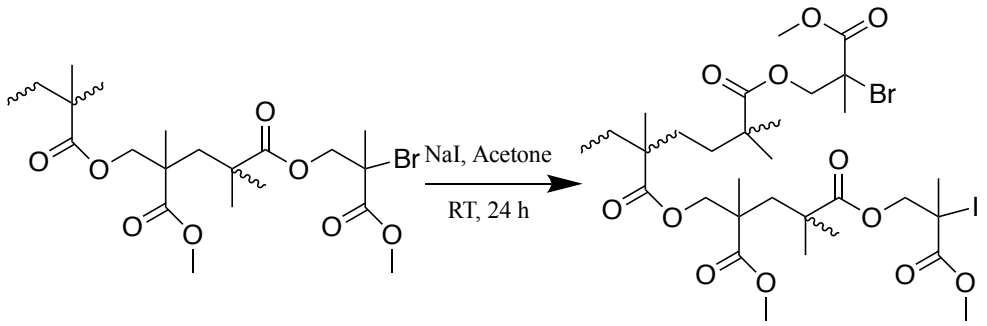



Figure 4.12 $^{13}C$ NMR spectrum of the hyperbranched poly(methyl methacrylate) from 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate via ATRP

4.10. Nucleophilic substitution with sodium iodide




Scheme 4.11 The nucleophilic substitution of hyperbranched poly(methyl methacrylate) with sodium iodide

The reaction between hyperbranched poly(methyl methacrylate) and sodium iodide (Scheme 4.11) can be only followed by $^{13}C$ NMR spectroscopy since the bromide and

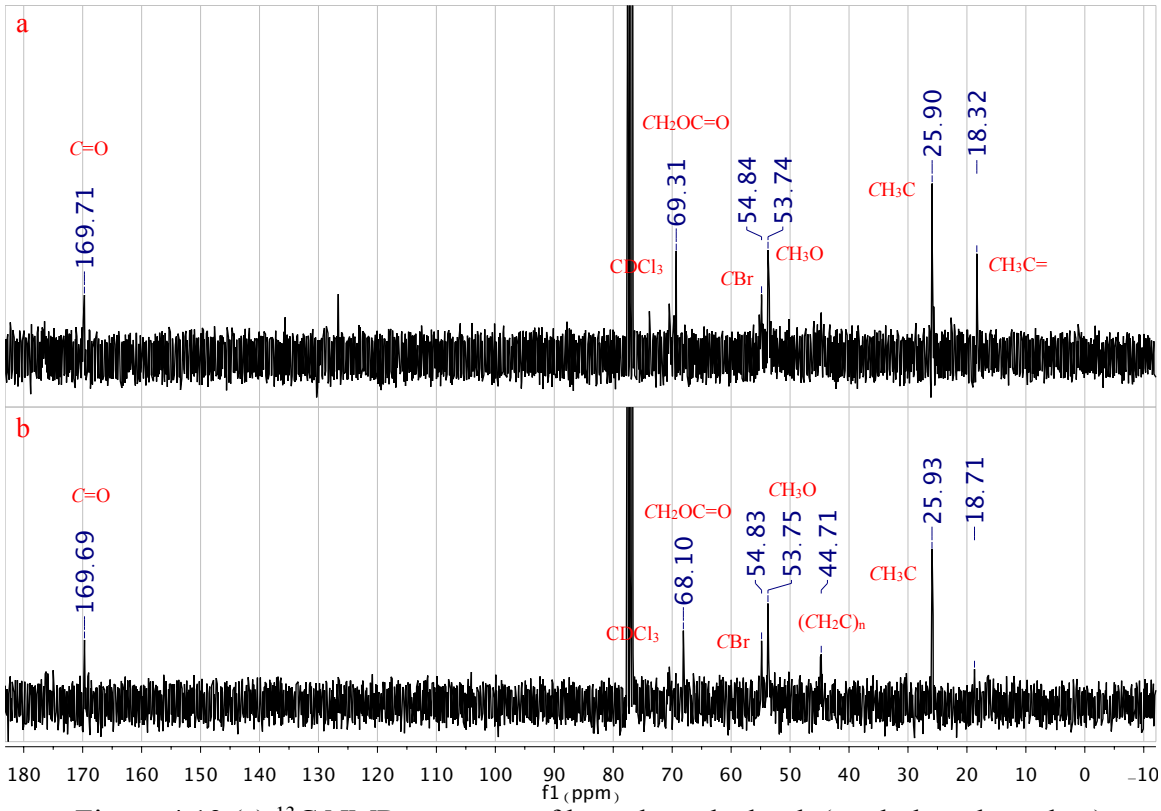
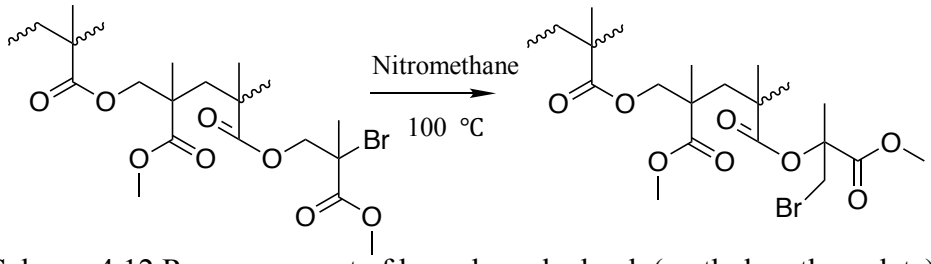



