SUPRAMOLECULAR BLOCK AND RANDOM COPOLYMERS IN MULTIFUNCTIONAL ASSEMBLIES

A Dissertation
Presented to
The Academic Faculty

by

Caroline Glenn Burd

In Partial Fulfillment
of the Requirements for the Degree
Ph.D in the
School of Chemistry and Biochemistry

Georgia Institute of Technology
August 2008

SUPRAMOLECULAR BLOCK AND RANDOM COPOLYMERS IN MULTIFUNCTIONAL ASSEMBLIES

Approved by:

Dr. Marcus Weck, Advisor
School of Chemistry and Biochemistry
Georgia Institute of Technology

Dr. Christine Payne
School of Chemistry and Biochemistry
Georgia Institute of Technology

Dr. Uwe Bunz
School of Chemistry and Biochemistry
Georgia Institute of Technology

Dr. David Collard
School of Chemistry and Biochemistry
Georgia Institute of Technology

Dr. Chris Jones
School of Chemical & Biomolecular Engineering
Georgia Institute of Technology

Date Approved: May 8, 2008

ACKNOWLEDGEMENTS

I cannot sufficiently thank my advisor, Dr. Marcus Weck, for providing extraordinary support, encouragement, and assistance for every undertaking during my years at Georgia Tech. His dedication to his career has inspired me. I can be a royal pain, and I greatly appreciate his patience with me. I would also like to thank colleagues and friends from the Weck group, past and present, for their assistance and support (and friendship), including Dr.MH, Dr. XZ, Dr.JP, Dr.AM, Dr.JC, Dr.WS, Dr.WG (especially for his patience and help in the beginning of my tenure), Dr.IW, Dr.XY, Dr.KY, Dr.NM, Dr.AA, KN, TP, KA, AK, and PG. I would also like to thank Dr. Andrew Lyon for his support and encouragement in the beginning of my graduate career. I would especially like to thank MNH, for our "Midcity Wednesdays" and her friendship.

Next, I would like to thank members of my thesis committee (Dr.Christopher Jones, Dr.Uwe.Bunz, Dr.Christine Payne, and Dr. David Collard) who have been generous with their time and assistance throughout my graduate career. I have greatly appreciated all the times that they have been willing to lend their time and insights into my various endeavors. Their thoughts, suggestions and support have also been an integral part of the successful completion of my work here at Georgia Tech.

Thank you to all the others who have helped me with various scientific endeavors. Many members of the School of Chemistry and Biochemistry provided access to and help with instrumentation, including Dr. Les Gelbaum, the Bunz, Collard, Hud, Lyon and Jones groups, and the Georgia Tech Mass Spectrometry Laboratory (MS experiments). I

would also like to especially thank Dr. Cam Tyson for supplying much appreciated encouragement, and support.

I would like to thank all of my friends (JTK, AG, SMcK, BV, ML, CK, GM, CN, SD, JD, AS, JMcG, JJM, DH, GM, JA, YS, PL, JJ, JA, AL, GG, JE), the "cool kids"(LD, JA, AMH, MD, AA, ABR, JG, RT3), and my "dinner group" (Dr.SW, Dr.TC, AR, FZ, Dr.MC, JJ, KF (now KG)) for their continued friendship despite my moodiness, absence, and my excuse of "I can't, I am working on the thesis" for over the last year.

Finally, this would not be complete without thanking my family for their encouragement, understanding, and support. I cannot sufficiently thank you all for everything you do for me. Also, I could never adequately express my gratitude to JTK for believing in me, encouraging me, supporting my crazy decisions, (especially those that made things more difficult for myself) and having the patience to still love me when I was a very moody girl.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

LIST OF SYMBOLS AND ABBREVIATIONS

μL	microliter
^{13}C NMR	carbon magnetic resonance
^{1}H NMR	proton magnetic resonance
A	acceptor (in hydrogen bonding)
Å	angstrom
ADA	acceptor-donor-acceptor
ATRP	atom transfer radical polymerization
bpy	2,2'-bipyridine
C	cytosine
CA	cyanuric acid
COD	cyclooctadiene
CT	chain terminator
CTA	chain-transfer agent
D-H	donor (in hydrogen bonding)
DAD	donor-acceptor-donor
DAP	diaminopyridine
DBTA	*O*,*O*′-dibenzoyl-D-tartaric acid
DCC	dicyclohexyl carbodiimide
DCM	dichloromethane
DDAA	donor-donor-acceptor-acceptor
DMAP	4-dimethylamino pyridine
DMF	*N*,*N*-dimethylformamide

DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DSC	differential scanning calorimetry
ECH	epichlorohydrin
EI	electron ionization
ESI	electrospray ionization
EtOAc	Ethyl acetate
FAB	fast atom bombardment
FT-IR	Fourier transform infrared
g	gram
G	guanine
GPC	gel-permeation chromatography
h	hour
HMTA	hexamethyltetraamine
HKR	hydrolytic kinetic resolution
HOMO	highest occupied molecular orbital
HRMS	high-resolution mass spectroscopy
HasAsm	*S. marcescens* holo-hemophore
Hz	hertz
IR	infrared
ITC	isothermal titration calorimetry
J	coupling constant
K*a*	association constant

Kcal	kilocalorie
*K*d	dissociation constant
*k*i	rate constant for initiation
*k*p	rate constant for propagation
KJ	kilojoule
L	liter
LDA	lithium diisopropylamide
LED	light-emitting diode
LUMO	lowest unoccupied molecular orbital
M	molar
m/z	mass-to-charge ratio
M^+	molecular ion
M^{-1}	inverse molar
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
MLCT	metal to ligand charge transfer
mmol	milimole
M_n	number-average molecular weight
mol	mole
MS	mass spectrometry
M_w	weight-average molecular weight

NBT	*N*-butylthymine
NMP	nitroxide-mediated polymerization
NMR	nuclear magnetic resonance
^{o}C	degrees centigrade
PAA	poly(acrylic acid)
PCL	poly(caprolactone)
PDI	polydispersity index
PEG	poly(ethylene glycol)
PEO	poly(ethylene oxide)
PI	poly(isoprene)
PIB	poly(isobutylene)s
PLA	poly(lactide)
PMMA	poly(methyl methacrylate)
POSS	polyhedral oligomeric silsesquioxane
ppm	parts per million
PS	poly(styrene)
PVP	poly(vinylpyridine)
py	pyridine
r.t.	room temperature
RAFT	reversible addition-fragmentation chain-transfer polymerization
RIPs	recognition induced polymersomes
RNA	ribonucleic acid

ROMP	ring-opening metathesis polymerization
SCS	sulfur-carbon-sulfur
sec	second
T	thymine
TBAF	tetrabutyl ammonium fluoride
TEMPO	2,2,6,6-Tetramethyl-piperidin-1-oxyl
TGA	thermogravimetric analysis
THF	tetrahydrofuran
THY	thymine
TLC	thin-layer chromatography
TOF	turnover frequency
TON	turnover number
trpy	2,2',2"-terpyridine
U	uracil
UPB	universal polymer backbone
UPy	2-ureido-4-pyrimidone
UV-VIS	ultraviolet-visible
δ	chemical shift

SUMMARY

This thesis begins with a brief overview of supramolecular chemistry and self-assembly and simple examples derived from Nature that provide the motivation for the work presented here. The concept of a synthetic noncovalent toolbox is then introduced. The discussion then focuses more explicitly on side-chain and main-chain functionalized motifs and the methodologies employed in supramolecular polymer functionalization. The primary hypothesis of the thesis is that the combination of supramolecular strategies, ring-opening metathesis polymerization, and a well-understood toolbox of functionalities capable of noncovalent interactions, comprises a method for generating bioinspired materials. This hypothesis was tested by synthesizing unique functionalized supramolecular polymers that allowed for a detailed understanding of the orthogonality of noncovalent interactions and how such interactions can begin to mimic the complexity of functional biomaterials. The strategies and methods discussed in the synthesis of these bioinspired materials are divided into three chapters: (1) an exploration of the self-sorting phenomena between two non-complementary pairs of hydrogen bonds along polymer side-chains, (2) the extension of the self-sorting concept to include a metal coordination moiety, and (3) the side-chain functionalization strategies of chapters 2 and 3 in combination with the main-chain ROMP methodologies discussed in chapter 1 to form orthogonally self-assembled multifunctional block copolymers. The main results of this thesis include the results that multifunctional block copolymers can be fashioned via ROMP, functionalized in both the main- and side-chains, and self-assembled in an orthogonal fashion. In addition, these studies have found that self-sorting between pairs

of non-complementary hydrogen bonding motifs can occur in supramolecular synthetic systems, that the interactions are extremely solvent dependent and that these interactions can result in unexpected phenomena. These results demonstrate the importance of a fully understood toolbox for the rapid development of supramolecular materials. The knowledge derived from this toolbox and presented in chapters 2, 3, and 4, allows for the careful selection of compounds for cleverly designed self-assembly materials inspired by Nature. Finally, conclusions are drawn to the success of the synthetic toolbox and the various strategies presented herein, and potential future directions are discussed.

.

CHAPTER 1
SELF-ASSEMBLY IN POLYMER SCIENCE

1.1 Abstract

This chapter defines self-assembly and supramolecular chemistry and the role they place in polymer science. It focuses on the field of supramolecular polymer chemistry relating specifically to recent advances in polymers containing hydrogen bonding and metal coordination moieties. While advances in π-π, ionic, and van der Waals interactions are important to the ultimate goal of mimicking biological complexity, they are not the focus of the work presented in this thesis and are largely omitted from this introduction chapter. A broad overview of methodologies for synthesizing end functionalized telechelic polymers is also presented. This chapter introduces the motivations and concepts of a synthetic toolbox. Subsequent chapters will serve to develop and further expand the understanding of the toolbox components in combination with novel polymer science methodologies. By developing a well-defined and well-understood synthetic toolbox scientists are one step closer to be able to mimic the complexity and function seen in nature.

1.2 Supramolecular Chemistry and Self-Assembly

Supramolecular chemistry is the chemistry of the noncovalent bond to form and direct molecular assemblies.[1] The most important feature of supramolecular chemistry is that the individual molecular components can be considered building blocks which are reversibly held together by noncovalent assemblies. Self-assembly is closely related to supramolecular chemistry and is defined as "the spontaneous association of molecules under equilibrium conditions into stable, structurally well-defined aggregates joined by

noncovalent bonds",[1] *i.e.* mixing molecules together that have complementary recognition groups results in the spontaneous formation of aggregates/architectures without the need for outside control. The principles that govern self-assembly are the foundation to supramolecular science. By studying the self-assembly behavior of noncovalent interactions in combinations we can begin to develop a collection of recognition motifs (or a toolbox) and understand how they interact in nature to form functional materials.

1.3 Nature's Inspiration

The self-assembly processes that govern nature's complexity can be broken down into many types of noncovalent interactions working in unison to create complex functional and mechanical structures. The use of noncovalent chemistry for the development of biopolymers such as DNA, RNA, and proteins such as connectin and silk allow for the diversity in both form and function of the materials that we have on earth today. The principles governing the formation and three-dimensional structure of these biopolymers are based on a limited number of building blocks (relying on weak and reversible interactions) to achieve a high degree of complexity in a very functional material.[2-4] By utilizing noncovalent interactions in simultaneous multistep self-assembly processes a diverse set of functional biological materials can be created.[2, 5-10] These self-assembly processes are reversible, selective, self-healing, and spontaneous. By enlisting noncovalent strategies such as hydrogen bonding, metal-coordination, π-π stacking, and van der Waals forces, nature has developed an elegant methodology that is able to screen biopolymer's activity and properties and to optimize them.

One of the best-known examples of self-assembled structures in nature is DNA. DNA exists in a double helical form whose two strands are held together by hydrogen bonds between the purine and pyrimidine bases and by π-π stacking interactions between the base pairs that make up the side-chains of the individual strands.[2] The double bonds formed between thymine and adenine and the triple hydrogen bonds between cytosine and guanine are essential in stabilizing the helical tertiary structure of DNA (Figure 1.1). Guanine and cytosine selectively interact with each other (as do thymine and adenine) because "mismatching" results in significantly weaker hydrogen bonding complexes.

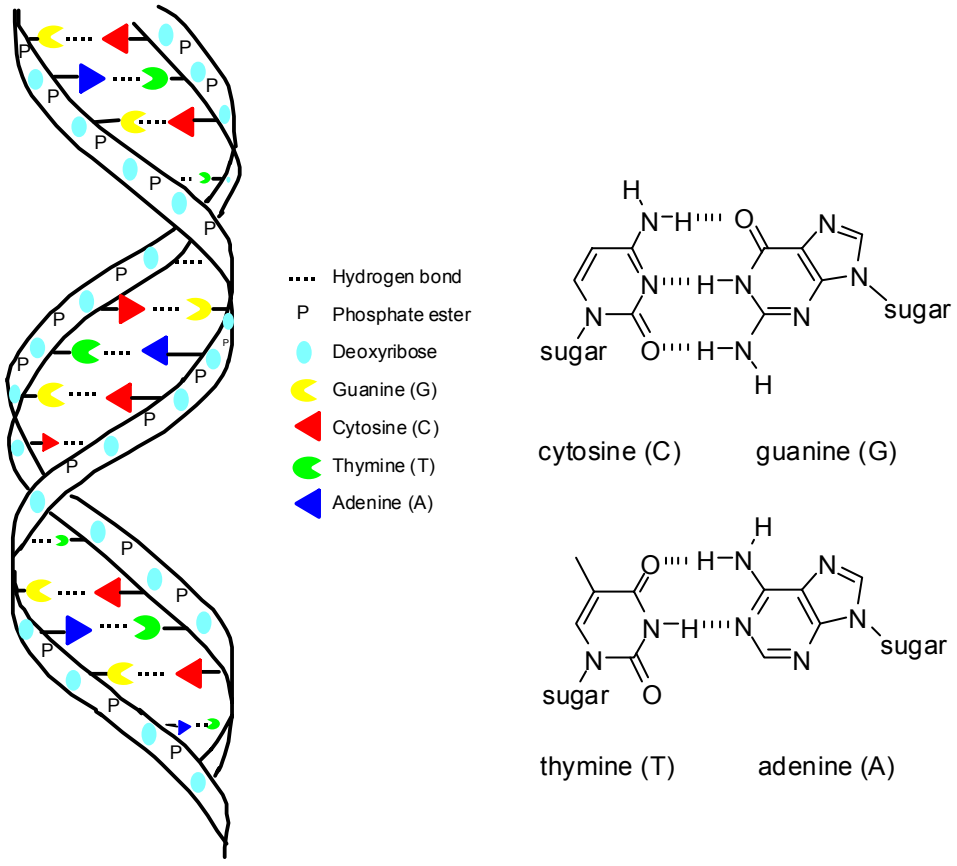


Figure 1.1. (a) DNA chain showing complementary base pairing. (b) Base pairing in DNA (guanine and cytosine form triple ADD-DDA hydrogen bonds; thymine and adenine form double AD-DA hydrogen bonds).

There are many examples of metal coordination in concert with other non-covalent interactions that can be found in nature. Another well-investigated and understood biological noncovalent nanostructure based on multiple noncovalent interactions in nature is the zinc finger.[11-16] A zinc finger is a protein domain that consists of 30 amino acid residues forming two anti-parallel β-sheets and an α-helix held together by a zinc ion. Thus combining metal coordination, hydrogen bonding, disulfide bridges, π-π stacking, and van der Waals forces to create functional complexity is the thrust behind nature's complexity. While the complicated morphology of a zinc finger might be hard to mimic with a synthetic polymer, the underlying principles governing structural biology can be utilized in synthetic polymer chemistry.

These translation of the lessons taught by nature into synthetic systems evolved into a subfield of chemistry known as supramolecular chemistry.[17-21] Supramolecular scientists expanded on these lessons by initially breaking down nature's complexity, using noncovalent interactions to develop macromolecular structures. Supramolecular chemistry has been extensively reviewed and encompasses a broad field that extends beyond the scope of this thesis.[22-40] This thesis will instead focus on the innovations of supramolecular *polymer* chemistry which is defined for the purpose of this thesis as a polymer consisting of a backbone that contains supramolecular components (i.e. noncovalent functionalities incorporated in the backbone, terminal ends or side-chains). By using noncovalent interactions to functionalize polymeric receptors with small molecule substrates the subfield of supramolecular *polymer* chemistry was created. Over the past twenty years, polymer chemists have only begun to explore how to mimic

nature's use of noncovalent chemistry to develop functional materials and for the fabrication of nanomaterials.

There are two strategies for fabricating nanomaterials: the "top-down" and the "bottom up" approaches. The top-down approach often uses traditional microfabrication methods where externally-controlled tools are employed to cut, mill and shape materials into the desired shape and order.[41, 42] In contrast, a "bottom up approach" (Figure 1.2) constructs macromolecular nanostructures beginning with small molecules specifically chosen for their propensity to form noncovalent interactions. The functional small molecules then often rely on a variety of noncovalent forces and the spatial "fitting" between these molecules to form supramolecular materials.[41-46]

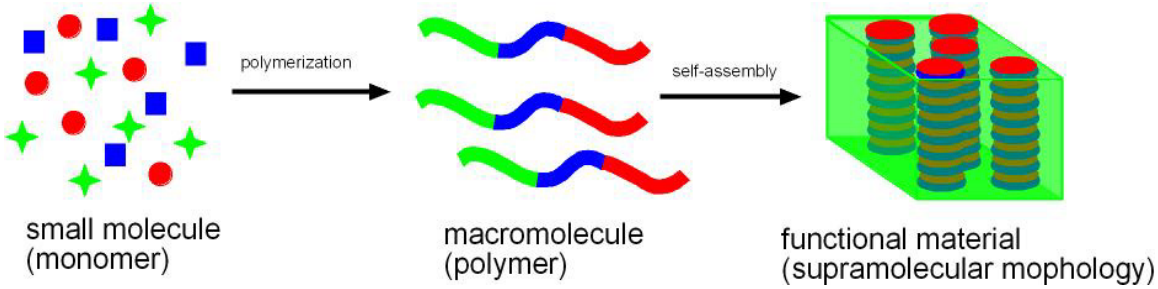


Figure 1.2. Schematic representation of the bottom up approach.

The "bottom up approach" has been inspired primarily from nature, as many biological structures are put together from a collection of small molecular components by means of noncovalent secondary interactions in a highly directional and controlled manner such as described above for DNA. In addition, the reversible nature of the noncovalent interactions that form the secondary structure of biopolymers, crucial to this approach, results in a material that is both self-forming and self-healing.

An unrealized goal of supramolecular chemists is to create artificial functional structures with the same specificity seen in nature. In order to accomplish these goals, it is important to have a detailed understanding of how synthetic molecules and structures interact with each other in a variety of environments, *i.e*. to develop structure property relationships between molecules, noncovalent interactions and the environment. Only after the development of such an understanding can we begin to construct functional materials using this knowledge. A collection of well-defined and understood noncovalent moieties could be used as a toolbox to design, construct, and build a multitude of functional nanomaterials with uses ranging from electronics to biotechnology. This thesis serves as a starting point towards the development of such a well-understood toolbox by borrowing ideas of the hydrogen bonded and metal coordination scaffolds seen in nature. Through the combination of developing a synthetic toolbox and using polymer methodology techniques, this thesis begins to explore how to effectively mimic biological complexity and to bring supramolecular science one step closer to understanding how multiple noncovalent interaction scaffolds interact with each other both in the synthetic and natural worlds.

1.4 Noncovalent Interactions

This part of the chapter will introduce two types of noncovalent interactions studied in this thesis, hydrogen bonds and metal coordination. While advances in π-π, ionic, and van der Waals interactions are important to the ultimate goal of mimicking biological complexity, they are not the focus of the work presented in this thesis and are omitted from this introduction chapter.

1.4.1. Hydrogen bonds

Hydrogen bonds are an important component of the molecular glue that binds proteins into their secondary and tertiary structures. Hydrogen bonds are also responsible for the properties of water, nature's vital solvent. Without hydrogen bonding the elegance we see in nature today would not be possible.

Hydrogen bonding occurs between a proton donating group (D-H) and a proton-accepting group (A). "D" is an electronegative atom such as oxygen or nitrogen (but can also be sulfur, phosphorous, carbon or a halogen). "A" is an electron lone pair of an electronegative atom or π-electrons of a conjugated system. A hydrogen bond is typically characterized as a proton shared by two electron lone pairs. Hydrogen bonds can be tuned, *i.e*. their strength tailored, through a number of variables including temperature and the solvent. Solvents that contain hydrogen bond donor or acceptor groups (typically polar protic solvents) are competitive inhibitors to binding. In the presence of a polar protic solvent such as water, the contribution a hydrogen bond makes to the molecular interactions is limited to the difference between the strength of the hydrogen bond:receptor and the hydrogen bond:solvent.

The strength of a typical single hydrogen bond is around 1-40 kJ/Mol,[47, 48] however the cumulative strength of hydrogen bonding arrays can form complexes with association constants as high as 10^9 M^{-1}.[47, 48] Figure 1.3 shows some typical hydrogen bonding arrays found in nature.

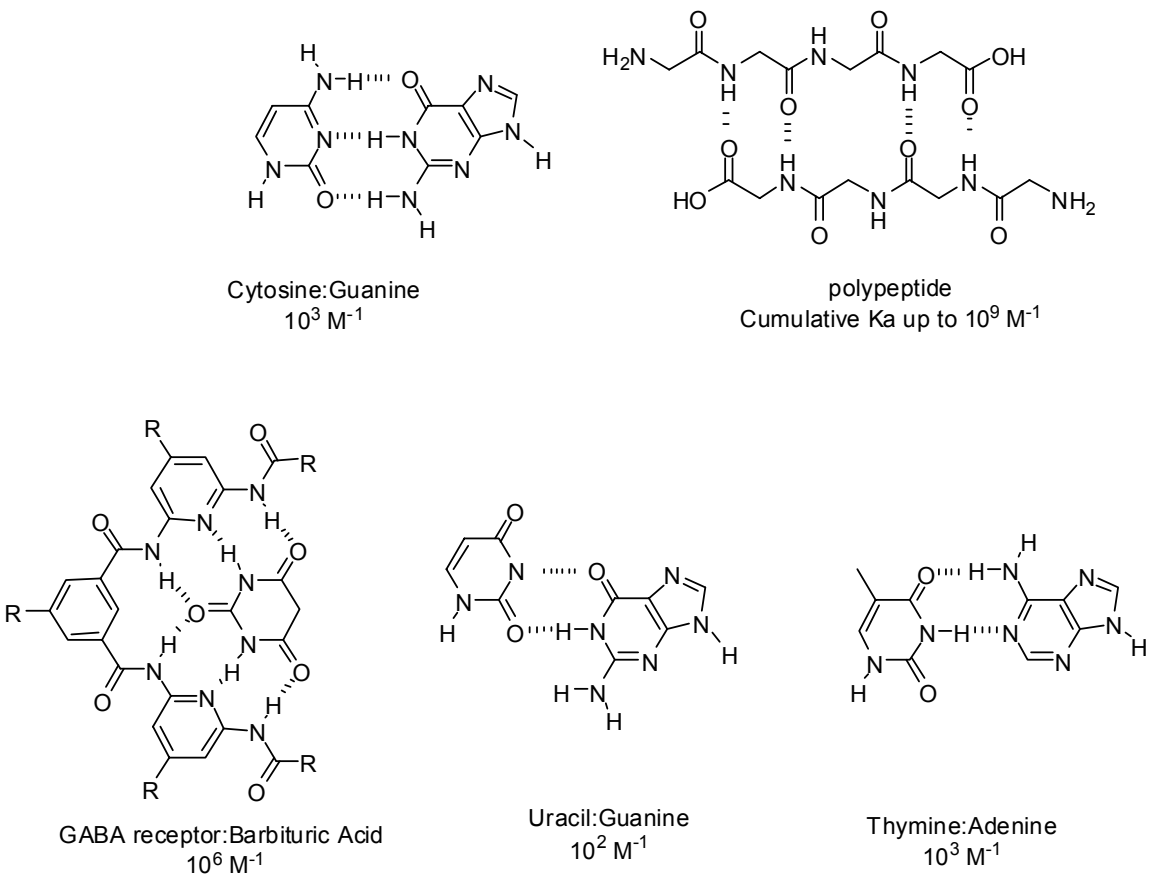


Figure 1.3. Complementary hydrogen bonding pairs found in nature. Association constants (K_a) are reported in chloroform.

The stability of hydrogen bonded assemblies is not only related to the number of hydrogen bonds incorporated, but also the arrangement of the donor and acceptor sites.[49] The differences in stability have largely been shown to be due to secondary attractive and repulsive interactions.[50, 51] Destabilization results from electrostatic repulsions between polarized atoms on adjacent hydrogen bonds. Figure 1.4 shows the differences in binding due to secondary interactions between ADA:DAD (10^3 M^{-1}) and DDA:ADD (10^2 M^{-1}) complexes. Alternating donor and acceptor moieties in a single hydrogen bonding motif results in a decreased binding in the complementary pair due to increased repulsive secondary interactions.

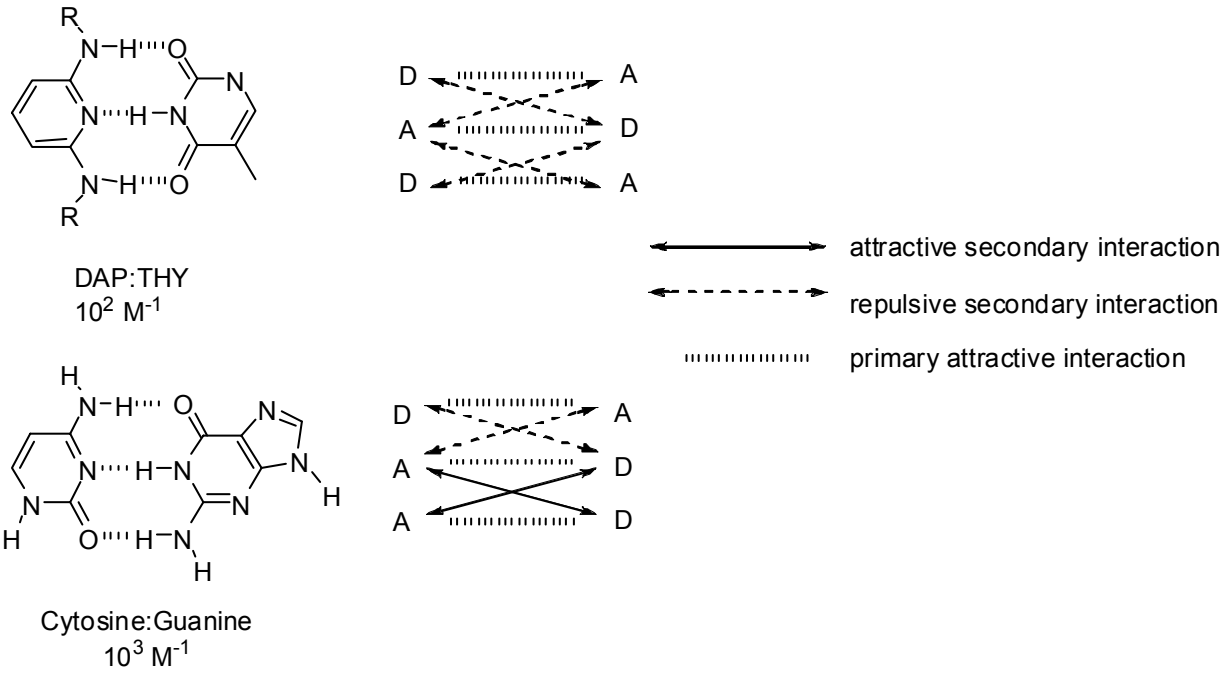


Figure 1.4. Attractive and Repulsive hydrogen bonding interactions between ADA:DAD and DDA:ADD complexes.

The DNA bases (figure 1.4) recognize their complementary bases to pair up even in the presence of other base pairs; this is called self-sorting. At the start of my studies, Isaacs and coworkers reported that a mixture of ureidopyrimidinone dimers, calixarene tetraurea capsules, calixarene bis(rosettes), and molecular clips exist in their associated forms despite the presence of competitive actors.[52] These molecules specifically associate with themselves or other molecules through noncovalent interactions in the presence of other competitive noncovalent forces are referred to as *self-sorting* molecules. This concept of self-sorting is key to the self-assembly that occurs in nature. Motivated by these studies I studied self-sorting between two hydrogen bonding moieties tethered onto a polymeric backbone. By gaining a synthetic understanding of this phenomenon, biomimetic materials can be more efficiently designed. Chapter 2 will explore *self-sorting* dynamics as a strategy for polymer multi-functionalization.

1.4.2. Metal coordination

Another class of noncovalent interactions seen in nature that has motivated supramolecular chemistry is metal coordination.[53-56] While hydrogen bonding is relatively weak, metal coordination is generally considered a significantly stronger binding interaction, however like hydrogen bonding, metal coordination is also highly solvent dependent. Metal coordination occurs when lone pair electrons from a ligand are donated to an empty orbital in a metal ion. As the strength of ligand binding to a metal ion increases, the rate at which the ligand binds and dissociates from the metal ion decreases. There are many broad classes of ligands such as classical, organo-metallic, cluster and bioinorganic.[57] Classical ligands can be found in nature, and are the only ligand-type reviewed in this thesis. A classical ligand, also called a Werner complex[57] after coordination chemistry's founder Alfred Werner, is a ligand that binds through the lone pairs of the main group atom of the ligand. Many metal-ligand interactions seen in nature are classical ligands (including water).

One example of a classical ligand that can be seen in nature is the histidine residues on proteins. For example, in numerous metalloproteins found in nature, such as hemeproteins (i.e. hemoglobin, myoglobin etc.), the lone pairs on the imidazole ring of the histidine moiety of the protein bind to the iron (Figure 1.5). The histidine residues serve as ligands that stabilize the heme complex to the protein allowing it's complex function. Metal coordination techniques based on classical ligands will be explored in both chapter 3 and 4.

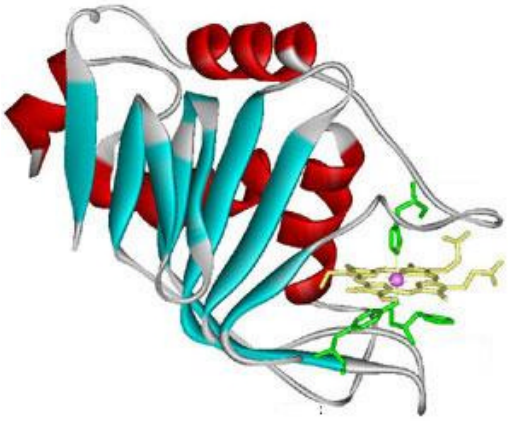


Figure 1.5. The 3D structure of the *S. marcescens* holo-hemophore (HasASM) shows that the heme iron atom is ligated by tyrosine and histidines.[58]

1.5 Self-Assembled Polymers

Supramolecular polymers are promising for materials fabrication because they can combine many of the positive attributes of conventional polymers with the properties that result from the dynamic equilibrium of reversible monomer units. Furthermore, the strength of the association constant of the noncovalent recognition unit can be tuned resulting ultimately in a high degree of control over polymeric properties such as the degree of polymerization.

Polypeptides are among nature's most important structures and frameworks for the biological machinery and can be considered supramolecular polymers that assembly into three-dimensional structures to form proteins.[2] Polypeptides are random copolymers consisting of twenty different monomers (amino acids) containing different side-chains. The amino acids can be considered nature's toolbox of monomer functionalities. The different functional groups capable of noncovalent interactions present on these side-chainsaid their self-assembly. Polypeptide chains fold into functional proteins using a library of noncovalent interactions. Clearly, the elegance that is developed from having a

single polymer backbone with multiple side-chain functionalities capable of undergoing folding patterns into well-defined 3D architectures is unrivaled in synthetic chemistry and one of the motivations for the development of a synthetic toolbox described in this thesis.

1.5.1 Strategies Towards Side-Chain Functionalized Polymers

Side-Chain Functionalization via Hydrogen Bonds

The accomplishments in the field of supramolecular side-chain polymers use the idea of breaking down nature's complexity by applying the same functionalities capable of noncovalent recognition interactions along the side-chains of a polymer. This was accomplished via the monofunctionalization of homopolymers *i.e.* the side-chains along the polymer backbone were noncovalently functionalized with small molecules. Therefore, by the simple addition of small molecules containing complementary recognition groups to the ones along the polymer backbone, a range of materials can be created and rapidly optimized as outlined in Figure 1.6.

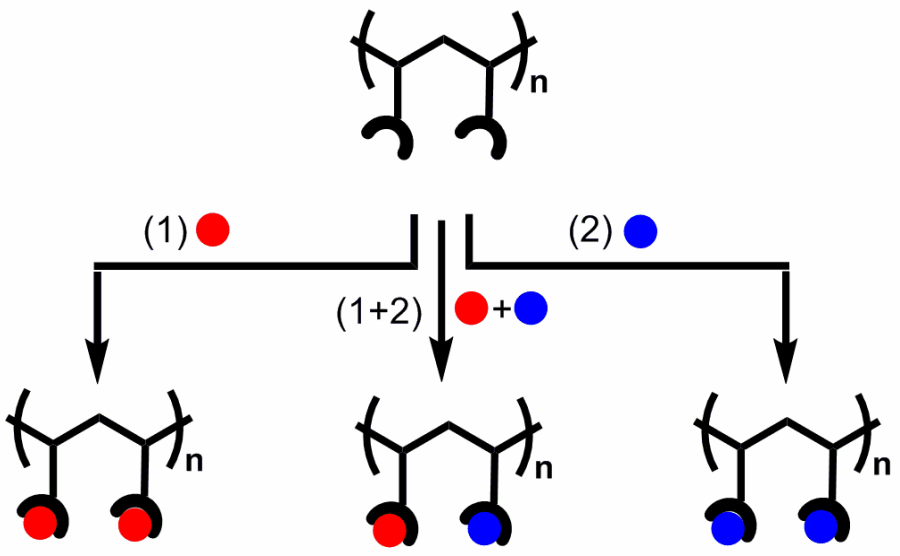


Figure 1.6. Noncovalent synthesis of different polymers from a generic homopolymer backbone. Via the addition of different recognition units a variety of polymers can be formed. Routes 1 and 2 are examples of different homopolymers that can be formed. Route 1+2 is an example of a copolymer containing more than one recognition unit.

The majority of reports on the monofunctionalization of polymers utilize hydrogen bonding as the self-assembly interaction.[59-67] The versatility of hydrogen bonding in polymer functionalization is owed primarily to the responsiveness of these bonds. Hydrogen bonds can be manipulated with a variety of external stimuli, including temperature, solvent, and pH.[47]

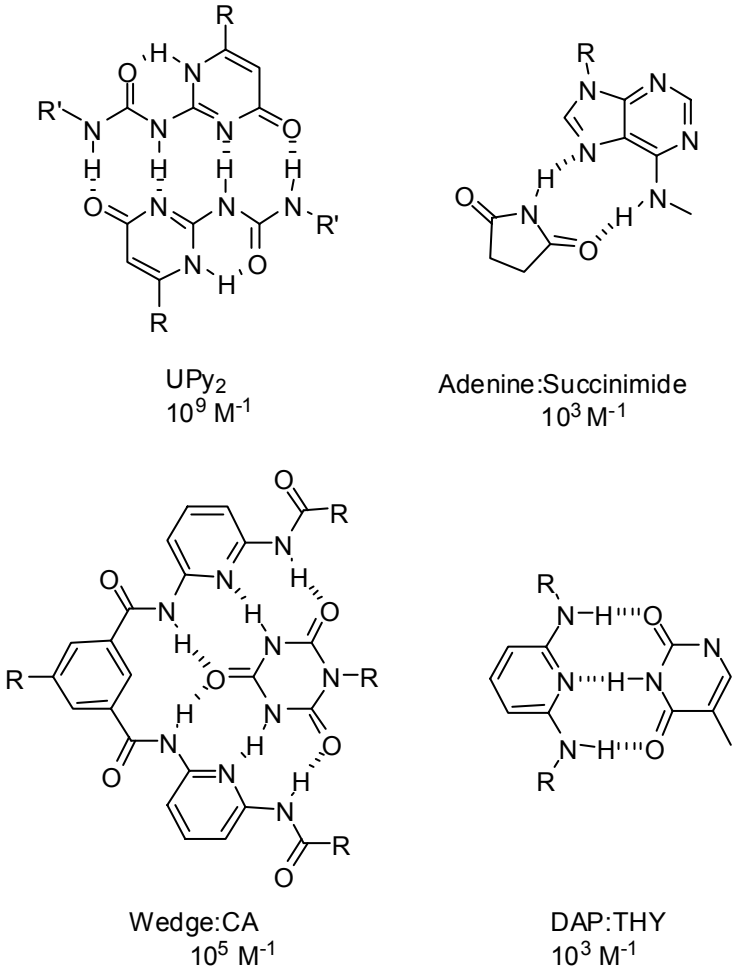
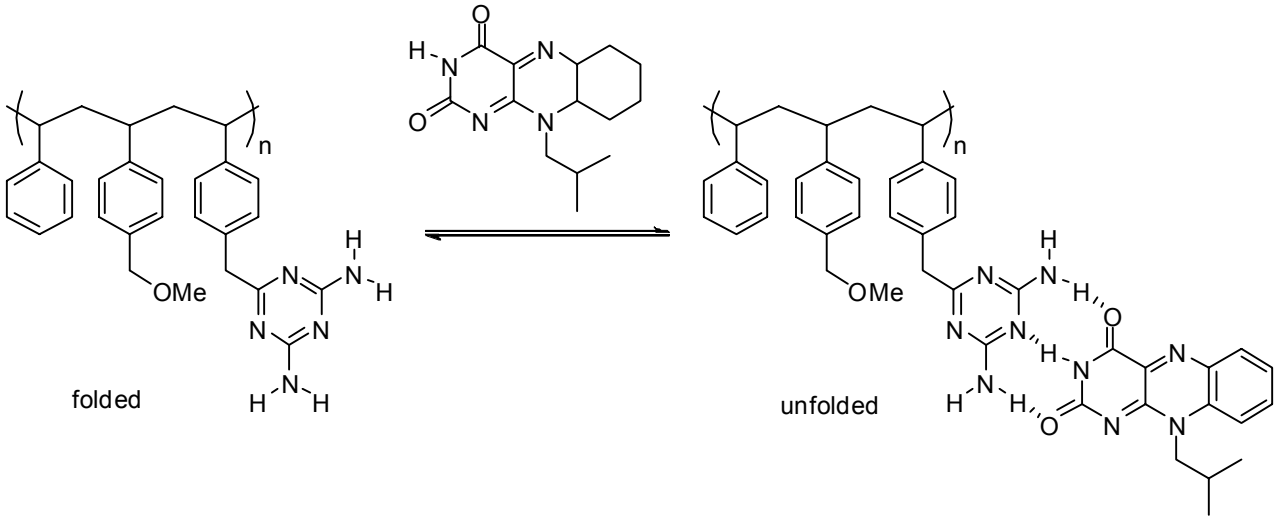


Figure 1.7. Complementary hydrogen bonding pairs frequently used in supramolecular assemblies. Association constants are measured in chloroform.

It is important to note that the strongest synthetic hydrogen bond arrays tend to originate from self-complementary systems (such as the UPy_2 recognition pair in Figure 1.7).[68-73] However, self-complementary recognition pairs are undesirable for polymer functionalization since they would result in uncontrolled crosslinking of the polymers and not in the controlled functionalization of the materials. Therefore, researchers have focused their attention on non self-complementary recognition pairs such as the DAP:THY, *i.e.* they have focused on hydrogen bond arrays originating from functional groups that have a low tendency to self-dimerize ($K_d < 50$ M^{-1}).[74-87]

Kato and Fréchet led the early work on the hydrogen bonding-based functionalization of polymers to synthesize liquid crystalline materials.[88-90] While these studies are instrumental to the field, they are mainly ten years old, have been reviewed extensively before and will not be reviewed in this thesis.[91] Furthermore, over the past decade the field has moved from liquid crystals to more general functionalized nano-functional systems motivated by nature. [91, 92]

Scheme 1.1. DAD-ADA hydrogen bonding recognition between diaminotriazine functionalized copolymer and flavin.



Among the leading research groups working on side-chain supramolecular polymer functionalization is the group of Rotello at UMass. The majority of their contributions are based on the post polymerization functionalization of poly(styrene)-based copolymers with hydrogen bonding sites followed by the noncovalent functionalization of these copolymers with a library of small molecules via hydrogen bonding.[65-67, 75-77, 93-115] Among the first examples of this group was the functionalization of a diaminotriazine-bearing poly(styrene) with flavin through a triple, non self-

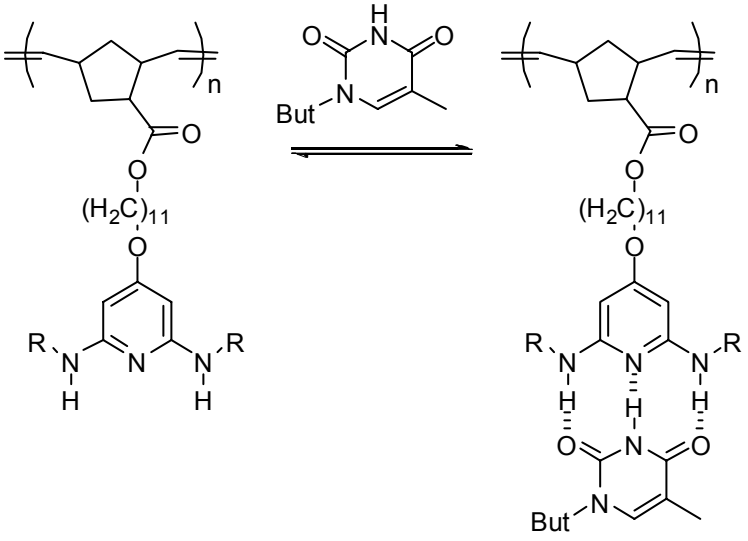
complementary hydrogen bond array (Scheme 1.1).[109] In this case, the polymer morphology changed from a folded state due to triazine dimerization, to a fully unfolded and functionalized copolymer upon the introduction of flavin. By controlling the morphology via the addition of additional noncovalent moieties, this is the first step to understanding a synthetic bioinspired structure. This simple synthetic analogy gives insight into the role of noncovalent interactions in the secondary structure of proteins. More general, the Rotello group coined the phrase "plug and play" to describe the modular noncovalent functionalization via hydrogen bonding.[64, 104, 116] This 'plug and play' approach used noncovalent synthesis to expand organic polymers into functional composite material using a variety of small molecules for functionalization.[104] Moreover, the versatility of this approach was readily extended to bulk materials. By using spin casting to kinetically trap host-guest complexes in poly(styrene) films, the Rotello group was able to demonstrate the noncovalent recognition of guests in various polymeric host systems.[64]

This methodology was then expanded further by Rotello into nanoscience by developing the "brick and mortar" strategy.[117] For example, poly(styrene) (mortar) functionalized with terminal thymine groups were hydrogen bonded to gold nanoparticles (brick) containing complementary diaminopyridine receptors. These polymer-gold nanoparticle assemblies served then as the basis for the exploration of multivalency with recognition induced polymersomes (RIPs).[118]

Similarly, the initial research efforts of the Weck laboratory focused on rapidly optimizing materials via functional polymer libraries inspired by nature.[119-121] The objectives were two-fold; (i) the employment of a fully functional group tolerant living

polymerization method that results in highly controllable and well-defined polymers and (ii) the use of a recognition unit that will allow for high yielding functional group attachment during the noncovalent functionalization steps. To achieve the first objective ring-opening metathesis polymerization (ROMP) a living and fully functional group tolerant polymerization method was employed.[74, 119-129] ROMP allows for the polymerization of monomers containing functional groups such as those found in nature eliminating the need for postpolymerization functionalization. This results in greater control of the polymer properties and quantitative polymer functionalization. Objective two was met with the introduction of thymine-based functional groups onto both diaminopyridine and diaminotriazine polymeric receptors (Scheme 1.2).[130]

Scheme 1.2. Noncovalent functionalization of diaminopyridine-based polymers with complementary thymine molecules.