Figure 4.13 (a) $^{13}C$ NMR spectrum of hyperbranched poly(methyl methacrylate) produced by ATRP of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate; (b) $^{13}C$ NMR spectrum of hyperbranched poly(methyl methacrylate) stirring with sodium iodide

iodide were not detectable on $^{1}H$ NMR spectroscopy. The possibility of this reaction was explored with 10 equivalents sodium iodide to bromide in acetone at room temperature. Figure 4.11 was the $^{13}C$ NMR of the hyperbranched poly(methyl methacrylate) before and after stirring with sodium iodide. The $^{13}C$ NMR spectrum showed a new resonate at 44.71 ppm after 24 hours, which also can be found in the $^{13}C$ NMR spectrum of hyperbranched poly(methyl methacrylate) of the methylene group located at polymer backbone. To determine whether the reaction happened, we need the support from the model compound (methyl 3-acetoxy-2-bromo-2-methylpropanoate) to located the resonance change.

4.11. Cationic Rearrangements of hyperbranched poly(methyl methacrylate)




Scheme 4.12 Rearrangement of hyperbranched poly(methyl methacrylate).

The cationic rearrangements were carried out in nitromethane which had a boiling point at 100 ℃ to 103 ℃ (Scheme 4.11). After stirring in 100℃ oil bath for 48 hours, new resonance resonated at the 3.60 ppm and 1.45 ppm, which might be the rearranged structure- a primary brominated methylene and a methyl group. Figure 4.14 was the $^{1}H$ NMR spectrums of hyperbranched poly(methyl methacrylate) before and after rearrangement.