These diaminopyridine and diaminotriazine functionalized polymers were then self-assembled with thymine-based molecules to create highly functionalized

materials.[131] The binding constants of the monomers did not significantly change as a result of the polymerization allowing for an efficient self-assembly onto the polymeric scaffolds. Furthermore, the polymer properties can be tuned by adding small molecule substrates to the polymeric receptors.[131] For example, the Weck group was able to easily tune the degree of crosslinking of the diaminotriazine polymer *via* complementary addition of the *N*-butylthymine substrates.

The Sleiman group also motivated by moieties found in nature, reported "DNA-mimetic polymers".[80, 132-136] They incorporated self-complementary adenine monomers in the polymeric backbone to form various polymer morphologies.[132] Using ROMP, they synthesized adenine functionalized copolymers that are able to fold into cylindrical morphologies arising from the self complementary hydrogen bonding motifs of the adenine units.[132] This idea of a self complementary backbone was explored further with a series of triblock copolymers containing diacetoamidopyridine and its complementary unit dicarboximide.[133] Similar to the concept of how different polypeptides fold into very different proteins, Sleiman reported that varying the triblock sequence and ratio resulted in different self-assembled architectures (Figure 1.8). These differences in properties were only recognized, however, in the aggregation behavior of the polymers and in the hydrodynamic radii without real control over the types of aggregations formed.[133] In order to fully reach our goals of synthetic biomimetic functional structures more noncovalent interactions need to be incorporated and a much deeper understanding of the interactions between the monomer units needs to be developed.

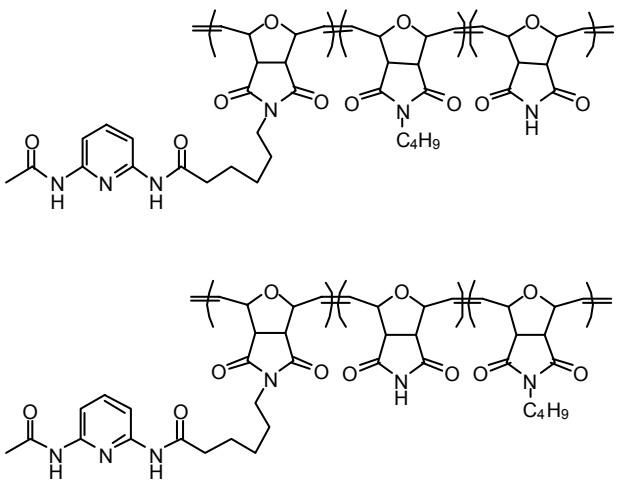


Figure 1.8. Variation in block sequence of self-complementary triblock copolymers.

Side-Chain Functionalization via Metal Coordination

Hydrogen bonding is not the only noncovalent interaction nature has in her toolbox. Therefore a second class of noncovalent interactions, metal coordination, was chosen to be included in the supramolecular synthetic toolbox developed in this thesis. Just as metal coordination is found in nature to hold together various protein morphologies, it has been used in main-chain supramolecular polymers to form polymeric architectures.[137-143] However, only in recent years has the use of metal coordination for the functionalization of side-chains supramolecular polymers been explored extensively.[144-150] The two most common classes of metal coordination polymers are based on either pyridine or pincer based ligands.

Pyridine Containing Side-Chain Functionalized Polymers

An obvious place to start investigating the viability of polymerizable metal complexes, and polymers functionalized through metal coordination are pyridyl-based systems, since a number of pyridine-based ligands are commercially available and many

pyridine based ligands can be structurally modified with little effort.[32, 140, 141, 149, 151-161] Moreover, pyridyl based complexes are prominent as actors in both nature and synthetic materials, ranging from metalloproteins to light-emitting materials and solar cells.[162, 163]

Bipyridine, a bidentate ligand, and terpyridine, a tridentate ligand, are known to coordinate a variety of metals including copper, zinc, iron, platinum, ruthenium, osmium.[141, 143, 144, 151, 154, 159, 161, 164-167] Both ligands can act as π acceptors to stabilize various oxidation states. The Weck group and others have explored the polymerization behavior of various norbornene-based transition metal complexes containing bipyridine monomers that can be polymerized via ROMP.[165, 166] Specifically, norbornene based monomers containing (tris-bipyridine) ruthenium (II), (bis-bipyridine) palladium (II), and heterolyptic ruthenium complexes (Figure 1.9) were synthesized and polymerized.

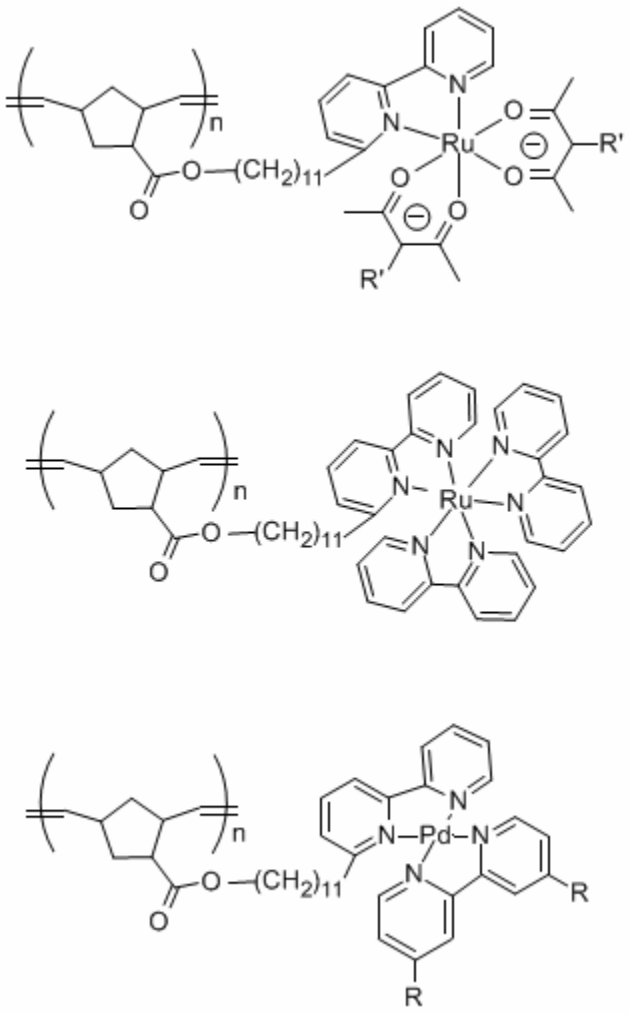


Figure 1.9. Bipyridine containing polymers reported in the literature.

Due to the ionic character of the $Ru(bpy)_3^{-2}$ complexes, homopolymerization and characterization of the resulting polymers were challenging. However, the solubility of the pendant bpy polymers can be tuned easily through the addition of alkyl substitutions on the ligands, allowing for the polymerization of all fully metal functionalized monomers via ROMP. Ru (II) tris bipyridine block copolymers synthesized by Sleiman were found to self-assemble in acetonitrile/toluene solutions to form micellar aggregates with luminescent properties similar to the monomeric analogues.[166]

While ROMP has been highly successful in producing well-defined polymers containing pyridyl based metal complexes, other polymerization methods have also been investigated.[32] Tew has demonstrated the controlled radical polymerization of terpyridine containing styrene monomers to yield trpy functionalized poly(styrene) copolymers. Postpolymerization modification via metal coordination of the copolymers proved to be a versatile route to metal complex containing polymers.[149]

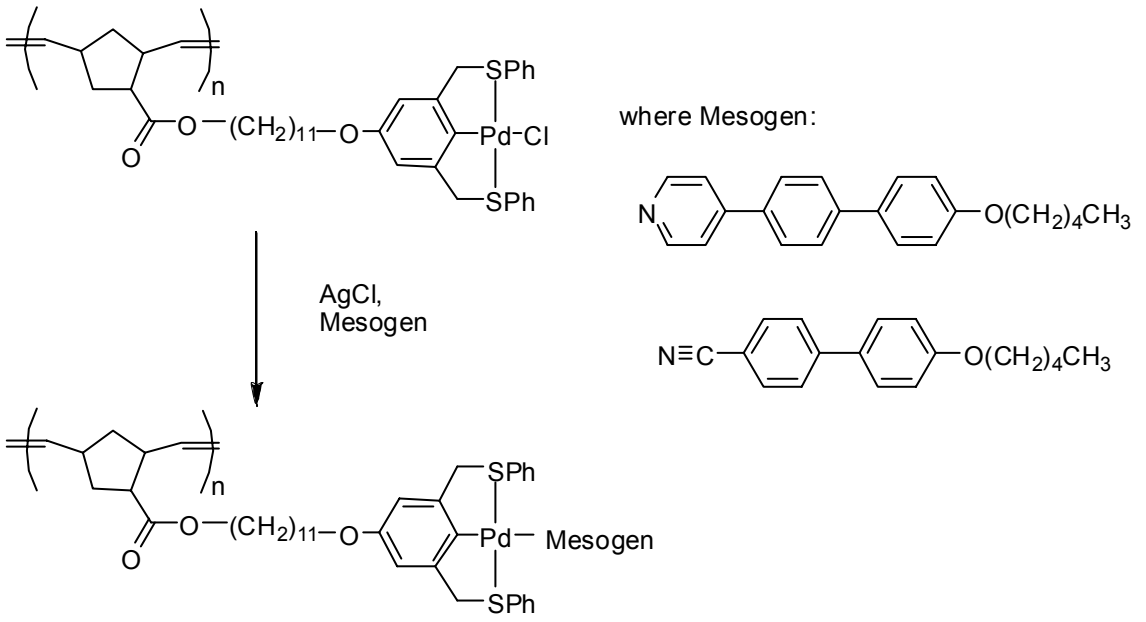
Side-Chain Functionalized Polymers through "Pincer" Complexation

"Pincer" type complexes containing platinum group metals have also become versatile tools in supramolecular science.[168] Just as nature has multiple functionalities for a single moiety, pincer complexes can be used as supramolecular synthons for a variety of applications in supramolecular chemistry and catalysis.[169-178] Pincer complexes are particularly attractive due to their stable tridentate coordination sphere, which can accommodate simple one-to-one addition of a variety of donor ligands, including nitriles, pyridines, and phosphines. Covalent tethering of pincer complexes to polymers should give rise to versatile and responsive materials *via* simple noncovalent functionalization. Pincer complexes containing a halide ligand are particularly useful for this goal, since the halide can serve as a "mask" for the coordination site during polymerization which then can be "unmasked" easily upon the addition of silver salts to the polymer allowing other ligands to be coordinated onto the polymeric receptors.

In 2002, the Weck group reported the first pincer side-chain functionalized polymer and a new addition to be studied for the synthetic toolbox.[123, 179, 180] The poly(norbornene) based Pd(II) pincer complexes could be functionalized easily and

quantitatively with a library of pyridines and nitrides resulting in the formation of fully soluble and highly functionalized metal-coordination polymers (Scheme 1.3).[180]

Scheme 1.3. Functionalization of Pincer containing homopolymers.



While it has been shown that rapid functionalization of polymers can be accomplished via side-chain self-assembly by either hydrogen bonding or metal coordination, the ultimate goal lies in extending these techniques to incorporate a number of different well-understood functionalities into highly complex materials. The living polymerization method outlined above coupled with multiple noncovalent recognition pairs along a single polymer backbone should allow for the realization of this goal.

1.5.2 Multiple Recognition Motifs

In order to fully grasp the complexity of nature and to develop a biotic systems with non-biological function, we must fully understand the intricacies of how types of complementary noncovalent interactions give both structure and function to

biomacromolecules. Developing an understanding of how the noncovalent moieties - contained in our synthetic toolbox - interact with each other, is key to forming non-biological materials that mimic the elegance of nature. By studying a polymer backbone that has multiple functionalities, we come one step closer to mimicking this complexity. Multifunctionalization can be carried out by incorporating two or more recognition units into the polymer backbone followed by the self-assembling (by the addition) of the complementary units. This addition can be carried out in a step-wise assembly or a one-step assembly.

Two Recognition Units

There have been a handful of groups who have explored multifunctionalizations to produce supramolecular structures based on noncovalent recognition motifs. For example, metal coordination has been combined with hydrogen bonding to synthesize dendrimers,[181] Cu-mediated DNA assemblies,[182] and hollow supramolecular frameworks.[183] Hydrogen bonding combined with ionic interactions have been used in the synthesis of thermotropic liquid-crystals,[184] three-dimensional supramolecular polymers,[185] self-organizing polymeric materials,[186] interwoven supramolecular arrays,[187] electrochemical switchable dyes,[188] and molecular elevators.[189]

However, to fully mimic the complexity and function of nature, a number of noncovalent interactions need to be present on a single backbone. There are fewer examples of multiple noncovalent interactions incorporated into polymeric side-chains. In one example, Ikkala and coworkers have combined metal coordination and ionic interactions to functionalized polymers.[190, 191] In these studies, zinc complexes were coordinated to poly(4-vinylpyridine). By selecting dodecylbenzenesulfonate counter ions the second ionic coordination gave rise to multicomb polymeric assemblies (Figure 1.10).

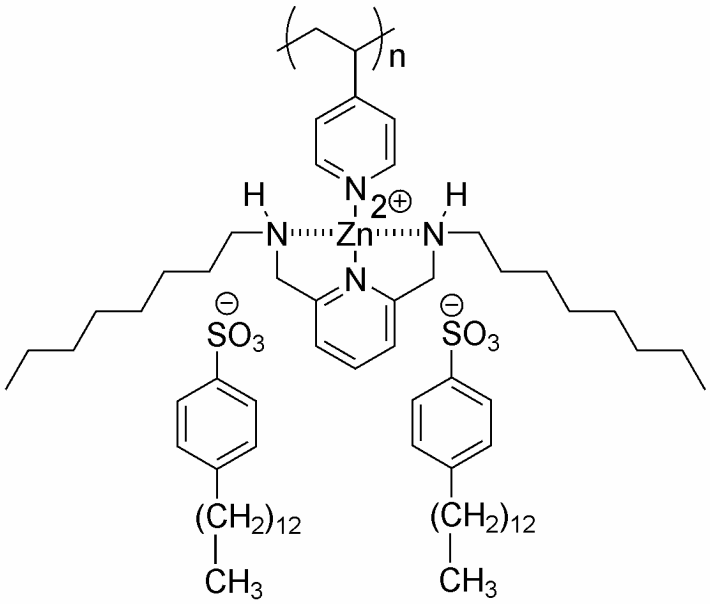


Figure 1.10. A multicomb polymer self-assembled by combining both metal coordination and ionic interactions.

One of the primary research foci of the Weck group is the exploration of multiple interactions along a polymer's side-chains. At the beginning of the work presented here, the Weck group had determined that the functionalization of polymers bearing two complementary units could be achieved in an orthogonal fashion.[192] While this was an elegant proof of concept, in order to reach our ultimate goal of functional materials capable of mimicking nature's elegance, more recognition units need to be incorporated into the polymeric systems and a detailed understanding of any interactions between these recognition groups needs to be developed.

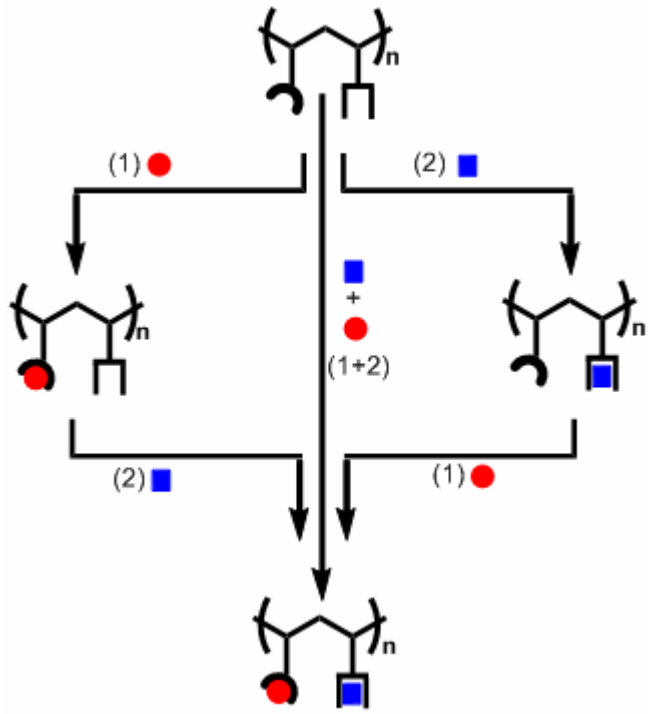
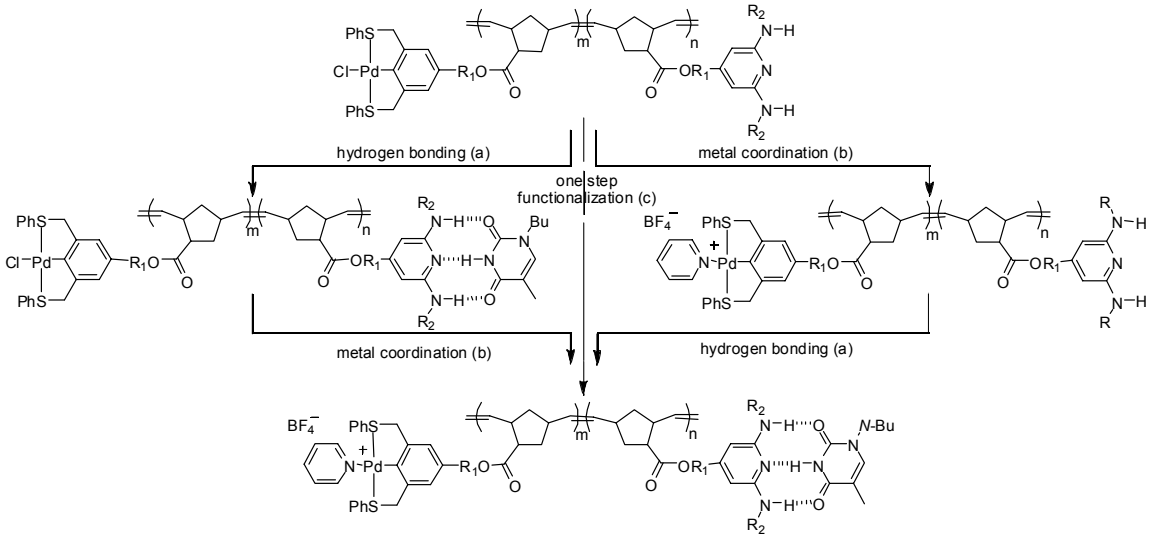


Figure 1.11. Generalized, orthogonal route to multifunctional polymers. Left side: addition of a substrate with recognition unit 1, followed by the addition of recognition unit 2; Right side: addition of a substrate with recognition unit 2, followed by the addition of recognition unit 1; Center: one-pot addition of both substrates 1 and 2 at the same time. Regardless of the route taken, the resulting polymer is the same.

Polymer Multifunctionalization via Metal Coordination and Hydrogen Bonding

The previous section has shown how polymers containing *one* noncovalent recognition unit along the polymer side-chains can be successfully functionalized. Several accounts from the Weck lab have explored metal coordination and hydrogen bonding together.[121, 124, 125, 193] At the start of the work presented here, Joel Pollino had shown the only account of this.[121, 124, 125, 193] He demonstrated that random copolymers having Pd(II) pincer complexes and diaminopyridine receptor side-chains could be functionalized both orthogonally and stepwise with its complementary receptors (pyridine and thymine respectively) as shown in Scheme 1.4.[192]

Scheme 1.4. Step-wise and one-step orthogonal functionalization of copolymers through metal coordination and hydrogen bonding.



Reagents and Conditions (a) *N*-butylthymine; (b) pyridine, $AgBF_4$; (c) *N*-butylthymine, pyridine, $AgBF_4$, one-step.