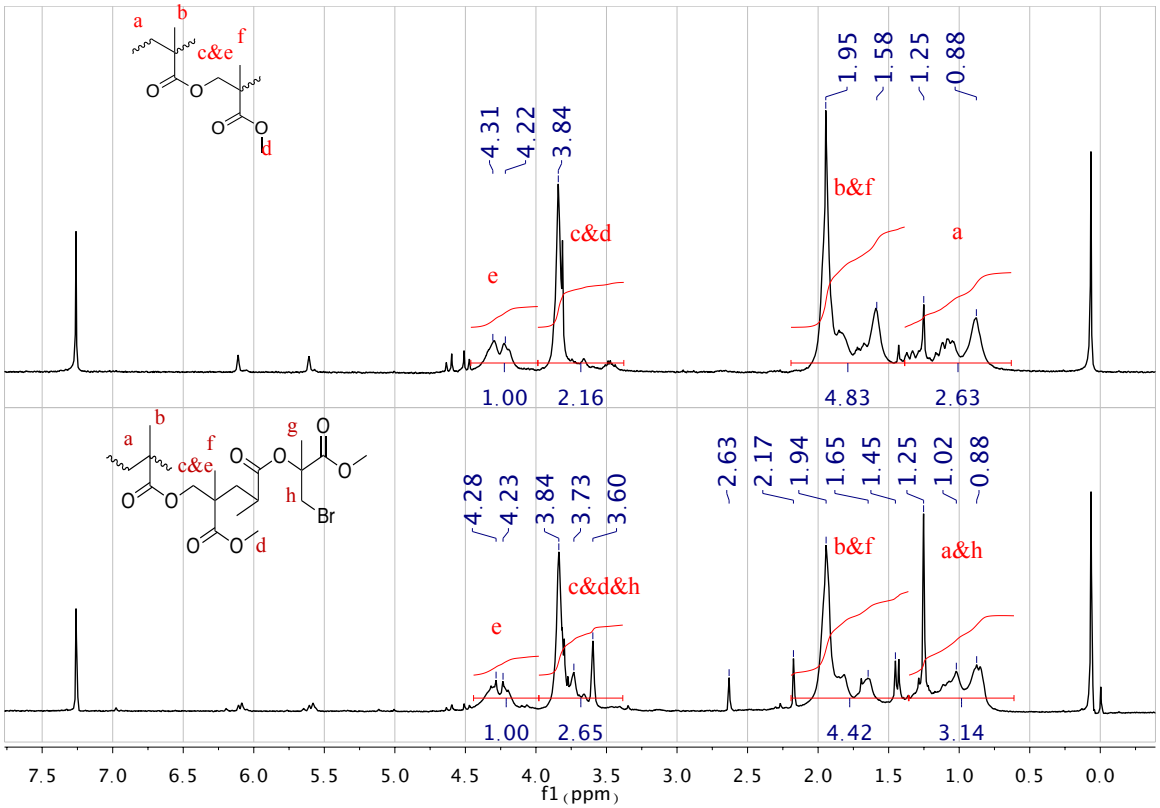



Figure 4.14 (a) $^{1}$H NMR spectrum of hyperbranched poly(methyl methacrylate) Polymer prepared by ATRP of 2-bromo-3-methoxy-2-methyl-3-oxopropyl methacrylate $M_n$= 3.41 kDa, $M_w$= 6.11 kDa.; (b) $^{1}$H NMR spectrum of rearranged

From Figure 4.14, we can see that the integral of each area's ratio to the whole was changing. Theoretically, the resonance at 4.00 ppm to 4.50 ppm would move upfield if an $\alpha$-bromine was produced and resonated at the area from 3.20 ppm to 4.00 ppm. The methyl group participating the rearrangement will move upfield since the directly bonding carbon was not substituted by a bromide. In theory, all of those integrals were changed during the rearrangement. Therefore, the conversion of this reaction was calculated by comparing the integrals' proportion to the total before and after the rearrangement. The total integral was calculated as the sum of the four integrals shown in Figure 4.14. The hydrogens that were

involved in the rearrangement belonged to the methylene group with unreacted initiation site and the methyl group. After the rearrangement, the new resonance was overlapped with the methoxy group and methylene group of the backbone. The calculation result was shown in Table 4.4. We could find the proportions' increasing matches the total decreasing. The conversion is calculated by the ratio changing divided by the whole hydrogen that could participating and about 22% ($Conversion = \frac{7\%}{52\% \times \frac{5}{8}} = 22\%$).

Table 4.4 the integral variance of hydrogens in Figure 4.14 before and after rearrangement at 100 ℃ in nitromethane 24 hours.

| Hydrogen code | before | after | Δ |
|---|---|---|---|
| b+e+f (4.0-4.5 ppm & 1.45-2.2 ppm) | 52% | 45% | -7% |
| a+g (1.0-1.45 ppm) | 27% | 31% | +4% |
| c+d+h (3.5-4.0 ppm) | 21% | 24% | +3% |

# CHAPTER V

## SUMMARY

The synthesis pathway of the inimer to produce hyperbranched poly(methacrylate) was developed by the previous student, Chenwei Liu. Starting from D,L-alanine, 2-amino-2-methyl-3-hydroxy propionic acid was synthesized via the Akabori reaction. The key intermediate, 2-bromo-3-hydroxy-2-methylpropionic acid, was successfully synthesized starting from 2-amino-2-methyl-3-hydroxypropionic acid under deaminohalogenation. After esterification of methacrylic anhydride and methanol, the methyl methacrylate inimer was made.

The polymerization of the hyperbranched poly(methyl methacrylate) by ATRP using Cu(I)Br as catalyst was not successful using PMDETA as ligand. Side reactions were found during polymerization at high temperature. Therefore, we moved to polyethyleneimine as ligand and THF as solvent to polymerize themethacrylate inimer. Suitable conditions were developed for the polymerization that successfully polymerized using polyethyleneimine as ligand in THF.

The post-polymerization reactivity of the hyperbranched poly(methyl methacrylate) was also explored. The nucleophilic substitution of the bromide group was not successful at room temperature with sodium iodide. During the cationic rearrangement, new resonances were observed in the $^{1}H$ NMR spectrum. More work needs to be done for the post-polymerization of hyperbranched polymethacrylate as post-polymerization was one of the

most popular ways to introduce functional groups into polymers, such as carrying out the nucleophilic substitution with better nucleophiles at higher temperature. The model compound should also be studies to help exploring the post-polymerization abilities of the hyperbranched polymethacrylate.

# REFERENCES


1. Gao, C.; Yan, D. *Prog. Polym. Sci.* Hyperbranched Polymers: From Synthesis To Applications. **2004,** *29*, 183-275.

2. Wang, J. S.; Matyjaszewski, K. *J. Am. Chem. Soc.* Controlled/" Living" Radical Polymerization. Atom Transfer Radical Polymerization In The Presence Of Transition-Metal Complexes. **1995,** *117*, 5614-5615.

3. Chang, H. T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* Proton-Transfer Polymerization: A New Approach To Hyperbranched Polymers. **1999,** *121*, 2313-2314.

4. Liu, C. Synthesis Of Hyperbranched Polymethacrylates By A Bromoinimer Approach. *Master Thesis*. University of Akron, 2018.

5. Yates, C.; Hayes, W. *Eur. Polym. J.* Synthesis And Applications Of Hyperbranched Polymers. **2004,** *40*, 1257-1281.

6. Kim, Y. H.; Webster, O. W. *Macromolecules*, Hyperbranched Polyphenylenes. **1992,** *25*, 5561-5572.

7. Frechet, J. M.; Henmi, M.; Gitsov, I.; Aoshima, S.; Leduc, M. R.; Grubbs, R. B. *Science* Self-Condensing Vinyl Polymerization: An Approach To Dendritic Materials. **1995,** *269*, 1080-1083.

8. Suzuki, M.; Ii, A.; Saegusa, T. *Macromolecules* Multibranching Polymerization: Palladium-Catalyzed Ring-Opening Polymerization Of Cyclic Carbamate To Produce Hyperbranched Dendritic Polyamine. 1992, 25, 7071-7072.

9. Magnusson, H.; Malmström, E.; Hult, A. *Macro. Rapid. Commu.* Synthesis Of Hyperbranched Aliphatic Polyethers Via Cationic Ring-Opening Polymerization Of 3 - Ethyl - 3 - (Hydroxymethyl) Oxetane. **1999,** *20*, 453-457.

10. Pugh, C.; Raveendra, B.; Singh, A.; Samuel, R.; Garcia, G. *Synth. Lett.* Design And Regioselective Synthesis Of (2-Bromo-2-Alkoxycarbonyl) Ethyl Acrylates As Inimers For Hyperbranched (Co) Polyacrylates. **2010,** *2010*, 1947-1950.

11. Pugh, C.; Singh, A.; Samuel, R.; Bernal Ramos, K. M. *Macromolecules* Synthesis Of Hyperbranched Polyacrylates By A Chloroinimer Approach. **2010,** *43*, 5222-5232.

12. Pugh, C. R.; Singh, A., Synthesis Of Inimers And Hyperbranched Polymers. U.S. Patent No. 8,524,942B2. Sep. 2013.

13. Widawski, G.; Rawiso, M.; François, B. *Nature* Self-Organized Honeycomb Morphology Of Star-Polymer Polystyrene Films. **1994,** *369*, 387.