Subsequently, Kamlesh Nair has studied a polymer where the two previous noncovalent units were switched on the backbone (*i.e*. the previous small molecule substrates were now the recognition units along the polymeric side-chains) to form a block copolymer (Figure 1.12).[125]

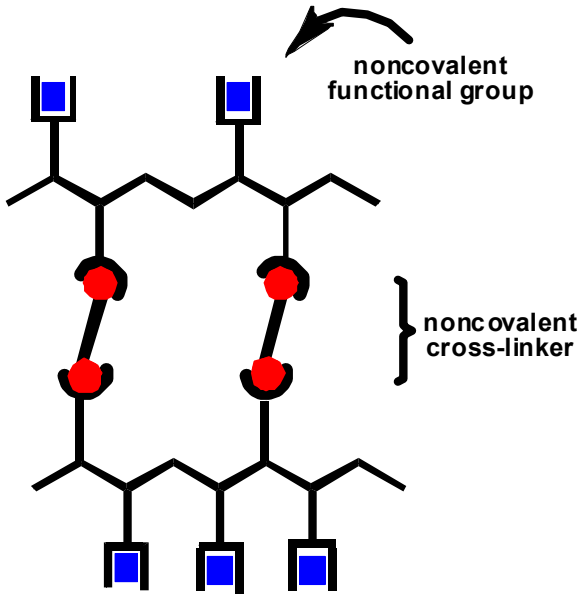
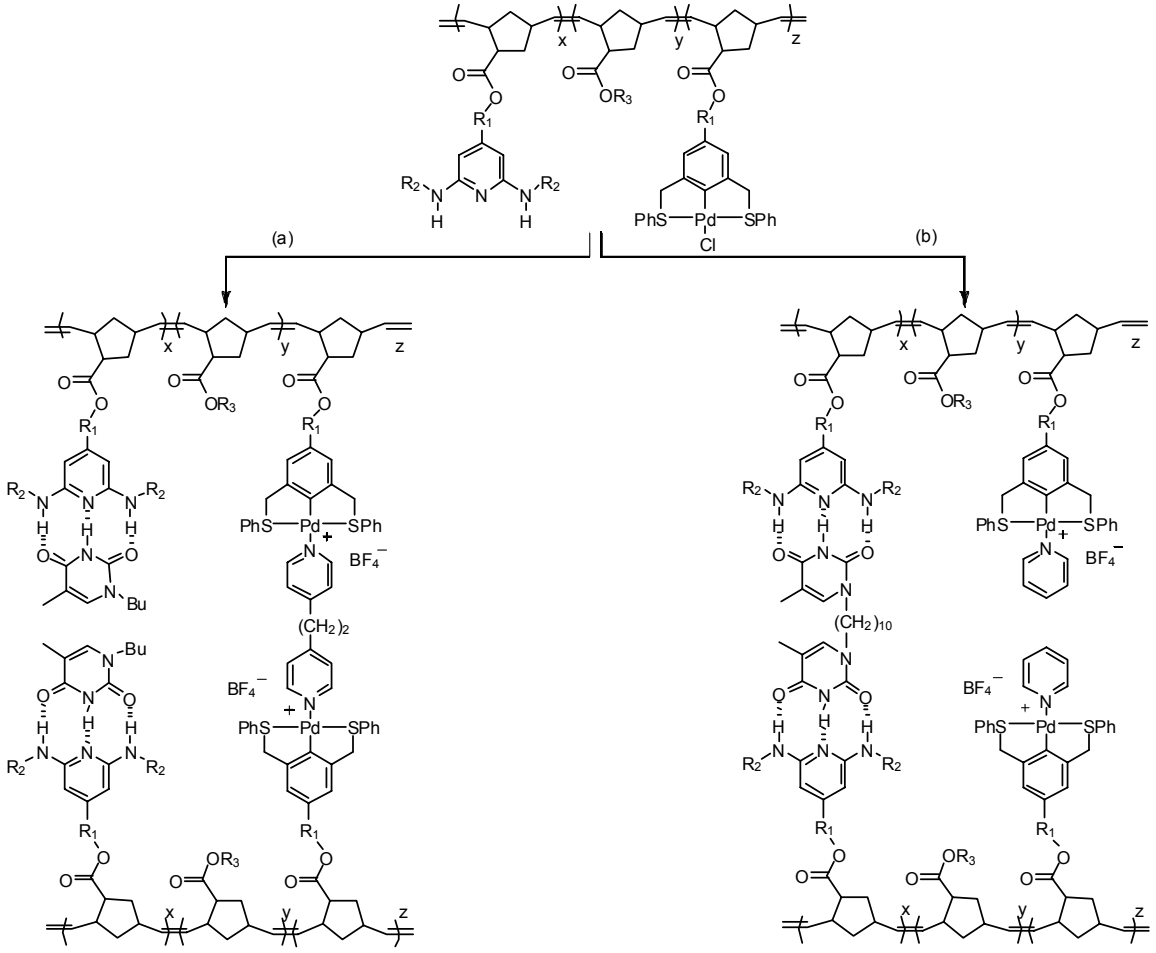


Figure 1.12. One example of a noncovalent synthetic approach to functionalized, cross-linked polymers. In this example non-complementary cross-linking units are employed. In other approaches (not shown) complementary interactions are used.

Kamlesh Nair confirmed that the functionalization was independent of the nature of the polymer backbone and that both the metal coordination and hydrogen bonding occurred independently. He then expanded this methodology, bringing us one step closer to the formation of dynamically cross-linked materials. By combining both hydrogen bonding and metal coordination in a cross-linked array, it was possible to tailor the degree of cross-linking (since the hydrogen bonding is temperature dependent) and to still functionalize the complexed array via the addition of a noncovalent receptor (Scheme 1.5).[179]

Scheme 1.5. Noncovalent cross-linking and functionalization through a combination of metal coordination and hydrogen bonding.



To form even more complicated materials mimicking the complexity of nature, the noncovalent toolbox would need to be extended to contain more noncovalent components. Copolymers containing three functional groups have been studied as potential drug carriers, cross-linking materials, molecular switches and as "smart" responsive materials as well as for curing applications. At the start of the work presented here I began to explore the possibility of adding an additional functional motif to Pollino's copolymer, *i.e.* to develop an orthogonal polymer containing three functional motifs. Chapter 3 will explore my work in this area.

While I was studying the work presented in chapter 3, Clint South in the Weck group reported the orthogonal functionalization of terpolymers using a combination of hydrogen bonding, metal-coordination, and pseudorotaxane formation (Figure 1.13).[121] The work presented in chapter 3 carries the idea of a terpolymer with recognition motifs a step further, presenting three interdependent recognition motifs capable of both intermolecular self-assembly and disassembly in response to various stimuli.

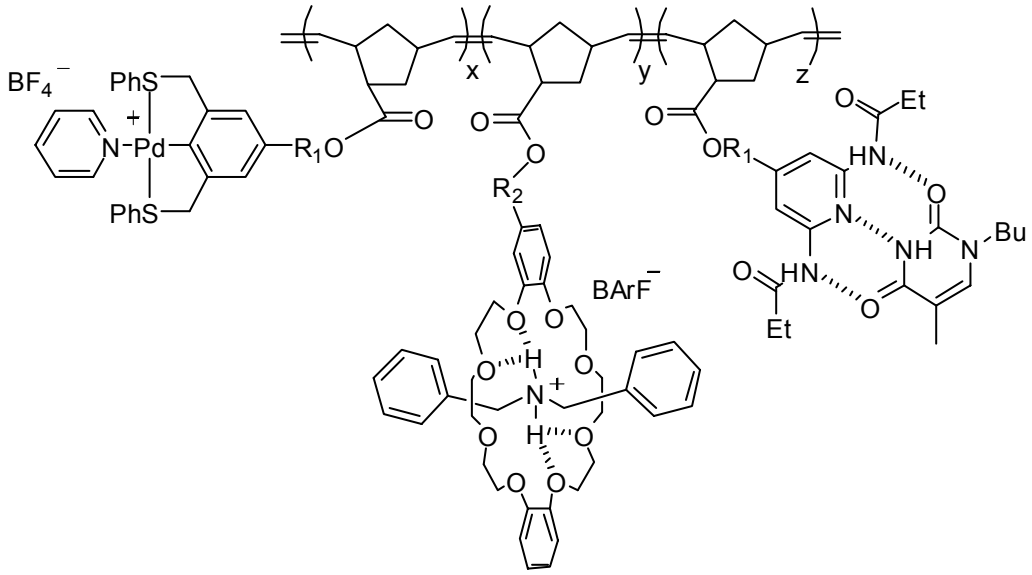


Figure 1.13. Triblock copolymer containing hydrogen bonding, metal-coordination, and pseudorotaxane formation

1.5.3 Main-Chain Functionalized Polymers

Main-chain Supramolecular polymers have been defined as polymers that are formed from repeating units that are held together by means *other than* covalent bonds.[194-196] Just as proteins are composed of polypeptides with functional side-chains, there are many examples in nature of a single recognition motif, functional terminal recognition motifs, and modular motifs. A subset of main-chain supramolecular

polymers, telechelic polymers, could be used to mimic some of the motifs found in nature.

The term "telechelic" originated from the Greek words "telos" (meaning far) and "chelos" (meaning claw). This term was used to describe a polymer chain having a "claw" to grip something at its far end.[197] A telechelic polymer is a polymer containing one or more reactive end groups at the end of the polymer chains. Not all telechelic polymers are supramolecular polymers, a "supramolecular" telechelic polymer's end groups contains a noncovalent recognition unit that can undergo self-assembly.

Telechelics provide a simple method for forming a wide array of block copolymers with different backbones and/or functionalities via self-assembly. There are many different types of polymers that can be generated from a telechelic polymer. For example, a telechelic polymer, A, could assemble with another telechelic polymer B that contains a recognition end unit complementary to that of A, to form an AB block copolymer. Another example is alternating block copolymers. By functionalizing both ends of polymer chains, A and B, one can form repeating ABAB block copolymers. A repeating block copolymer can be used to mimic the modularity found in many biopolymers such as titin.

There are many popular means for making telechelic polymers. These include post polymerization modification, macroinitators, chain-terminating units, and chain-transfer units. However, there are still limitations with many of the methodologies that have been developed. These limitations include: limited control during the polymerization, the choice of monomer, temperance for monomer functionality, poor yields and harsh conditions associated with post-polymerization modification, and simply the lack of versatility and simplicity found in nature. To overcome these limitations, a

new strategy needs to be implemented. The strategy described in chapter 4 of this thesis will provide a method for simple end-group functionalization while also allowing for the incorporation of functional side-chains. In addition, at the beginning of the work presented here, there were no examples in the literature of the formation of a true AB block copolymer or an ABA block copolymer via the combination of ROMP and supramolecular methodologies. A route for their rapid synthesis is also presented in chapter 4.

Main-Chain Functionalization via Post-polymerization Modifications

Some of the first telechelic polymers were developed using post polymerization modification methods. [198-200] The Meijer group synthesized a self-complementary hydrogen bonding moiety based on the ureido-pyrimidone unit.[198-200] The ureido-pyrimidone unit dimerizes through quadruple hydrogen bonds with an association constant of 10^6 M^{-1} in chloroform. Meijer's group used poly(dimethylsiloxane)s that were functionalized with the self-complementary ureidopyrimidone (UPy) at the ends (Figure 1.14).[196] The self-assembly of the functionalized ends lead to a strong modification of the material properties viewable in particular in significant increases in solution viscosity at higher concentrations of the self-assembling polymer. [196]Meijer expanded this to include polymers with rigid-rod and coil-like segments terminated with ureidotriazine units to access interesting morphological behaviors.[92, 194, 201] A limitation with this method is that the functional group is self-complementary meaning that well-defined block copolymers cannot be formed.

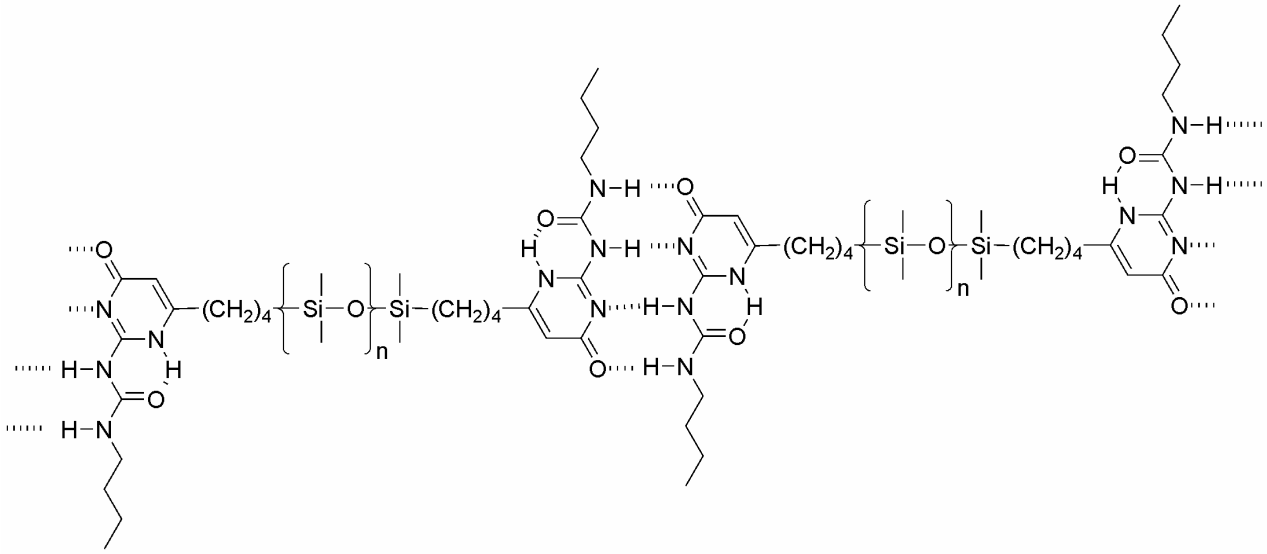


Figure 1.14. Block formation of supramolecular telechelic polymers via self-complementary UPy hydrogen bonding.

One elegant study inspired by the biopolymer titin, known for it's mechanical strength, toughness, and elasticity, contains UPy in the polymer backbone. The Guan group has developed multidomain polymers end functionalized with UPy groups that were then tethered to each other via flexible linkers.[202] Studies of the polymer showed the unfolding of the loops UPy units as the polymer was stretched and found that the polymer was more elastic and tough than that without the supramolecular component. This biomimetic polymer is one example of how supramolecular interactions plays an important role in developing advanced materials.

The Long group has also end-functionalized polymers such as poly(styrene) (PS), poly(isoprene) (PI), and microphase-separated PS-*b*-PI block copolymers with hydrogen bonding units including UPy groups.[204-206] They studied the relationship between end group structure and physical properties such as glass-transition temperature, melt viscosity, morphology, and dissociation temperatures of the resultant polymers. The

hydrogen bonded-terminated polymers formed thermoreversible aggregates and showed that complete dissociation that could be tuned by varying the structure of the hydrogen bonding units.

The Schubert group has functionalized various polymeric precursors with terpyridine units at the ends.[140, 142, 143, 155] Terpyridine can form stable bis-complexes with a large variety of transition metal ions. Via the addition of ruthenium, they could control the bifunctional assembly of the terpyridine units to form AB block copolymers. Ruthenium terpyridine based metal-coordination requires a high temperature reflux and has long reaction times. These reaction conditions significantly limit the versatility of this methodology.

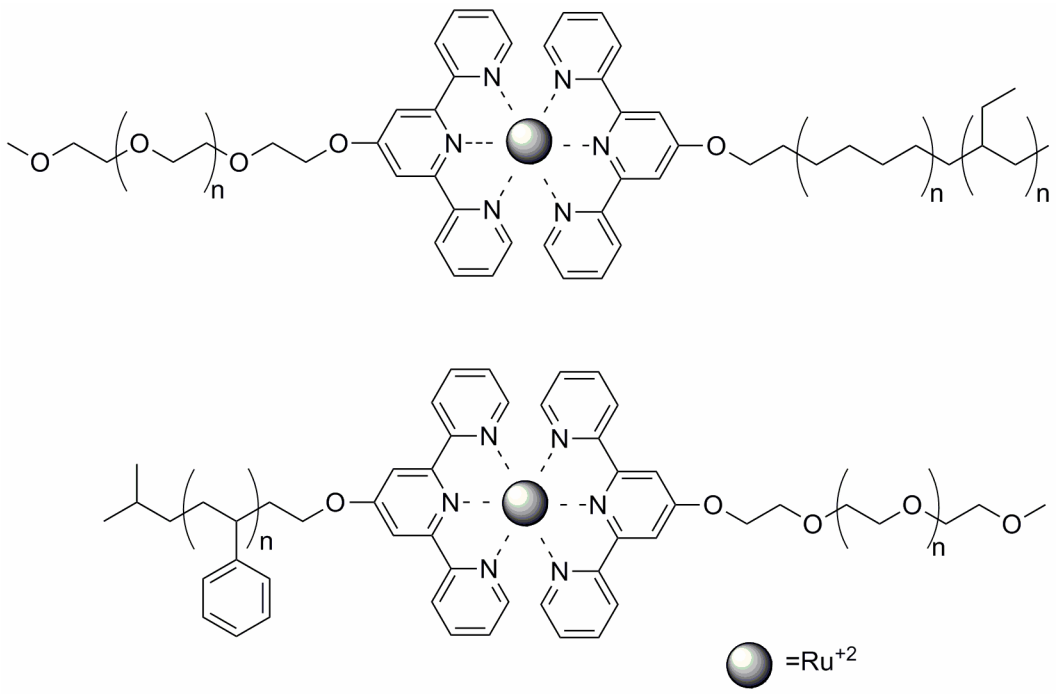


Figure 1.16. Metallo-supramolecular PEO-[Ru]-PEB and PS-[Ru]-PEO block copolymers.

The terpyridine end functionalized polymers can also be combined with polymers functionalized with self-complementary 2-ureido-4[1*H*]-ureidopyrimidinone (UPy) units to form hydrogen bonded metallo-supramolecular polymers.[140]

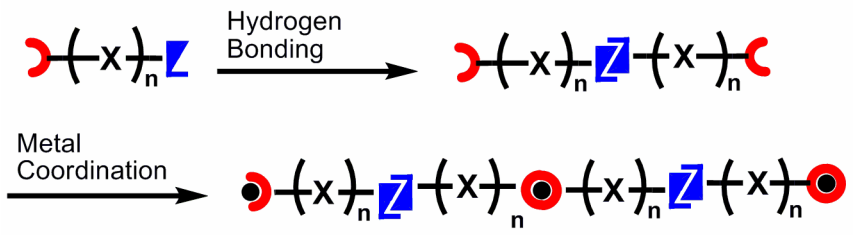


Figure 1.17. Representation of a supramolecular telechelic polymer containing both hydrogen bonding and metal coordination units. The hydrogen bonding end functionalized portion (blue) was first self-assembled via complementary hydrogen bonding. Next the addition of a metal salt (black) to form the metal coordination portion of the polymer.

During the work presented here, the Binder group reported the synthesis of telechelic poly(isobutylene)s (PIB) with hydrogen bonding motifs. Nucleobases such as thymine, uracil, cytosine and as well as chelate-type hydrogen bonding motifs containing both donors and acceptors (Hamilton wedge type) were affixed onto the end groups of the PIB.[207-210] In contrast to the work of Meijer, the hydrogen bonding recognition units are *non-complementary*. By using non-complementary recognition units, they were able to ensure simple and efficient *AB block copolymer* formation.

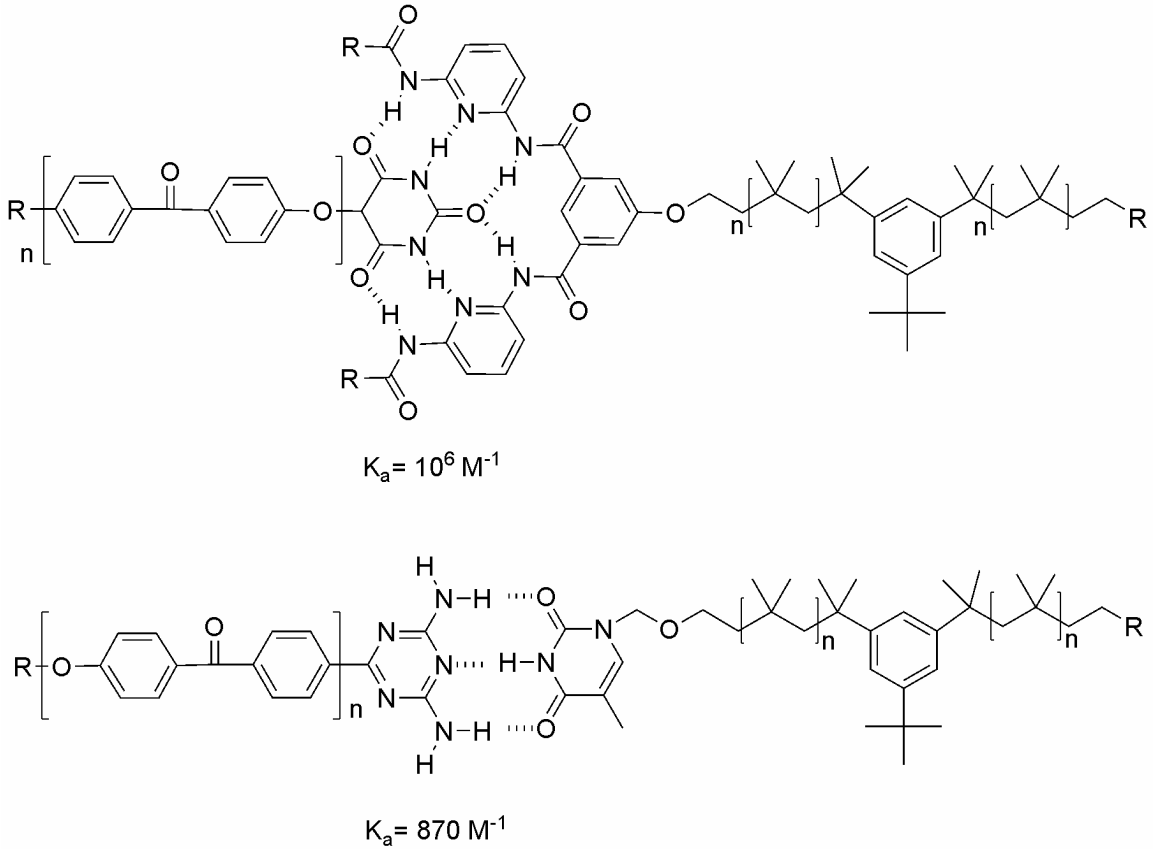
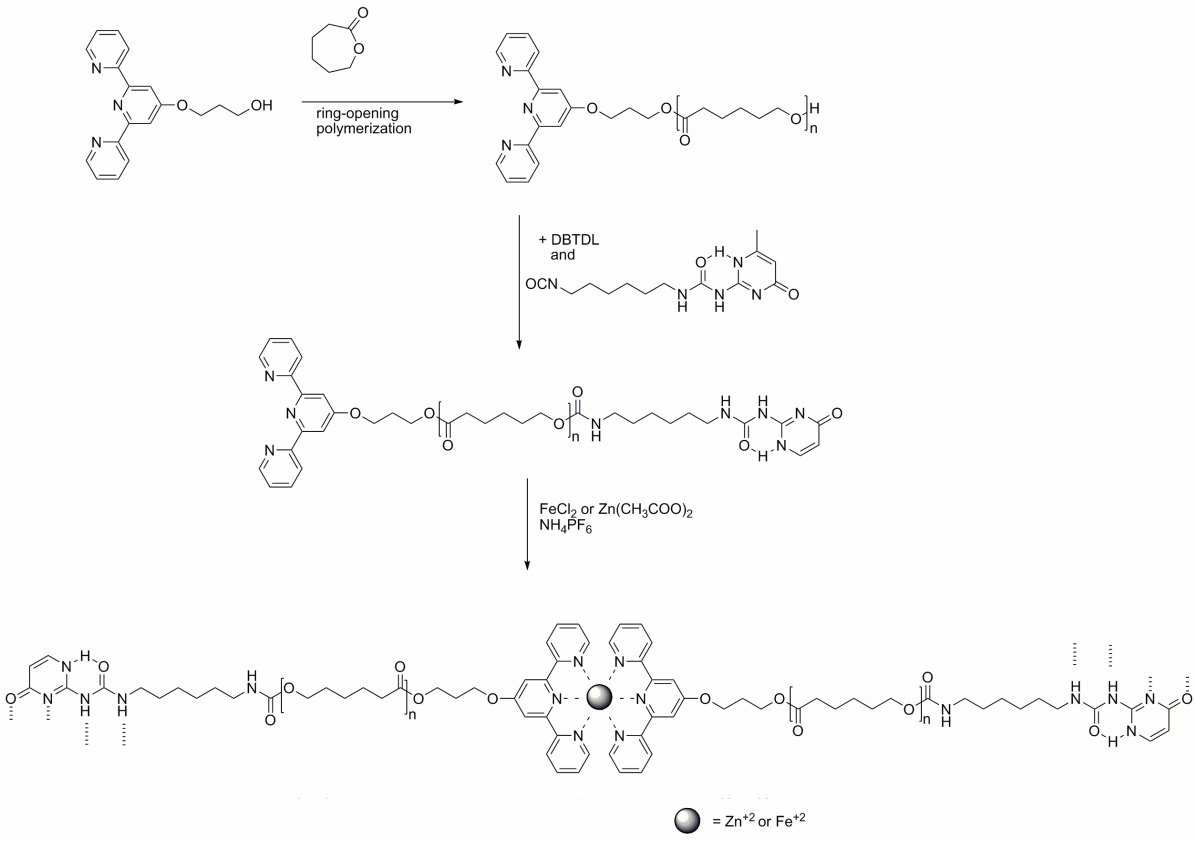