14. Roovers, J. *Polymer* Synthesis And Dilute Solution Characterization Of Comb Polystyrenes. **1979,** *20*, 843-849.

15. Roovers, J.; Comanita, B., Dendrimers And Dendrimer-Polymer Hybrids. In *Branched Polymers I*, Springer: 1999; 179-228.

16. Gitsov, I.; Wooley, K. L.; Hawker, C. J.; Ivanova, P. T.; Frechet, J. M. J. *Macromolecules* Synthesis And Properties Of Novel Linear-Dendritic Block Copolymers. Reactivity Of Dendritic Macromolecules Toward Linear Polymers. **1993,** *26*, 5621-5627.

17. Shu, L.; Schlüter, A. D.; Ecker, C.; Severin, N.; Rabe, J. P. *Angewa. Chem.* Extremely Long Dendronized Polymers: Synthesis, Quantification Of Structure Perfection, Individualization, And SFM Manipulation. **2001,** *113*, 4802-4805.

18. Barnes, K. A.; Douglas, J. F.; Liu, D. W.; Bauer, B.; Amis, E. J.; Karim, A. *Polym. International* Influence Of Generation Number On The Dewetting Of Hypergraft Poly (2-Ethyl-2-Oxazoline) Films. **2000,** *49*, 463-468.

19. Jikei, M.; Kakimoto, M. a. *Prog. Polym. Sci.* Hyperbranched Polymers: A Promising New Class Of Materials. **2001,** *26*, 1233-1285.

20. Caminade, A. M.; Yan, D.; Smith, D. K. *Chem. Soc. Rev.* Dendrimers And

Hyperbranched Polymers. **2015,** *44*, 3870-3873.

21. Webster, O. W. *Science*, Living Polymerization Methods. **1991,** *251*, 887-893.

22. Zetterlund, P. B.; Kagawa, Y.; Okubo, M. *Chem. Rev.* Controlled/Living Radical

Polymerization In Dispersed Systems. **2008,** *108*, 3747-3794.

23. Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux, B. *Prog. Polym. Sci.* Nitroxide-Mediated Polymerization. **2013,** *38*, 63-235.

24. Chiefari, J.; Chong, Y.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P.; Mayadunne, R. T.; Meijs, G. F.; Moad, C. L.; Moad, G. *Macromolecules* Living Free-Radical Polymerization

By Reversible Addition− Fragmentation Chain Transfer: The RAFT Process. **1998,** *31*,

5559-5562.

25. Matyjaszewski, K. *Macromolecules*, Atom Transfer Radical Polymerization (ATRP):

Current Status And Future Perspectives. **2012,** *45*, 4015-4039.

26. Jikei, M.; Chon, S. H.; Kakimoto, M.-a.; Kawauchi, S.; Imase, T.; Watanebe, J. *Macromolecules* Synthesis Of Hyperbranched Aromatic Polyamide From Aromatic Diamines And Trimesic Acid. **1999,** *32*, 2061-2064.

27. Yan, D.; Gao, C. *Macromolecules* Hyperbranched Polymers Made From A2 And BB '2 Type Monomers. 1. Polyaddition Of 1-(2-Aminoethyl) Piperazine To Divinyl Sulfone. **2000,** *33*, 7693-7699.

28. Dax, S. L.; McNally, J. J.; Youngman, M. A. *Current Medical Chem.* Multi-Component Methodologies Synthesis. **1999,** *6*, 255.

29. Flory, P. J. *J. Am. Chem. Soc.* Molecular Size Distribution In Three Dimensional Polymers. VI. Branched Polymers Containing A—R—Bf-1 Type Units. **1952,** *74*, 2718-2723.

30. Flory, P. J. J. N. Y., Principles Of Polymer Science. **1953**.

31. Turner, S. R.; Walter, F.; Voit, B. I.; Mourey, T. H. *Macromolecules* Hyperbranched Aromatic Polyesters With Carboxylic Acid Terminal Groups. **1994,** *27*, 1611-1616.

32. Morikawa, A. *Macromolecules* Preparation And Properties Of Hyperbranched Poly (Ether Ketones) With A Various Number Of Phenylene Units. **1998,** *31*, 5999-6009.

33. Uhrich, K.; Boegeman, S.; Fréchet, J.; Turner, S. *Polym. Bull.* The Solid-Phase Synthesis Of Dendritic Polyamides. **1991,** *25*, 551-558.

34. Wieland, P. C.; Nuyken, O.; Schmidt, M.; Fischer, K. *Macro. Rapid Commu.* Amphiphilic Graft Copolymers And Hyperbranched Polymers Based On (3 - Vinylphenyl) Azomethyl - Malonodinitrile. **2001,** *22*, 1255-1260.

35. Liu, M.; Vladimirov, N.; Fréchet, J. M. *Macromolecules* A New Approach To Hyperbranched Polymers By Ring-Opening Polymerization Of An AB Monomer: 4-(2-Hydroxyethyl)-ε-Caprolactone. **1999,** *32*, 6881-6884.

36. Emrick, T.; Chang, H. T.; Fréchet, J. M. J. *J. Polym. Sci. A: Polym. Chem.* The Preparation Of Hyperbranched Aromatic And Aliphatic Polyether Epoxies By Chloride - Catalyzed Proton Transfer Polymerization From Abn And A2+ B3 Monomers. **2000,** *38*, 4850-4869.

37. Nuyken, O.; Gruber, F.; Pask, S. D.; Riederer, A.; Walter, M. *Macro. Chem. Phys.* The Synthesis of α -*tert*-Butyl- Ω -[pVinylphenyl]-Terminated Poly(2-Methylpropene) Macromonomers. **1993,** *194*, 3415-3432.

38. Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* Functional Polymers By Atom Transfer Radical Polymerization. **2001,** *26*, 337-377.

39. Boaen, N. K.; Hillmyer, M. A. *Chem. Soc. Rev.* Post-Polymerization Functionalization Of Polyolefins. **2005,** *34*, 267-275.

40. Mayo, F. R.; Walling, C. *Chem. Rev.* Copolymerization. **1950,** *46*, 191-287.

41. Mayo, F. R.; Lewis, F. M. *J. Am. Chem. Soc.* Copolymerization. I. A Basis For Comparing The Behavior Of Monomers in Copolymerization; The Copolymerization Of Styrene And Methyl Methacrylate. **1944,** *66*, 1594-1601.

42. Günay, K. A.; Theato, P.; Klok, H. A. *J. Polym. Chem.* Standing On The Shoulders Of Hermann Staudinger: Post-Polymerization Modification From Past To Present. **2013,** *51*, 1-28.

43. Coessens, V.; Matyjaszewski, K. *Macro. Sci.* A. End Group Transformation Of Polymers Prepared By ATRP, Substitution To Azides. **1999,** *36*, 667-679.

44. Coessens, V.; Pyun, J.; Miller, P. J.; Gaynor, S. G.; Matyjaszewski, K. *Macro. Rapid Rev.* Functionalization Of Polymers Prepared By ATRP Using Radical Addition Reactions. **2000,** *21*, 103-109.

45. Wright, C. Functional PLA Based Systems. *Doctoral Dissertation,* University of Akron, 2015.

46. Keller, R.; Wrcoff, H.; Marchi, L. E., Copper (I) Chloride. *Inorganic syntheses* **1946,** *2*, 1-4.

47. Otani, T. T.; Winitz, M., *Archives of biochemistry and biophysic,* Studies On Hydroxyamino Acids. I. Synthesis Of Some A-Alkylated Serines. *s* **1960,** *90*, 254-259.

48. Belikov, V.; Vitt, S.; Kuznetsova, N.; Bezrukov, M.; Saporovskaya, M., *Rus. Chem. Bull.* Reaction Of The Copper Complex Of L-Alanine With Acetaldehyde And The Mechanism Of The Akabori Reaction. **1969,** *18*, 2371-2375.

49. Bruckner, A., *Acta Chirurgica Academiae Scientiarum Hungaricae* Additions of Halogen by Means of N-Bromosuccinimide. III. Preparation of Aliphatic α,β-Dihalo CarboxylicAcids, **1966**, 49, 287-90.