Figure 1.18. Supramolecular AB telechelic alternating copolymers containing non-complementary hydrogen bonding units

While the above examples demonstrate the concept of employing noncovalent interactions to prepare self-assembled polymers, the recognition motifs above were all incorporated via a post-polymerization step. A major disadvantage to post-polymerization modification is that the yields of the postpolymerization step are often not quantitative. Many post-polymerization reactions require harsh reaction conditions and thus extremely stable polymers. In addition to poor yields and harsh conditions, this approach is complicated, lacks versatility in functional groups and is a long way from mimicking nature's elegance and simplicity. To overcome these disadvantages other strategies have been developed that allow for simple end group functionalization and the incorporation of the end group *during* the polymerization.

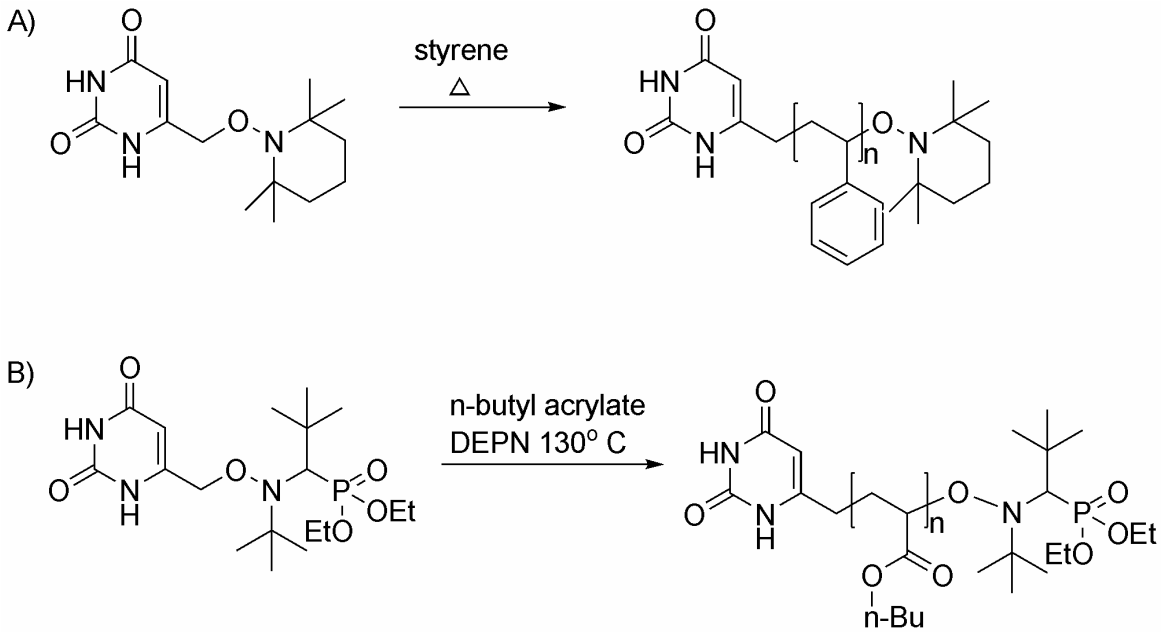
Main-Chain Functionalized Polymers via Functional Initiators

One strategy to avoid the harsh reaction conditions is the use of a functionalized initiator. The Schubert group expanded on their hydrogen bonded metallo-supramolecular polymer techniques to make poly(L-lactide)s from terpyridine initiators through various polymerization methods.[211, 212] In one example, they employed 4-hydroxypropyloxyterpyridine, for the tin octanoate-catalyzed ring-opening polymerization of ε-caprolactone,[138] followed by post-polymerization modification of the terminal hydroxyl group to incorporate a hydrogen bonding moiety. Scheme 1.6 shows the ring-opening synthesis of ε-caprolactone and the subsequent post-polymerization modification. By combining these two techniques, Schubert and coworkers were able to ensure that every polymer is functionalized differently at the terminal and proximal ends (via functional initiation and post polymerization reactions).



Scheme 1.6. Functional initiation and subsequent post-polymerization modification to form a hydrogen bonded metallo-supramolecular polymer.

Motivated by nature, the Long group has introduced uracil hydrogen bonding units into styrenic and acrylic polymers using a new family of functionalized initiators (Scheme 1.7).[213]



Scheme 1.7. Formation of end-functionalized polymers: Using A) a uracil-TEMPO initiator followed by a TEMPO-catalyzed poly(styrene) polymerization and B) a uracil-DEPN Initiator followed by a the formation of poly(*n*-butyl acrylate).

These hydrogen bonding initiators were used in the stable free radical polymerization of styrene and *n*-butyl acrylate. The resulting hydrogen bonding polymers exhibited narrow and controlled molecular weight distributions that are characteristic of controlled free radical polymerizations.[213]

The Hawker group has developed methodologies towards controlled radical polymerizations using alkoxyamine (TEMPO) radical initiators, which can be functionalized via a variety of organic transformations.[213] The Rotello group then used this methodology to synthesize tri-DAP end-functionalized poly(styrene) (triDAP-PS) (Figure 1.19).[214] They then adhered these brush-like polymers onto thymine-silane derivatized silica surfaces. The polymers they created displayed morphology changes based on the solvent that was used during the absorption.

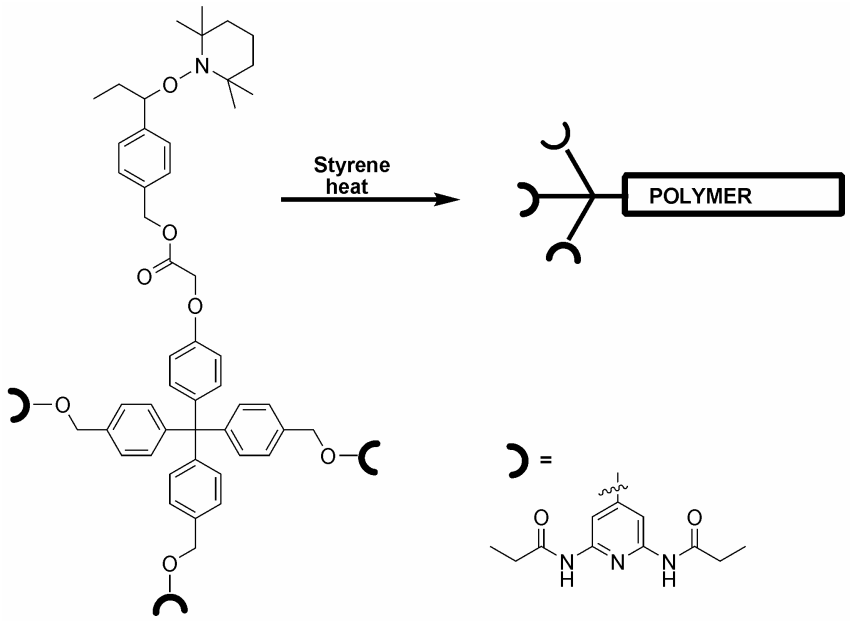


Figure 1.19. Tri-functionalized initiator resulting in tri-end-functionalized polymers .

These methodologies while elegant, are limited to a few classes of monomers and also lack functional group tolerance. In order to fully grasp the complexity of nature and to develop abiotic functional materials, we must be able to incorporate a variety of functional groups.

Main-chain Functionalized Polymers via ROMP Techniques

Ruthenium-catalyzed ROMP polymerization is a technique that is highly functional group tolerant, allowing for the incorporation of nearly any functional group onto either the ends or the side-chains of the polymer. ROMP is a process by which a strained cyclic olefin, such as norbornene, is broken and reformed in the presence of an organometallic initiator (Figure 1.20). Other examples of strained olefins typical polymerized via ROMP are cyclooctenes, cyclobutenes, and oxanorbornenes. ROMP can be initiated via a variety of metal initiators including tungsten and ruthenium alkylidines (Figure 1.20)A standard ruthenium-catalyzed ROMP polymerization is typically terminated via the addition of ethyl vinyl ether to give methylene end groups.

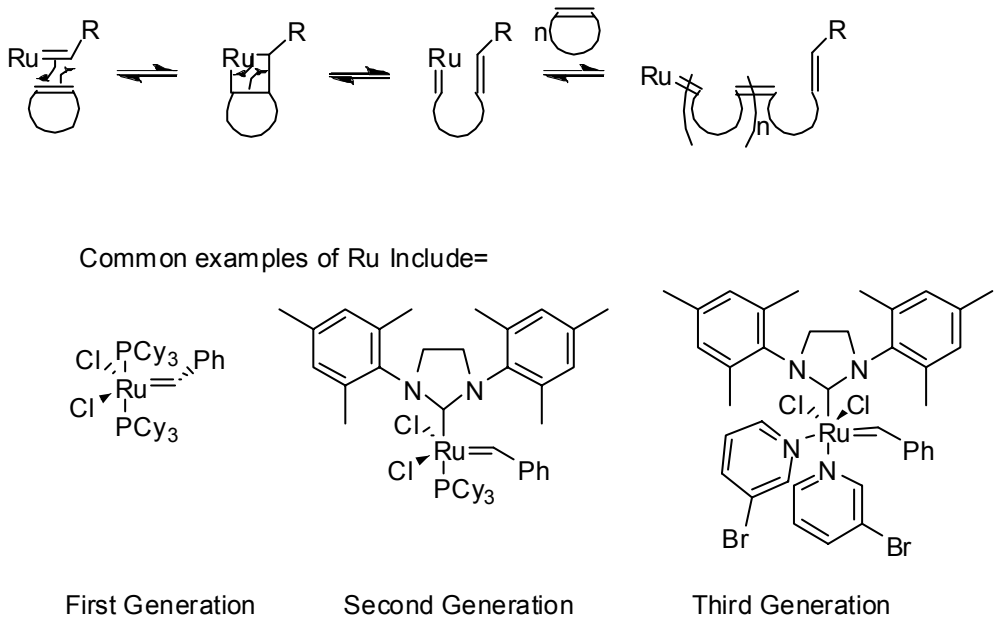


Figure 1.20. Ring-opening metathesis polymerization mechanism. Common ROMP initiators including Grubbs' first, second, and third generation initiators.

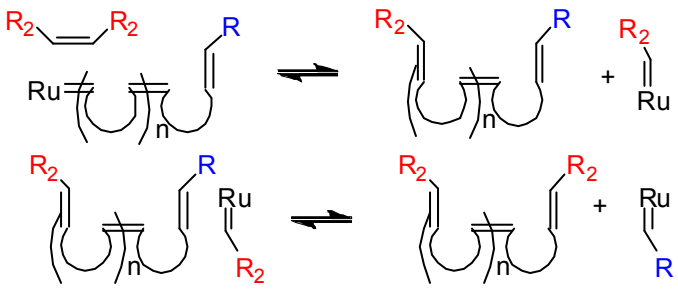
One of the first methods used to end-functionalize a ROMP polymer is by exposing the living (non-terminated) polymer to molecular oxygen. [215] Oxygen exposure results in an aldehyde end group. The aldehyde end group can then be transformed via organic reactions into a variety of functional moieties.[215] This technique however, still requires the problematic post-polymerization transformations discussed above and lacks nature's simplicity. To overcome these limitations, and to form end-functionalized polymers via ROMP, chain-transfer agents (CTA) and chain-terminators (CT) have been developed.

Telechelic Polymers Via Chain-Transfer Agents

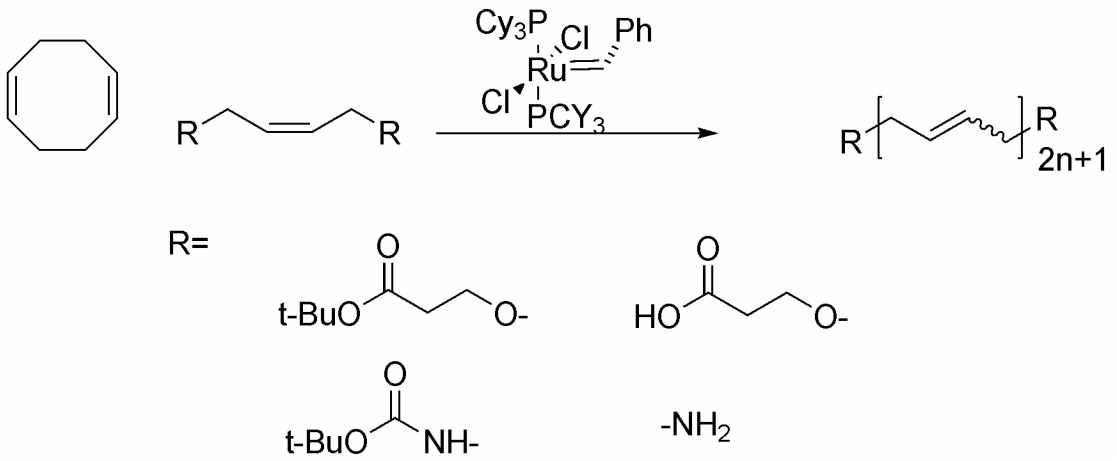
A chain-transfer agent (CTA) is an acyclic alkene that can be used during ROMP allowing for complete functionalization of the polymer end-groups. By including a CTA containing functional groups (such as noncovalent recognition motifs) a telechelic supramolecular polymer can be attained (Scheme 1.6). The CTA allows for control of

the molecular weight of the desired polymer by varying the chain-transfer agent to monomer ratio.[216] Ruthenium alkylidene initiated reactions conducted in the presence of a chain-transfer agent can result in symmetrically terminated, well-defined homopolymers.

Scheme 1.8. ROMP mechanism showing the incorporation of a chain-transfer agent.



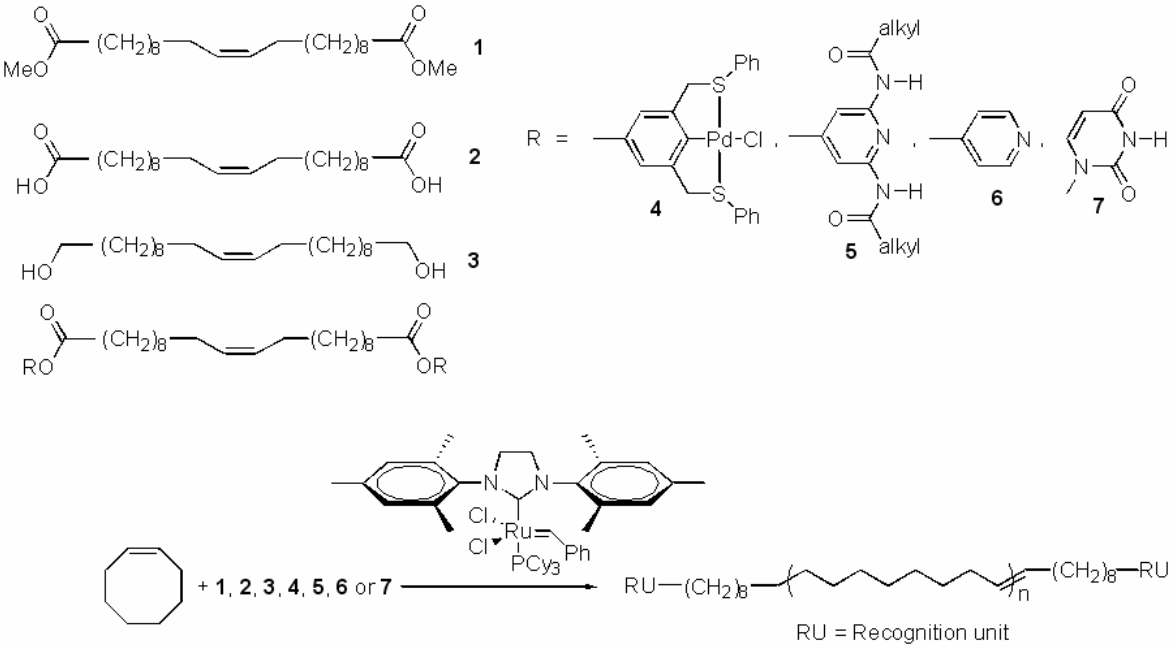
The Grubbs group reported the synthesis of hydroxyl terminated telechelic poly(butadiene)s via the ruthenium-catalyzed ROMP of COD in the presence of *cis*-1,4-bis(acetoxy)- 2-butene followed by a post-polymerization deprotection step.[217] They extended this approach to carboxyl- and amino-terminated telechelic polymers by employing appropriately functionalized CTAs (Scheme 1.9).[217]



Scheme 1.9. Cyclooctene polymerization with a CTA.

Gibson and Okada have also utilized this methodology to form poly(norbornene) macromonomers functionalized with hydroxyl groups at the terminal ends.[218] These hydroxyl-functionalized polymers were then employed in polycondensation reactions to form highly controlled polymers.

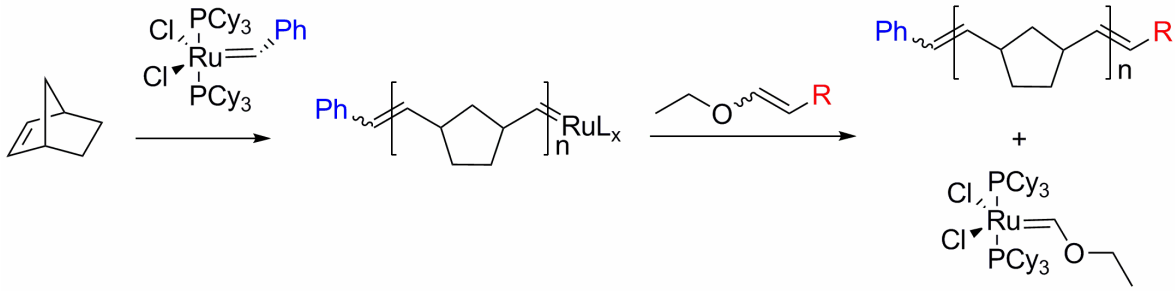
Mary-Nell Higley in the Weck group first utilized this CTA methodology for the formation of block copolymers.[216] Telechelic homopolymers of cyclooctene derivatives end-functionalized with hydrogen bonding or metal-coordination sites were formed through the combination of ROMP with a corresponding functional CTA. These telechelic homopolymers were then self-assembled with their complement homopolymer or small molecule analogue to form block-copolymer architectures. In addition, the homopolymers were synthesized with a high control over molecular weight and without the need for post-polymerization procedures (Scheme 1.10). Bert Meijer also formed telechelic block copolymers through the combination of ROMP with a corresponding functional self-complementary CTA.[219]



Scheme 1.10. Examples of telechelic end-functionalized polymers containing hydrogen bonding and metal coordination motifs.

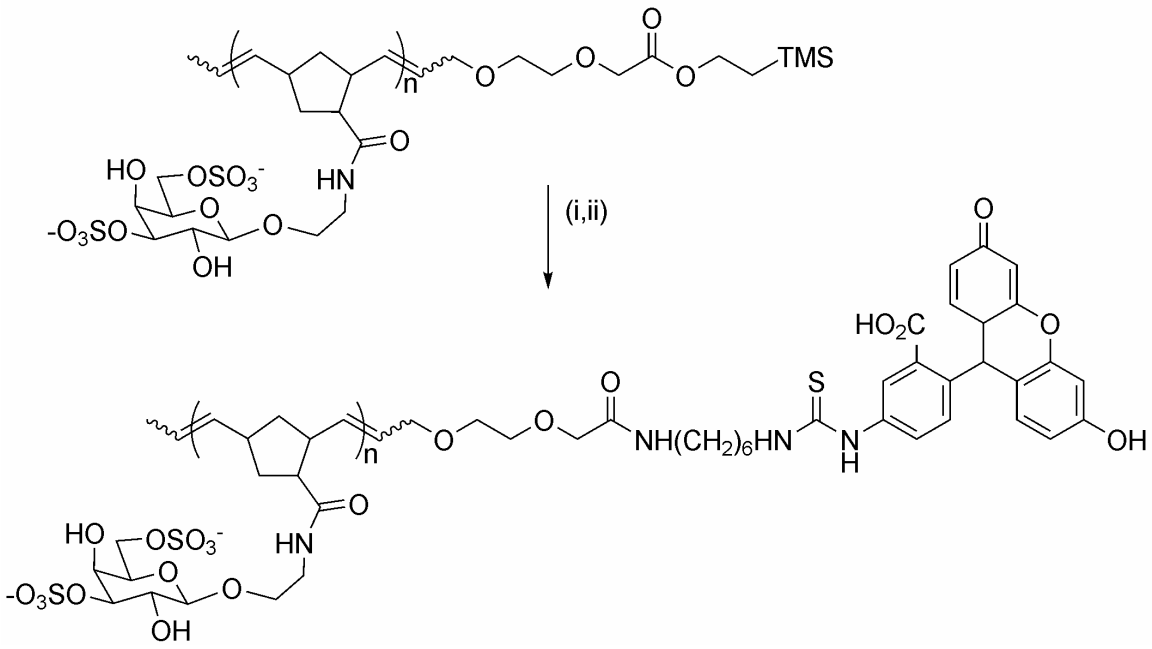
Telechelic Polymer Formation Via Chain-Terminating Units

Another means for synthesizing end-functionalized polymers is through the use of a chain-terminating (CT) unit. In a living ROMP polymerization, an active carbene remains at the terminal end of the fully polymerized polymer chain. The metal alkylidene can undergo other transformations and then be cleaved from the chain via an enol-ether (Scheme 1.11). In contrast to the chain-transfer agents discussed above, a chain-terminated polymer results in a *single* functionalization at the *terminal end* of the polymer. Using this methodology, virtually any functional unit can be incorporated onto the end of the polymer chain.



Scheme 1.11. Termination of ruthenium carbene-initiated ROMP reaction with an enol-ether resulting in an end-functionalized material.

In one example motivated by nature, the Kiessling group employed this methodology in combination with postpolymerization modifications to synthesize end-labeled polymers used for exploring cell–surface receptor-ligand interactions to inhibit cell-surface L-selectin interactions.[220] The terminated polymer was then conjugated to fluorescein (Scheme 1.12). Using fluorescence microscopy they were able to visualize the neoglycopolymer binding specifically to the cell surface L-selectin.



Scheme 1.12. Synthesis of fluorescent end-functionalized neoglycopolymer (i) NaOH (ii) 5-((5-aminopentyl)-thioureidyl) fluorescein, EDCl, N-hydroxysulfosuccinimide, water.

The Sleiman's group later used the same methodology to synthesize a biotin terminated polymer.[158] This polymer was then self-assembled with strepavidin as a crosslinking agent for the formation of nanospheres. This is an elegant example of forming a functional three-dimensional structure from the "bottom up" combining supramolecular chemistry with these polymerization methodologies (Figure 1.21).

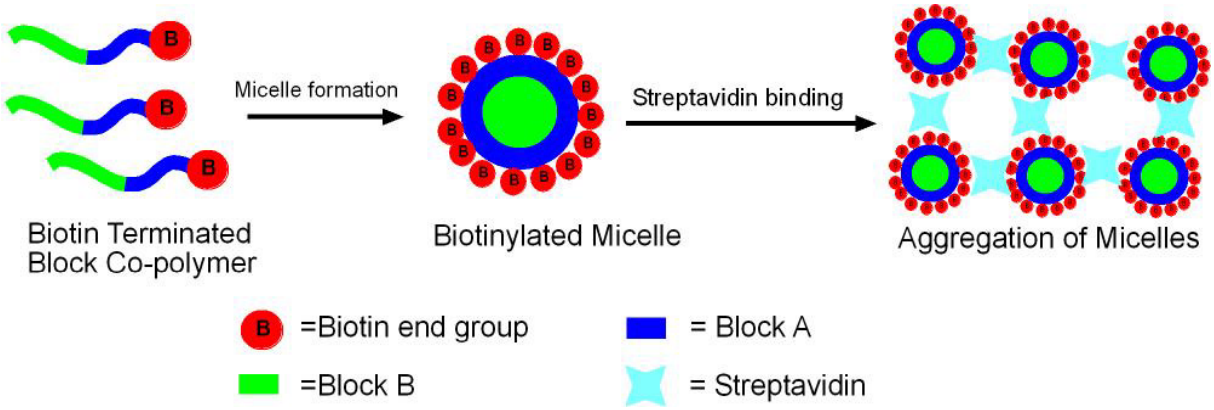


Figure 1.21. Schematic representation of the aggregation of biotinylated micelles by Streptavidin.

However, while there are many elegant uses of this methodology to probe into biological systems, there are no accounts reported using these methodologies for AB and ABA block copolymers. In order to obtain our ultimate goal of mimicking nature's simplicity in forming complex materials, this methodology will need to be further explored. In addition, there are no accounts of the combination of the main chain and side-chain interactions reported. The combination of noncovalent interactions carefully chosen for both main-chain and side-chain interactions is crucial to developing more and more complex materials, and has yet to be explored. Chapter 4 will expand on the toolbox components developed in chapters 2 and 3 and combine these to make the first side-chain and main-chain functionalized block copolymers. The primary hypothesis of this thesis is that the combination of supramolecular strategies, ring-opening metathesis

polymerization, and a well-understood toolbox of functionalities capable of noncovalent interactions, comprises a method for generating bioinspired materials. This hypothesis will be tested in chapters 2, 3, and 4 by synthesizing unique functionalized supramolecular polymers that allowed for a detailed understanding of the orthogonality of noncovalent interactions and how such interactions can begin to mimic the complexity of functional biomaterials.

1.6. Conclusion

Supramolecular chemistry has taken lessons from nature to formulate a promising field that concerns itself with mimicking and understanding the complexity and elegance of materials nature has designed. By building complicated structures from the bottom up, the elegance of nature's materials has only begun to be understood.

In the past decades, supramolecular chemists have expanded the toolbox of noncovalent interactions synthetically accessible. They are only now beginning to develop an understanding of how they interact with each other. Only through this deeper understanding can we combine materials based on recognition unit compatibility, solvent dependence, and selectivity. This thesis aims to understand how these noncovalent tools behave with each other and to further develop existing polymeric methodologies in order to develop more complicated functional materials such as those found in nature. More specifically it aims to develop a toolbox containing both metal coordination and multiple pairs of non-complementary hydrogen bonding recognition units that are well-defined and understood with respect to their interactions with each other. In addition, this thesis aims to use these toolbox interactions to develop novel polymer methodologies

based on ROMP. In doing so, the elegance of nature can be better understood and synthetically recreated to create a wide variety of functional and complex materials.

1.7 **References**

1. Whitesides, G. M.; Mathias, J. P.; Seto, C. T., Molecular Self-Assembly And Nanochemistry: A Chemical Strategy For The Synthesis Of Nanostructures, *Science* **1991**, *254*, 1312-1319.

2. John Moore, R. L., *Biochemistry For Dummies*. Wiley, John & Sons, Incorporated: 2008.

3. Donald, A. M., Why Should Polymer Physicists Study Biopolymers? *J. Polym. Sci., Part B: Polym. Phys.* **2007**, *45*, 3257-3262.

4. Semenova, M. G., Thermodynamic Analysis Of The Impact Of Molecular Interactions On The Functionality Of Food Biopolymers In Solution And In Colloidal Systems *Food Hydrocol.* **2007**, *21*, 23-45.

5. Channon, K.; Macphee, C. E., Possibilities For 'Smart' Materials Exploiting The Self-Assembly Of Polypeptides Into Fibrils *Soft Matter* **2008**, *4*, 647-652.

6. Chau, Y.; Luo, Y.; Cheung, A. C. Y.; Nagai, Y.; Zhang, S. G.; Kobler, J. B.; Zeitels, S. M.; Langer, R., Incorporation Of A Matrix Metalloproteinase-Sensitive Substrate Into Self-Assembling Peptides - A Model For Biofunctional Scaffolds *Biomaterials* **2008**, *29*, 1713-1719.

7. Santucci, R.; Sinibaldi, F.; Fiorucci, L., Protein Folding, Unfolding And Misfolding: Role Played By Intermediate States *Mini. Rev. Med. Chem.* **2008**, *8*, 57-62.

8. Sabil, H. R., Chaperone Machines In Action *Curr. Opin. Struct. Biol.* **2008**, *18*, 35-42.

9. Tewari, A. K.; Dubey, R., Emerging Trends In Molecular Recognition: Utility Of Weak Aromatic Interactions *Bioorg. Med. Chem.* **2008**, *16*, 126-143.

10. Roth, J.; Yam, G. H. F.; Fan, J. Y.; Hirano, K.; Gaplovska-Kysela, K.; Le Fourn, V.; Guhl, B.; Santimaria, R.; Torossi, T.; Ziak, M.; Zuber, C., Protein Quality Control: The Who's Who, The Where's And Therapeutic Escapes *Histochem. Cell Bio.* **2008**, *129*, 163-177.

11. Brayer, K. J.; Segal, D. J., Keep Your Fingers Off My DNA: Protein-Protein Interactions Mediated By C2H2 Zinc Finger Domains *Cell Biochem. Biophys.* **2008**, *50*, 111-131.

12. Cobaleda, C.; Perez-Caro, M.; Vicente-Duenas, C.; Sanchez-Garcia, I., Function Of The Zinc-Finger Transcription Factor SNAI2 In Cancer And Development *Annu. Rev. Genet.* **2007**, *41*, 41-61.

13. Morrison, A. A.; Viney, R. L.; Ladomery, M. R., The Post-Transcriptional Roles Of WT1, A Multifunctional Zinc-Finger Protein *Biochim. Biophys. Acta., Rev. Cancer* **2008**, *1785*, 55-62.

14. Dion, S.; Veronique, M.; Renault, S., Zinc Finger Proteins: Tools For Site-Specific Correction Or Modification Of The Genome *M S-Medecine Sciences* **2007**, *23*, 834-839.

15. Edelstein, L. C.; Collins, T., The SCAN Domain Family Of Zinc Finger Transcription *Gene* **2005**, *359*, 1-17.

16. Hall, T. M. T., Multiple Modes Of RNA Recognition By Zinc Finger Proteins *Curr. Opin. Struct. Biol.* **2005**, *15*, 367-373.

17. Konig, H. M.; Kilbinger, A. F. M., Learning From Nature: Beta-Sheet-Minnicking Copolymers Get Organized *Angew. Chem. Int. Ed.* **2007**, *46*, 8334-8340.

18. Sivakova, S.; Rowan, S. J., Nudeobases As Supramolecular Motifs *Chem. Soc. Rev.* **2005**, *34*, 9-21.

19. Lehn, J.-M., Toward Self-Organization And Complex Matter *Science* **2002**, *295*, 2400-2403.

20. Lehn, J.-M., Supramolecular Polymer Chemistry - Scope And Perspectives *Polym. Int.* **2002**, *51*, 825-839.

21. Lehn, J.-M., *Supramolecular Chemistry*. Wiley-VCH: 1995.

22. Lehn, J. M., Supramolecular Chemistry - Scope And Perspectives Molecules, Supermolecules, And Molecular Devices *Angew. Chem. Int. Ed.* **1988**, *27*, 89-112.

23. Lehn, J. M., Perspectives In Supramolecular Chemistry - From Molecular Recognition Towards Molecular Information-Processing And Self-Organization *Angew. Chem. Int. Ed.* **1990**, *29*, 1304-1319.

24. Daniel, M. C.; Astruc, D., Gold Nanoparticles: Assembly, Supramolecular Chemistry, Quantum-Size-Related Properties, And Applications Toward Biology, Catalysis, And Nanotechnology *Chem. Rev.* **2004**, *104*, 293-346.

25. Beer, P. D.; Gale, P. A., Anion Recognition And Sensing: The State Of The Art And Future Perspectives *Angew. Chem. Int. Ed.* **2001**, *40*, 486-516.

26. Albrecht, M., "Let's Twist Again" - Double-Stranded, Triple-Stranded, And Circular Helicates *Chem. Rev.* **2001**, *101*, 3457-3497.

27. Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, J. F., Dynamic Covalent Chemistry *Angew. Chem. Int. Ed.* **2002**, *41*, 898-952.

28. Davis, J. T.; Spada, G. P., Supramolecular Architectures Generated By Self-Assembly Of Guanosine Derivatives *Chem. Soc. Rev.* **2007**, *36*, 296-313.

29. Anslyn, E. V., Supramolecular Analytical Chemistry *J. Org. Chem.* **2007**, *72*, 687-699.

30. Gimeno, N.; Vilar, R., Anions As Templates In Coordination And Supramolecular Chemistry *Coord. Chem. Rev.* **2006**, *250*, 3161-3189.

31. Nitschke, J. R., Construction, Substitution, And Sorting Of Metallo-Organic Structures Via Subcomponent Self-Assembly *Acc. Chem. Res.* **2007**, *40*, 103-112.

32. Constable, E. C., 2,2 ': 6 ',2 "-Terpyridines: From Chemical Obscurity To Common Supramolecular Motifs *Chem. Soc. Rev.* **2007**, *36*, 246-253.

33. Ruben, M.; Lehn, J. M.; Muller, P., Addressing Metal Centres In Supramolecular Assemblies *Chem. Soc. Rev.* **2006**, *35*, 1056-1067.

34. Hannon, M. J., Supramolecular DNA Recognition *Chem. Soc. Rev.* **2007**, *36*, 280-295.

35. Suzuki, M.; Yumoto, M.; Shirai, H.; Hanabusa, K., Supramolecular Gels Formed By Amphiphilic Low-Molecular-Weight Gelators Of N-Alpha,N-Epsilon-Diacyl-L-Lysine Derivatives *Chem. Eur. J.* **2008**, *14*, 2133-2144.

36. Sallas, F.; Darcy, R., Amphiphilic Cyclodextrins - Advances In Synthesis And Supramolecular Chemistry *Eur. J. Org. Chem.* **2008**, 957-969.

37. Kinge, S.; Crego-Calama, M.; Reinhoudt, D. N., Self-Assembling Nanoparticles At Surfaces And Interfaces *Chemphyschem* **2008**, *9*, 20-42.

38. Balzani, V.; Credi, A.; Venturi, M., Molecular Machines Working On Surfaces And At Interfaces *Chemphyschem* **2008**, *9*, 202-220.

39. Wan, Y.; Sho, Y.; Zhao, D., Supramolecular Aggregates As Templates: Ordered Mesoporous Polymers And Carbons *Chem. Mater.* **2008**, *20*, 932-945.

40. Schneider, H. J.; Yatsimirsky, A. K., Selectivity In Supramolecular Host-Guest Complexes *Chem. Soc. Rev.* **2008**, *37*, 263-277.

41. Lazzari, M.; Rodriguez-Abreu, C.; Rivas, J.; Lopez-Quintela, M. A., Self-Assembly: A Minimalist Route To The Fabrication Of Nanomaterials *J. Nanosci. Nanotech.* **2006**, *6*, 892-905.

42. Zhang, S. G., Fabrication Of Novel Biomaterials Through Molecular Self-Assembly *Nature Biotech.* **2003**, *21*, 1171-1178.

43. Euliss, L. E.; Dupont, J. A.; Gratton, S.; Desimone, J., Imparting Size, Shape, And Composition Control Of Materials For Nanomedicine *Chem. Soc. Rev.* **2006**, *35*, 1095-1104.

44. Mitsuishi, M.; Matsui, J.; Miyashita, T., Functional Organized Molecular Assemblies Based On Polymer Nano-Sheets *Poly. J.* **2006**, *38*, 877-896.

45. Vayssieres, L., Designing Ordered Nanoarrays From Aqueous Solutions *Pure Appl. Chem.* **2006**, *78*, 1741-1747.

46. Liu, Y. J.; Ma, Z. W.; Ramakrishna, S., One Dimensional Nanomaterials: Preparation, Structures, And Assembly *Curr. Nanosci.* **2006**, *2*, 71-78.

47. Jeffery, G. A., *An Introduction To Hydrogen Bonding*. Oxford University Press, USA: 1997.

48. South, C. R.; Burd, C.; Weck, M., Modular And Dynamic Functionalization Of Polymeric Scaffolds *Acc. Chem. Res.* **2007**, *40*, 63-74.

49. Jorgenson, W. L.; Pranata, J., Importance Of Secondary Interactions In Triply Hydrogen Bonded Complexes: Guanine-Cytosine Vs Uracil-2,6-Diaminopyridine *J. Am. Chem. Soc.* **1990**, *112*, 2008-2010.

50. Jorgensen, W. L.; Pranata, J., Importance Of Secondary Interactions In Triply Hydrogen-Bonded Complexes - Guanine-Cytosine Vs Uracil-2,6-Diaminopyridine *J. Am. Chem. Soc.* **1990**, *112*, 2008-2010.

51. Pranata, J.; Wierschke, S. G.; Jorgensen, W. L., Opls Potential Functions For Nucleotide Bases - Relative Association Constants Of Hydrogen-Bonded Base-Pairs In Chloroform *J. Am. Chem. Soc.* **1991**, *113*, 2810-2819.

52. Wu, A. X.; Isaacs, L., Self-Sorting: The Exception Or The Rule? *J. Am. Chem. Soc.* **2003**, *125*, 4831-4835.

53. Giedroc, D. P.; Arunkumar, A. I., Metal Sensor Proteins: Nature's Metalloregulated Allosteric Switches *Dalton Trans.* **2007**, 3107-3120.

54. Mantion, A.; Massuger, L.; Rabu, P.; Palivan, C.; Mccusker, L. B.; Taubert, A., Metal-Peptide Frameworks (Mpfs): "Bioinspired" Metal Organic Frameworks *J. Am. Chem. Soc.* **2008**, *130*, 2517-2526.

55. Jiang, D. L.; Aida, T., Bioinspired Molecular Design Of Functional Dendrimers *Pro. Poly. Sci.* **2005**, *30*, 403-422.

56. Mandel, A.; Schmitt, W.; Womack, T. G.; Bhalla, R.; Henderson, R. K.; Heath, S. L.; Powell, A. K., A Bioinspired Approach To Control Over Size, Shape And Function Of Polynuclear Iron Compounds *Coord. Chem. Rev.* **1999**, *192*, 1067-1083.

57. Bowman-James, K., Alfred Werner Revisited: The Coordination Chemistry Of Anions *Acc. Chem. Res.* **2005**, *38*, 671-678.

58. Wandersman, C., Hasa Tridimensional Structure. In *Http://Www.Pasteur.Fr/Recherche/RAR/RAR2001/Mbbact-En.Html*, Structure, H. T., Ed. 2001.

59. Kim, H. J.; Lim, Y. B.; Lee, M., Self-Assembly Of Supramolecular Polymers Into Tunable Helical Structures *J. Poly. Sci., Part A: Polym. Chem.* **2008**, *46*, 1925-1935.

60. Weck, M., Side-Chain Functionalized Supramolecular Polymers *Poly. Intl.* **2007**, *56*, 453-460.

61. Sivakova, S.; Bohnsack, D. A.; Mackay, M. E.; Suwanmala, P.; Rowan, S. J., Utilization Of A Combination Of Weak Hydrogen-Bonding Interactions And Phase Segregation To Yield Highly Thermosensitive Supramolecular Polymers *J. Am. Chem. Soc.* **2005**, *127*, 18202-18211.

62. Yagai, S.; Iwashima, T.; Karatsu, T.; Kitamura, A., Synthesis And Noncovalent Polymerization Of Self-Complementary Hydrogen-Bonding Supramolecular Synthons: N,N '-Disubstituted 4,6-Diamino-Pyrimidin-2(1H)-Ones *Chem. Commun.* **2004**, 1114-1115.

63. Berl, V.; Schmutz, M.; Krische, M. J.; Khoury, R. G.; Lehn, J. M., Supramolecular Polymers Generated From Heterocomplementary Monomers Linked Through Multiple Hydrogen-Bonding Arrays - Formation, Characterization, And Properties *Chem. Eur. J.* **2002**, *8*, 1227-1244.

64. Ilhan, F.; Gray, M.; Rotello, V. M., Reversible Side Chain Modification Through Noncovalent Interactions. "Plug And Play" Polymers *Macromolecules* **2001**, *34*, 2597-2601.

65. Rotello, V.; Thayumanavan, S., In Focus: Recognition Mediated Self-Assembly *Polym. Int.* **2007**, *56*, 435-435.

66. Carroll, J. B.; Frankamp, B. L.; Srivastava, S.; Rotello, V., Polyhedral Oligomeric Silsesquioxane (POSS) Units As Molecular Recognition Elements *Abs. Am. Chem. Soc.* **2004**, *228*, U48-U49.

67. Cooke, G.; Rotello, V., Methods Of Modulating Hydrogen Bonded Interactions In Synthetic Host-Guest Systems *Chem. Soc. Rev.* **2003**, *32*, 56-57.

68. Ligthart, G.; Guo, D. W.; Spek, A. L.; Kooijman, H.; Zuilhof, H.; Sijbesma, R. P., Ureidobenzotriazine Multiple H-Bonding Arrays: The Importance Of Geometrical Details On The Stability Of H-Bonds *J. Org. Chem.* **2008**, *73*, 111-117.

69. Li, J. H.; Viveros, J. A.; Wrue, M. H.; Anthamatten, M., Shape-Memory Effects In Polymer Networks Containing Reversibly Associating Side-Groups *Adv. Mater.* **2007**, *19*, 2851-+.

70. Mather, B. D.; Elkins, C. L.; Beyer, F. L.; Long, T. E., Morphological Analysis Of Telechelic Ureidopyrimidone Functional Hydrogen Bonding Linear And Star-Shaped Poly(Ethylene-Co-Propylene)S *Macromol. Rapid Commun.* **2007**, *28*, 1601-1606.

71. Karikari, A. S.; Mather, B. D.; Long, T. E., Association Of Star-Shaped Poly(D,L-Lactide)S Containing Nucleobase Multiple Hydrogen Bonding *Biomacromolecules* **2007**, *8*, 302-308.

72. Keizer, H. M.; Van Kessel, R.; Sijbesma, R. P.; Meijer, E. W., Scale-Up Of The Synthesis Of Ureidopyrimidinone Functionalized Telechelic Poly(Ethylenebutylene) *Polymer* **2003**, *44*, 5505-5511.

73. Sijbesma, R. P.; Meijer, E. W., Quadruple Hydrogen Bonded Systems *Chem. Commun.* **2003**, 5-16.

74. Burd, C.; Weck, M., Solvent Influence On The Orthogonality Of Noncovalently Functionalized Terpolymers *J. Poly. Sci., Part A: Polym. Chem.* **2008**, *46*, 1936-1944.

75. Nakade, H.; Ilker, M. F.; Jordan, B. J.; Uzun, O.; Lapointe, N. L.; Coughlin, E. B.; Rotello, V. M., Duplex Strand Formation Using Alternating Copolymers *Chem. Commun.* **2005**, 3271-3273.

76. Carroll, J. B.; Frankamp, B. L.; Rotello, V. M., Self-Assembly Of Gold Nanoparticles Through Tandem Hydrogen Bonding And Polyoligosilsequioxane (POSS)-POSS Recognition Processes *Chem. Commun.* **2002**, 1892-1893.

77. Jeoung, E.; Carroll, J. B.; Rotello, V. M., Surface Modification Via 'Lock And Key' Specific Self-Assembly Of Polyhedral Oligomeric Silsequioxane (POSS) Derivatives To Modified Gold Surfaces *Chem. Commun.* **2002**, 1510-1511.

78. Beijer, F. H.; Sijbesma, R. P.; Vekemans, J.; Meijer, E. W.; Kooijman, H.; Spek, A. L., Hydrogen-Bonded Complexes Of Diaminopyridines And Diaminotriazines: Opposite Effect Of Acylation On Complex Stabilities *J. Org. Chem.* **1996**, *61*, 6371-6380.

79. Mather, B. D.; Baker, M. B.; Beyer, F. L.; Berg, M. A. G.; Green, M. D.; Long, T. E., Supramolecular Triblock Copolymers Containing Complementary Nucleobase Molecular Recognition *Macromolecules* **2007**, *40*, 6834-6845.

80. Ishihara, Y.; Bazzi, H. S.; Toader, V.; Godin, F.; Sleiman, H. F., Molecule-Responsive Block Copolymer Micelles *Chem. Eur. J.* **2007**, *13*, 4560-4570.

81. Binder, W. H.; Zirbs, R., Supramolecular Polymers And Networks With Hydrogen Bonds In The Main- And Side-Chain. In *Hydrogen Bonded Polymers*, 2007; Vol. 207, Pp 1-78.

82. Ohkawa, H.; Ligthart, G.; Sijbesma, R. P.; Meijer, E. W., Supramolecular Graft Copolymers Based On 2,7-Diamido-1,8-Naphthyridines *Macromolecules* **2007**, *40*, 1453-1459.

83. Keck, C. G.; Kendall, J. L.; Caster, K. C., Cross-Linkers For Improved High Temperature Performance Of ROMP Adhesives *Adv. Synt. Catal.* **2007**, *349*, 165-174.

84. Krakovsky, I.; Lokaj, J.; Sedlakova, Z.; Ikeda, Y.; Nishida, K., Hydrogen Bonding Interactions Of Styrene-Maleimide Copolymers With Diaminotriazine Derivatives *J. Appl. Poly. Sci.* **2006**, *101*, 2338-2346.

85. Nair, K. P.; Pollino, J. M.; Weck, M., Noncovalently Functionalized Block Copolymers Possessing Both Hydrogen Bonding And Metal Coordination Centers *Macromolecules* **2006**, *39*, 931-940.

86. Gong, H. G.; Krische, M. J., Duplex Molecular Strands Based On The 3,6-Diaminopyridazine Hydrogen Bonding Motif: Amplifying Small-Molecule Self-Assembly Preferences Through Preorganization And Iterative Arrangement Of Binding Residues *J. Am. Chem. Soc.* **2005**, *127*, 1719-1725.

87. Binder, W. H.; Kluger, C., Combining Ring-Opening Metathesis Polymerization (ROMP) With Sharpless-Type "Click" Reactions: An Easy Method For The Preparation Of Side Chain Functionalized Poly(Oxynorbornenes) *Macromolecules* **2004**, *37*, 9321-9330.

88. Kato, T.; Fréchet, J. M. J., Stabilization Of A Liquid-Crystalline Phase Through Noncovalent Interaction With A Polymer Side Chain *Macromolecules* **1989**, *22*, 3818-3819.

89. Kumar, U.; Kato, T.; Fréchet, J. M. J., Use Of Intermolecular Hydrogen Bonding For The Induction Of Liquid Crystallinity In The Side Chain Of Polysiloxanes *J. Am. Chem. Soc.* **1992**, *114*, 6630-9.

90. Kato, T.; Hirota, N.; Fujishima, A.; Fréchet, J. M. J., Supramolecular Hydrogen-Bonded Liquid-Crystalline Polymer Complexes. Design Of Side-Chain Polymers And A Host-Guest System By Noncovalent Interaction *J. Poly. Sci., Part A: Polym. Chem.* **1996**, *34*, 57-62.

91. Kato, T.; Mizoshita, N.; Kishimoto, K., Functional Liquid-Crystalline Assemblies: Self-Organized Soft Materials *Angew. Chem. Int. Ed.* **2006**, *45*, 38-68.

92. Gohy, J.-F.; Lohmeijer, B. G. G.; Schubert, U. S., From Supramolecular Block Copolymers To Advanced Nano-Objects *Chem. Eur. J.* **2003**, *9*, 3472-3479.

93. Boal, A. K.; Galow, T. H.; Ilhan, F.; Rotello, V. M., Binary And Ternary Polymer-Mediated Bricks And Mortar Self-Assembly Of Gold And Silica Nanoparticles *Adv. Funct. Mater.* **2001**, *11*, 461-465.

94. Arumugam, P.; Xu, H.; Srivastava, S.; Rotello, V. M., 'Bricks And Mortar' Nanoparticle Self-Assembly Using Polymers *Polym. Int.* **2007**, *56*, 461-466.

95. Boal, A. K.; Gray, M.; Ilhan, F.; Clavier, G. M.; Kapitzky, L.; Rotello, V. M., Bricks And Mortar Self-Assembly Of Nanoparticles *Tetrahedron* **2002**, *58*, 765-770.

96. Ilhan, F.; Gray, M.; Blanchette, K.; Rotello, V. M., Control Of Polymer Solution Structure Via Intra- And Intermolecular Aromatic Stacking *Macromolecules* **1999**, *32*, 6159-6162.

97. Jeoung, E.; Galow, T. H.; Schotter, J.; Bal, M.; Ursache, A.; Tuominen, M. T.; Stafford, C. M.; Russell, T. P.; Rotello, V. M., Fabrication And Characterization Of Nanoelectrode Arrays Formed Via Block Copolymer Self-Assembly *Langmuir* **2001**, *17*, 6396-6398.

98. Drechsler, U.; Thibault, R. T.; Rotello, V. M., Formation Of Recognition - Induced Polymersomes Uding Complementary Rigid Random Copolymers *Macromolecules* **2002**, *35*, 9621-9623.

99. Drechsler, U.; Thibault, R. J.; Rotello, V. M., Formation Of Recognition-Induced Polymersomes Using Complementary Rigid Random Copolymers *Macromolecules* **2002**, *35*, 9621-9623.

100. Ilhan, F.; Galow, T. H.; Clavier, G.; Rotello, V. M., Giant Vesicle Formation Through Self-Assembly Of Complementary Random Copolymers *J. Am. Chem. Soc.* **2000**, *122*, 5895-5896.

101. Cooke, G.; Rotello, V. M., Methods Of Modulating Hydrogen Bonded Interactions In Synthetic Host-Guest Systems *Chem. Soc. Rev.* **2002**, *31*, 275-286.

102. Shenhar, R.; Rotello, V. M., Nanoparticles: Scaffolds And Building Blocks *Acc. Chem. Res.* **2003**, *36*, 549-561.

103. Carroll, J. B.; Waddon, A. J.; Nakade, H.; Rotello, V. M., "Plug And Play" Polymers. Thermal And X-Ray Characterizations Of Noncovalently Grafted Polyhedral Oligomeric Silsesquioxane (POSS) - Polystyrene Nanocomposites *Macromolecules* **2003**, *36*, 6289-6291.

104. Carroll, J. B.; Waddon, A. J.; Nakade, H.; Rotello, V. M., "Plug And Play" Polymers. Thermal And X-Ray Characterizations On Noncovalently Grafted Polyhedral

Oligomeric Silsesquioxane (POSS)-Polystyrene Nanocomposites *Macromolecules* **2003**, *36*, 6289-6291.

105. Galow, T. H.; Ilhan, F.; Cooke, G.; Rotello, V. M., Recognition And Encapsulation Of An Electroactive Guest Within A Dynamically Folded Polymer *J. Am. Chem. Soc.* **2000**, *122*, 3595-3598.

106. Xu, H. H., R.; Lu, T.; Uzun, O.; Rotello, V., Recognition-Directed Orthogonal Self-Assembly Of Polymers And Nanoparticles On Patterned Surfaces *J. Am. Chem. Soc.* **2006**, *128*, 3162-3163.

107. Uzun, O.; Frankamp, B. L.; Sanyal, A.; Rotello, V. M., Recognition-Mediated Assembly Of Nanoparticle-Diblock Copolymer Micelles With Controlled Size *Chem. Mater.* **2006**, *18*, 5404-5409.

108. Frankamp, B. L.; Uzun, O.; Ilhan, F.; Boal, A. K.; Rotello, V. M., Recognition-Mediated Assembly Of Nanoparticles Into Micellar Structures With Diblock Copolymers *J. Am. Chem. Soc.* **2002**, *124*, 892-893.

109. Deans, R.; Ilhan, F.; Rotello, V. M., Recognition-Mediated Unfolding Of A Self-Assembled Polymeric Globule *Macromolecules* **1999**, *32*, 4956-4960.

110. Ilhan, F.; Gray, M.; Rotello, V. M., Reversible Side Chain Modification Through Noncovalent Interaction. "Plug And Play" Polymers *Macromolecules* **2001**, *34*, 2597-2601.

111. Boal, A. K.; Ilhan, F.; Derouchey, J. E.; Thurn-Albrecht, T.; Russell, T. P.; Rotello, V. M., Self-Assembly Of Nanoparticles Into Structured Spherical And Network Aggregates *Nature* **2000**, *404*, 746-748.

112. Thibault, R. J.; Galow, T. H.; Turnberg, E. J.; Gray, M.; Hotchkiss, P. J.; Rotello, V. M., Specific Interactions Of Complementary Mono- And Multivalent Guests With Recognition-Induced Polymersomes *J. Am. Chem. Soc.* **2002**, *124*, 15249-15254.

113. Thibault, R. J.; Hotchkiss, P. J.; Gray, M.; Rotello, V. M., Thermally Reversible Formation Of Microspheres Through Non-Covalent Polymer Cross-Linking *J. Am. Chem. Soc.* **2003**, *125*, 11249-11252.

114. Cooke, G.; Garety, J. F.; Hewage, S. G.; Jordan, B. J.; Rabani, G.; Rotello, V. M.; Woisel, P., Tunable Side-Chain Supramolecular Polymer *Org. Lett.* **2007**, ASAP.

115. De Cremiers, H. A.; Clavier, G.; Ilhan, F.; Cooke, G.; Rotello, V. M., Tuneable Electrochemical Interactions Between Polystyrenes With Anthracenyl And Tetrathiafulvalenyl Sidechains *Chem. Commun.* **2001**, 2232 - 2233.

116. Carroll, J. B.; Waddon, A. J.; Nakade, H.; Rotello, V. M., "Plug And Play" Polymers. Thermal And X-Ray Characterizations Of Noncovalently Grafted Polyhedral

Oligomeric Silsesquioxane (POSS)-Polystyrene Nanocomposites *Macromolecules* **2003**, *36*, 6289-6291.

117. Boal, A. K.; Ilhan, F.; Derouchey, J. E.; Thurn-Albrecht, T.; Russell, T. P.; Conticello, V. P., Self-Assembly Of Nanoparticles Into Structured Spherical And Network Aggregates *Nature* **2000**, *404*, 746-748.

118. Thibault, R. J.; Galow, T. H.; Turnberg, E. J.; Gray, M.; Hotchkiss, P. J.; Rotello, V. M., Specific Interactions Of Complementary Mono- And Multivalent Guests With Recognition-Induced Polymersomes *J. Am. Chem. Soc.* **2002**, *124*, 15249-15254.

119. Gerhardt, W.; Crne, M.; Weck, M., Multifunctionalization Of Synthetic Polymer Systems Through Self-Assembly *Chem. Eur. J.* **2004**, *10*, 6212-6221.

120. Weck, M.; Pollino, J. M.; Higley, M. N.; Nair, K. P.; Burd, C., Functional Polymer Design Via Multi-Site Self-Assembly. *Abstracts Am. Chem. Soc.* **2005**, *229*, U526-U526.

121. South, C. R.; Leung, K. C. F.; Lanari, D.; Stoddart, J. F.; Weck, M., Noncovalent Side-Chain Functionalization Of Terpolymers *Macromolecules* **2006**, *39*, 3738-3744.

122. Grubbs, R. H., *Handbook Of Metathesis*. Wiley-VCH: Wilheim, 2003.

123. Pollino, J. M.; Stubbs, L. P.; Weck, M., Living ROMP Of Exo-Norbornene Esters Possessing Pd(II) SCS Pincer Complexes Or Diaminopyridines *Macromolecules* **2003**, *36*, 2230-2234.

124. South, C. R.; Higley, M. N.; Leung, K. C.-F.; Lanari, D.; Nelson, A.; Grubbs, R. H.; Stoddart, J. F.; Weck, M., Self-Assembly With Block Copolymers Through Metal Coordination Of SCS-Pdii Pincer Complexes And Pseudorotaxane Formation. *Chem. Eur. J.* **2006**, *12*, 3789-3797.

125. Nair, K. P.; Pollino, J. M.; Weck, M., Noncovalently Functionalized Block Copolymers Possessing Both Hydrogen Bonding And Metal Coordination Centers *Macromolecules* **2006**, *39*, 931-940.

126. Burd, C.; Weck, M., Self-Sorting In Polymers *Macromolecules* **2005**, *38*.

127. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Crosslinked And Functionalized Universal Polymer Backbones Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly. *Tetrahedron* **2004**, *60*, 7205-7215.

128. Nair, K. P.; Breedveld, V.; Weck, M., Tunable Thermo-Reversible Polymer Networks By Multifunctional Hydrogen Bonding Self-Assembly. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **2007**, *48*, 46-347.

129. Pollino, J. M.; Stubbs, L. P.; Weck, M., Living ROMP Of Exo-Norbornene Esters Possessing Pdii SCS Pincer Complexes Or Diaminopyridines *Macromolecules* **2003**, *36*, 2230-2234.

130. Stubbs, L. P.; Weck, M., A Polymeric Scaffold For The Self-Assembly Of Receptors Through Hydrogen Bonding *Chem. Eur. J.* **2003**, *9*, 992-999.

131. Stubbs, L. P.; Weck, M., Towards A Universal Polymer Backbone: Design And Synthesis Of Polymeric Scaffolds Containing Terminal Hydrogen-Bonding Recognition Motifs At Each Repeating Unit *Chem. Eur. J.* **2003**, *9*, 992-999.

132. Bazzi, H. S.; Sleiman, H. F., Adenine-Containing Block Copolymers Via Ring-Opening Metathesis Polymerization: Synthesis And Self-Assembly Into Rod Morphologies *Macromolecules* **2002**, *35*, 9617-9620.

133. Bazzi, H. S.; Bouffard, J.; Sleiman, H. F., Self-Complementary ABC Triblock Copolymers Via Ring-Opening Metathesis Polymerization *Macromolecules* **2003**, *36*, 7899-7902.

134. Rakotondradany, F.; Palmer, A.; Toader, V.; Chen, B. Z.; Whitehead, M. A.; Sleiman, H. F., Hydrogen-Bond Self-Assembly Of DNA-Analogues Into Hexameric Rosettes *Chem. Commun.* **2005**, 5441-5443.

135. Aldaye, F.; Sleiman, H., Assembling Nanocomponents One By One With DNA *J. Biomol. Struct. Dyn.* **2007**, *24*, 700-701.

136. Yang, H.; Sleiman, H., Templated Synthesis Of Metal-DNA Crossover Points - Unusual Stability And Dynamic Character *J. Biomol. Struct. Dyn.* **2007**, *24*, 704-705.

137. Suijkerbuijk, B.; Aerts, B. N. H.; Dijkstra, H. P.; Lutz, M.; Spek, A. L.; Van Koten, G.; Gebbink, R., "Click" 1,2,3-Triazoles As Tunable Ligands For Late Transition Metal Complexes *Dalton Trans.* **2007**, 1273-1276.

138. Hofmeier, H.; Hoogenboom, R.; Wouters, M. E. L.; Schubert, U. S., High Molecular Weight Supramolecular Polymers Containing Both Terpyridine Metal Complexes And Ureidopyrimidinone Quadruple Hydrogen-Bonding Units In The Main Chain *J. Am. Chem. Soc.* **2005**, *127*, 2913-2921.

139. Larrow, J. F.; Jacobsen, E. N., Asymmetric Processes Catalyzed By Chiral (Salen)Metal Complexes *Top. Organomet. Chem.* **2004**, *6*, 123-152.

140. Hofmeier, H.; El-Ghayoury, A.; Schenning, A. P. H. J.; Schubert, U. S., New Supramolecular Polymers Containing Both Terpyridine Metal Complexes And Quadruple Hydrogen Bonding Units *Chem. Commun.* **2004**, 318-319.

141. Smith, A. P.; Fraser, C. L., Synthesis Of Bipyridine-Centered Diblock Copolymers *Macromolecules* **2003**, *36*, 2654-2660.

142. Meier, M. A. R.; Lohmeijer, B. G. G.; Schubert, U. S., Characterization Of Defined Metal-Containing Supramolecular Block Copolymers *Macromol. Rapid Commun.* **2003**, *24*, 852-857.

143. Schubert, U. S.; Eschbaumer, C., Macromolecules Containing Bipyridine And Terpyridine Metal Complexes: Towards Metallosupramolecular Polymers *Angew. Chem. Int. Ed.* **2002**, *41*, 2892-2926.

144. Carlise, J. R.; Weck, M., Side Chain Funcitonalized Polymers Containing Bipyridine Coordination Sites *J. Poly. Sci., Part A: Polym. Chem.* **2004**, *42*, 2973-2984.

145. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Cross-Linked And Functionalized 'Universal Polymer Backbones' Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

146. Pollino, J. M.; Weck, M., Supramolecular Side-Chain Functionalized Polymers: Synthesis And Self-Assembly Behavior Of Polynorbornenes Bearing Pdii SCS Pincer Complexes *Synthesis* **2002**, *9*, 1277-1288.

147. Meyers, A.; Weck, M., Design And Synthesis Of Alq3-Functionalized Polymers *Macromolecules* **2003**, *36*, 1766-1768.

148. Calzia, K. J.; Tew, G. N., Methacrylate Polymers Containing Metal Binding Ligands For Use In Supramolecular Materials: Random Copolymers Containing Terpyridines *Macromolecules* **2002**, *35*, 6090.

149. Aamer, K. A.; Tew, G. N., Synthesis Of Terpyridine-Containing Polymers With Blocky Architecture *Macromolecules* **2004**, *37*, 1990-1993.

150. Stupp, S. I.; Keser, M.; Tew, G. N., Functionalized Supramolecular Materials *Polymer* **1998**, *39*, 4505-4509

151. Jampolsky, L. M.; Baum, M.; Kaiser, S.; Sternbach, L. H.; Goldberg, M. W., The Synthesis Of 2,2'- And 4,4'-Polymethylenebipyridines *J. Am. Chem. Soc.* **1952**, *74*, 5222-5224.

152. Kickham, J. E.; Loeb, S. J., Simultaneous First- And Second-Sphere Coordination. Organopalladium Crown Ether Complexes As Metalloreceptors For O-Aminopyridine Derivatives *Inorg. Chem.* **1994**, *33*, 4351 - 4359.

153. Schubert, U. S.; Hien, O.; Eschbaumer, C., Functionalized Polymers With Metal Complexing Segments: A Simple And High-Yield Entry Towards 2,2:6,2-Terpyridine-Based Oligomers *Macromol. Rapid Commun.* **2000**, *21*, 1156-1161.

154. Wu, X.; Fraser, C. L., Architectural Diversity Via Metal Template-Assisted Polymer Synthesis: A Macroligand Chelation Approach To Linear And Star-Shaped Polymeric Ruthenium Tris(Bipyridine) Complexes *Macromolecules* **2000**, *33*, 4053-4060.

155. Schubert, U. S.; Eschbaumer, C.; Hien, O.; Andres, P. R., 4'-Functionalized 2,2':6',2?-Terpyridines As Building Blocks For Supramolecular Chemistry And Nanoscience *Tetrahedron Lett.* **2001**, *42*, 4705-4707.

156. Heller, M.; Schubert, U. S., Polystyrene With Pendant Mixed Functional Ruthenium(II)-Terpyridine Complexes *Macromol. Rapid Commun.* **2002**, *23*, 411-415.

157. Meier, M. A. R.; Schubert, U. S., Terpyridine-Modified Poly(Vinyl Chloride): Possibilities For Supramolecular Grafting And Crosslinking *J. Poly. Sci., Part A: Polym. Chem.* **2003**, *41*, 2964-2973.

158. Chen, B. Z.; Metera, K.; Sleiman, H. F., Biotin-Terminated Ruthenium Bipyridine Ring-Opening Metathesis Polymerization Copolymers: Synthesis And Self-Assembly With Streptavidin *Macromolecules* **2005**, *38*, 1084-1090.

159. Kokil, A.; Yao, P.; Weder, C., Organometallic Networks Based On 2,2'-Bipyridine-Containing Poly(P-Phenylene Ethynylene)S *Macromolecules* **2005**, *38*, 3800-3807.

160. Ott, C.; Lohmeijer, B. G. G.; Wouters, D.; Schubert, U. S., Terpyridine-Terminated Homo And Diblock Copolymer LEGO Units By Nitroxide-Mediated Radical Polymerization *Macromol. Chem. Phys.* **2006**, *207*, 1439-1449.

161. Pfister, A.; Fraser, C. L., Synthesis And Unexpected Reactivity Of Iron Tris(Bipyridine) Complexes With Poly(Ethylene Glycol) Macroligands *Biomacromolecules* **2006**, *7*, 459-468.

162. Kalyanasundaram , K., Photophysics, Photochemistry And Solar Energy Conversion With Tris(Bipyridyl)Ruthenium(II) And Its Analogues *Coord. Chem. Rev.* **1982**, *46*, 159-244.

163. Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Venturi, M., Artificial Molecular-Level Machines: Which Energy To Make Them Work? *Acc. Chem. Res.* **2001**, *34*, 445-455.

164. Nguyen, J. V.; Jones, C. W., Design, Behavior, And Recycling Of Silica-Supported Cubr-Bipyridine ATRP Catalysts *Macromolecules* **2004**, *37*, 1190-1203.

165. Carlise, J. R.; Weck, M., Side-Chain Functionalized Polymers Containing Bipyridine Coordination Sites: Polymerization And Metal Coordination Studies *J. Polym. Sci. Part A: Polym. Chem.* **2004**, *42*, 2973-2984.

166. Chen, B.; Sleiman, H. F., Ruthenium Bipyridine-Containing Polymers And Block Copolymers Via Ring-Opening Metathesis Polymerization *Macromolecules* **2004**, *37*, 5866-5872.

167. Belbakra, A.; Goeb, S.; De Nicola, A.; Ziessel, R.; Sabatini, C.; Barbieri, A.; Barigelletti, F., Spectroscopic And Redox Properties Of Novel D(6)-Complexes

Engineered From All Z-Ethenylthiophene-Bipyridine Ligands *Inorg. Chem.* **2007**, *46*, 839-847.

168. Singleton, J. T., The Uses Of Pincer Complexes In Organic Synthesis *Tetrahedron* **2003**, *59*, 1837-1857.

169. Yu, K.; Sommer, W.; Weck, M.; Jones, C. W., Silica And Polymer-Tethered Pd-SCS-Pincer Complexes: Evidence For Precatalyst Decomposition To Form Soluble Catalytic Species In Mizoroki-Heck Chemistry *J. Catal.* **2004**, *226*, 101-110.

170. Suijkerbuijk, B.; Lutz, M.; Spek, A. L.; Van Koten, G.; Gebbink, R., Pincer-Porphyrin Hybrids *Org. Lett.* **2004**, *6*, 3023-3026.

171. Gerhardt, W. W.; Zucchero, A. J.; South, C. R.; Bunz, U. H. F.; Weck, M., Controlling Polymer Properties Through Dynamic Metal-Ligand Interactions: Supramolecular Cruciforms Made Easy *Chem. Eur. J.* **2007**, *13*, 4467-4474.

172. Gerhardt, W. W.; Weck, M., Investigations Of Metal-Coordinated Peptides As Supramolecular Synthons *J. Org. Chem.* **2006**, *71*, 6333-6341.

173. Gerhardt, W. W.; Zucchero, A. J.; Wilson, J. N.; South, C. R.; Bunz, U. H. F.; Weck, M., Supramolecular Cruciforms *Chem. Commun.* **2006**, 2141-2143.

174. South, C. R.; Pinon, V.; Weck, M., Erasable Coordination Polymer Multilayers On Gold *Angew. Chem. Int. Ed.* **2008**, *47*, 1425-1428.

175. Adhikari, D.; Mossin, S.; Basuli, F.; Huffman, J. C.; Szilagyi, R. K.; Meyer, K.; Mindiola, D. J., Structural, Spectroscopic, And Theoretical Elucidation Of A Redox-Active Pincer-Type Ancillary Applied In Catalysis *J. Am. Chem. Soc.* **2008**, *130*, 3676-3682.

176. Zhao, C. Q.; Jennings, M. C.; Puddephatt, R. J., A Hemilabile Binucleating Pincer Ligand For Self-Assembly Of Coordination Oligomers And Polymers *Dalton Trans.* **2008**, 1243-1250.

177. Traff, A.; Nilsson, G. N.; Szabo, K. J.; Eriksson, L., Application Of Iridium Pincer Complexes In Hydrogen Isotope Exchange Reactions *J. Organomet. Chem.* **2007**, *692*, 5529-5531.

178. Albrecht, M.; Van Koten, G., Platinum Group Organometallics Based On "Pincer" Complexes: Sensors, Switches, And Catalysts *Angew. Chem. Int. Ed.* **2001**, *40*, 3750-3781.

179. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Cross-Linked And Functionalized 'Universal Polymer Backbones' Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

180. Pollino, J. M.; Weck, M., Supramolecular Side-Chain Functionalized Polymers: Synthesis And Self-Assembly Behavior Of Polynorbornenes Bearing Pd^{ii} SCS Pincer Complexes *Synthesis* **2002**, 1277-1285.

181. Huck, W. T. S.; Hulst, R.; Timmerman, P.; Veggel, F. C. J. M. V.; Reinhoudt, D. N., Noncovalent Synthesis Of Nanostructures: Combining Coordination Chemistry And Hydrogen Bonding *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1006-1008.

182. Liu, D. R.; Schultz, P. G., Generating New Molecular Function: A Lesson From Nature *Angew. Chem. Int. Ed.* **1999**, *38*, 36-54.

183. Peng, Z.; Gharavi, A. R.; Yu, L., Synthesis And Characterization Of Photorefractive Polymers Containing Transition Metal Complexes As Photosensitizer *J. Am. Chem. Soc.* **1997**, *119*, 4622 - 4632.

184. Guan, L.; Zhao, Y., Self-Assembly Of A Liquid Crystalline Anisotropic Gel *Chem. Mater.* **2000**, *12*, 3667-3673.

185. Fromm, K. M., "Synthesis And Crystal Structure Of The One-Dimensional Polymer Compound {[Ba(Otf)3(Thf)3]2[Ba(Otf)3(Thf)2]}1-Dim (Otf = CF3SO3-) - Excerpts From A Three-Dimensional Structure As An Access To New Materials?" *Chem. Eur. J.* **2001**, *7*, 2236-2244.

186. Ruokolainen, J. M.; Torkkeli, M.; Ma¨Kela¨, T.; Serimaa,R.; Tenbrinke, G.; Ikkala, O. , Switching Supramolecular Polymeric Materials With Multiple Length Scales *Science* **1998**, *289*, 557-560.

187. Fyfe, M. C. T. S., J. F, Interwoven Supramolecular Arrays Via The Noncovalent Polymerization Of Pseudorotaxanes. *Coord. Chem. Rev.* **1999**, *183*, 139-155.

188. Deng, W.-Q. F., A. H.; Stoddart, J. F.; Goddard, W. A., III An Electrochemical Color-Switchable RGB Dye: Tristable [2]Catenane. *J. Am. Chem. Soc.* **2005**, *127*, 15994-15995.

189. Badjic, J.; Stoddart, J. F.; Balzani, V.; Silvi, S.; Credi, A.; Operating Molecular Elevators. *J. Am. Chem. Soc.* **2006**, *128*, 1489-1499.

190. Valkama, S.; Lehtonen, O.; Lappalainen, K.; Kosonen, H.; Castro, P.; Repo, T.; Torkkeli, M.; Serimaa, R.; Ten Brinke, G.; Ikkala, O., Multicomb Polymeric Supramolecules And Their Self-Organization: Combination Of Coordination And Ionic Interactions *Macromol. Rapid. Commun.* **2003**, *24*, 556-560.

191. Ikkala, O.; Ten Brinke, G., Hierarchical Self-Assembly In Polymeric Complexes: Towards Functional Materials *Chem. Commun.* **2004**, 2131-2137.

192. Pollino, J. M.; Stubbs, L. P.; Weck, M. W., One-Step Multifunctionalization Of Random Copolymers Via Self-Assembly *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

193. Pollino, J. M.; Stubbs, L. P.; Weck, M., One-Step Multifunctionalization Of Random Copolymers Via Self-Assembly *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

194. Folmer, B. J. B.; Sijbesma, R. P.; Versteegen, R. M.; Van Der Rijt, J. A. J.; Meijer, E. W., Supramolecular Polymer Materials: Chain Extension Of Telechelic Polymers Using A Reactive Hydrogen-Bonding Synthon *Adv. Mater.* **2000**, *12*, 874-878.

195. Hirschberg, J. H. K. K.; Ramzi, A.; Sijbesma, R. P.; Meijer, E. W., Ureidotriazine-Based Supramolecular Copolymers *Macromolecules* **2003**, *36*, 1429-1432.

196. Hirschberg, J. H. K. K.; Beijer, F. H.; Van Aert, H. A.; Magusin, P. C. M. M.; Sijbesma, R. P.; Meijer, E. W., Supramolecular Polymers From Linear Telechelic Siloxanes With Quadruple-Hydrogen-Bonded Units *Macromolecules* **1999**, *32*, 2696-2705.

197. Goethals, E. J., *Telechelic Polymers: Synthesis And Applications*. CRC Press: Boca Raton, 1988.

198. Beijer, F. H.; Kooijman, H.; Spek, A. L.; Sijbesma, R. P.; Meijer, E. W., Self-Complementarity Achieved Through Quadruple Hydrogen Bonding *Angew. Chem. Int. Ed.* **1988**, *37*, 75-78.

199. Lange, R. F. M.; Meijer, E. W., Supramolecular Polymer Interactions Based On The Alternating Copolymer Of Styrene And Maleimide *Macromolecules* **1995**, *28*, 782 - 783.

200. Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Brinke, G. T.; Folmer, B. J. B.; Hirschberg, J. H. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W., Reversible Polymers Formed From Self-Complementary Monomers Using Quadruple Hydrogen Bonding *Science* **1997**, *278*, 1601-1604.

201. Dijkstra, H. P.; Meijer, M. D.; Patel, J.; Kreiter, R.; Van Klink, G. P. M.; Lutz, M.; Spek, A. L.; Canty, A. J.; Van Koten, G., Design And Performance Of Rigid Nanosize Multimetallic Cartwheel Pincer Compounds As Lewis-Acid Catalysts *Organomettalics* **2001**, *20*, 3159-3168.

202. Guan, Z. B.; Roland, J. T.; Bai, J. Z.; Ma, S. X.; Mcintire, T. M.; Nguyen, M., Modular Domain Structure: A Biomimetic Strategy For Advanced Polymeric Materials *J. Am. Chem. Soc.* **2004**, *126*, 2058-2065.

203. Roland, J. T.; Guan, Z. B., Synthesis And Single-Molecule Studies Of A Well-Defined Biomimetic Modular Multidomain Polymer Using A Peptidomimetic Beta-Sheet Module *J. Am. Chem. Soc.* **2004**, *126*, 14328-14329.

204. Yamauchi, K.; Lizotte, J. R.; Long, T. E., Thermoreversible Poly(Alkyl Acrylates) Consisting Of Self-Complementary Multiple Hydrogen Bonding *Macromolecules* **2003**, *36*, 1083-1088.

205. Yamauchi, K.; Lizotte, J. R.; Long, T. E., Synthesis And Characterization Of Novel Complementary Multiple-Hydrogen Bonded (CMHB) Macromolecules Via A Michael Addition *Macromolecules* **2002**, *35*, 8745-8750.

206. Mckee, M. G.; Elkins, C. L.; Long, T. E., Influence Of Self-Complementary Hydrogen Bonding On Solution Rheology/Electrospinning Relationships *Polymer* **2004**, *45*, 8705-8715.

207. Binder, W. H.; Kunz, M. J.; Kluger, C.; Hayn, G.; Saf, R., Synthesis And Analysis Of Telechelic Polyisobutylenes For Hydrogen-Bonded Supramolecular Pseudo-Block Copolymers *Macromolecules* **2004**, *37*, 1749-1759.

208. Farnik, D.; Kluger, C.; Kunz, M. J.; Machl, D.; Petraru, L.; Binder, W. H., Synthesis And Self Assembly Of Hydrogen-Bonded Supramolecular Polymers *Macromol. Symp.* **2004**, *217*, 247-266.

209. Binder, W. H.; Bernstorff, S.; Kluger, C.; Petraru, L.; Kunz, M. J., Tunable Materials From Hydrogen-Bonded Pseudo Block Copolymers *Adv. Mater.* **2005**, *17*, 2824-2828.

210. Binder, W. H., Polymeric Ordering By H-Bonds. Mimicking Nature By Smart Building Blocks *Monatsh. Chem.* **2005**, *136*, 1-19.

211. Schubert, U. S.; Heller, M., Metallo-Supramolecular Initiators For The Preparation Of Novel Functional Architectures *Chem. Eur. J.* **2001**, *7*, 5252-5259.

212. Heller, M.; Schubert, U. S., Terpyridines As Supramolecular Initiators For Living Polymerization Methods *Macromol. Symp.* **2002**, *177*, 87-96.

213. Mather, B. D.; Lizotte, J. R.; Long, T. E., Synthesis Of Chain End Functionalized Multiple Hydrogen Bonded Polystyrenes And Poly(Alkyl Acrylates) Using Controlled Radical Polymerization *Macromolecules* **2004**, *37*, 9331-9337.

214. Xu, H.; Norsten, T. B.; Uzun, O.; Jeoung, E.; Rotello, V. M., Stimuli Responsive Surfaces Through Recognition-Mediated Polymer Modification *Chem. Commun.* **2005**, 5157-5159.

215. Mitchell, J. P.; Gibson, V. C.; Schrock, R. R., Chain-End Functionalization Of Living Polymers Formed By The Ring-Opening Metathesis Polymerization Of Norbornene *Macromolecules* **1991**, *24*, 1220-1221.

216. Higley, M. N.; Pollino, J. M.; Hollembeak, E.; Weck, M., A Modular Approach Toward Block Copolymers *Chem. Eur. J.* **2005**, *11*, 2946-2953.

217. Hillmyer, M. A.; Grubbs, R. H., Chain Transfer In The Ring-Opening Metathesis Polymerization Of Cyclooctadiene Using Discrete Metal Alkylidenes *Macromolecules* **1995**, *28*, 8662-8667.

218. Gibson, V. C.; Okada, T., Synthesis Of End-Functionalized Polynorbornenes And Polynorbornanes Via Metathesis: Novel Macromonomers For Polycondensation Reactions *Macromolecules* **2000**, *33*, 655-656.

219. Scherman, O. A.; Ligthart, G.; Ohkawa, H.; Sijbesma, R. P.; Meijer, E. W., Olefin Metathesis And Quadruple Hydrogen Bonding: A Powerful Combination In Multistep Supramolecular Synthesis *Proc. Nat. Acad. Sci. U.S.A.* **2006**, *103*, 11850-11855.

220. Owen, R. M.; Gestwicki, J. E.; Young, T.; Kiessling, L. L., Synthesis And Applications Of End-Labeled Neoglycopolymers *Org. Lett.* **2002**, *4*, 2293-2296.

.

CHAPTER 2

SELF-SORTING IN POLYMERS

2.1 Abstract

Random and block copolymers containing two different classes of hydrogen-bonding side-chains have been prepared by ring-opening metathesis polymerization. The resulting copolymers can be viewed as 'universal polymer backbones'[1] based solely on two competitive hydrogen-bonding pairs. The hydrogen-bonding side-chains containing thymine and cyanuric acid based recognition motifs are shown to self-assemble with their complementary diamido pyridine and isophthalic wedge moieties, respectively, even in the presence of competitive recognition sites, *i.e.* selective functionalization of the copolymers can be accomplished via a one-step orthogonal self-assembly approach displaying self-sorting in a competitive environment. These results clearly demonstrate for the first time the concept of self-sorting in synthetic polymers and suggest the design of complex polymeric materials containing competitive noncovalent interactions.

2.2 Introduction

Self-sorting is the ability of objects such as molecules to find and self-assemble selectively with their corresponding recognition units. From complex systems described in chapter 1, to simple phenomena, like oil-water phase separation, self-sorting is evident throughout our daily lives. In synthetic systems, self-sorting based on hydrogen-bonding has been explored as a general phenomenon in low molecular weight organic molecules.[2-8] However, to date, the principle of self-sorting in polymeric and complex un-natural systems that can be viewed as simple synthetic analog to biopolymers such as DNA has not been explored. While in polymer science many reports in the literature outline the

use of pendant side-chain polymers based on multiple recognition units,[1, 9-12] these examples however are in highly controlled systems without the presence of a competitive recognition unit. This simple analog demonstrates the interactions of multiple types of hydrogen bonding pairs along a single macromolecule, and brings us a step closer to being able to mimic Nature's supramolecular complexity.

In this chapter, I investigate the concept of self-sorting in polymers by employing norbornene copolymers composed of two different hydrogen-bonding side-chains. These hydrogen-bonding side-chains contain thymine and cyanuric acid based recognition units that are able to self-assemble with diamido pyridine[13-23] and isophthalic wedge moieties,[24-31] respectively. This chapter demonstrates that the principle of self-sorting can be translated to synthetic side-chain functionalized polymers, *i.e.* copolymer side-chains self-assemble with their corresponding recognition unit in the presence of competitive recognition sites.

The concept of self-sorting in polymers is essential for replication and translation of genetic material. The specific interactions within these complementary pairs play a key role in the storage and decoding of genetic material. Recent research efforts have focused on the manipulation of the Watson-Crick base pairs of DNA[32] and employing them as a synthetic tool, using complementary DNA oligomers as a template to bring reactants together thereby discovering new reactions.[33-35] Other investigations have utilized hydrogen-bonding moieties as enzyme mimics to induce catalytic activity.[1, 36-38] In these examples, the inherent self-sorting of hydrogen-bonding receptors is key. The polymeric system presented herein follows this trend by relying on hydrogen-bonded dimers and a hydrogen-bonded enzyme-mimic as recognition units.

The copolymers introduced in this chapter are an extension of Joel Pollino's 'universal polymer backbone' concept[1] and are based solely on hydrogen-bonded recognition motifs that are able to self-assemble with their corresponding receptor molecule in the presence of competitive recognition units. The copolymers are based on two monomers that encompass three design elements: (1) norbornene as the polymerizable unit that propagates in a living fashion via ring-opening metathesis polymerization (ROMP),[39] (2) a spacer molecule to increase solubility and to decouple the polymer from the hydrogen-bonding recognition units, and (3) the recognition units themselves that are either thymine derivatives that can undergo three hydrogen bonds to self-assemble with diaminopyridines[13-23] or cyanuric acids that are able to self-assemble with isophthalic wedge type receptor via six hydrogen bonds (Figure 2.1).[24-31, 40]

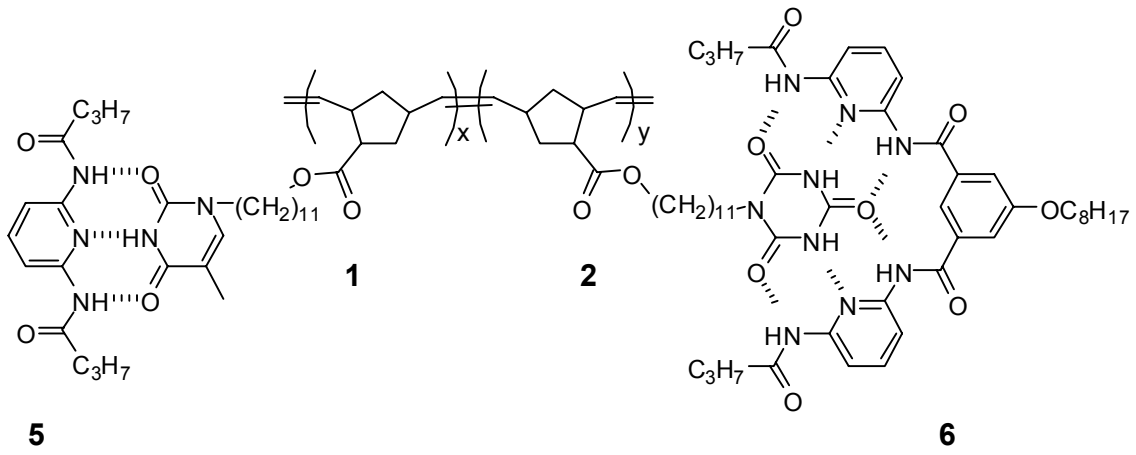


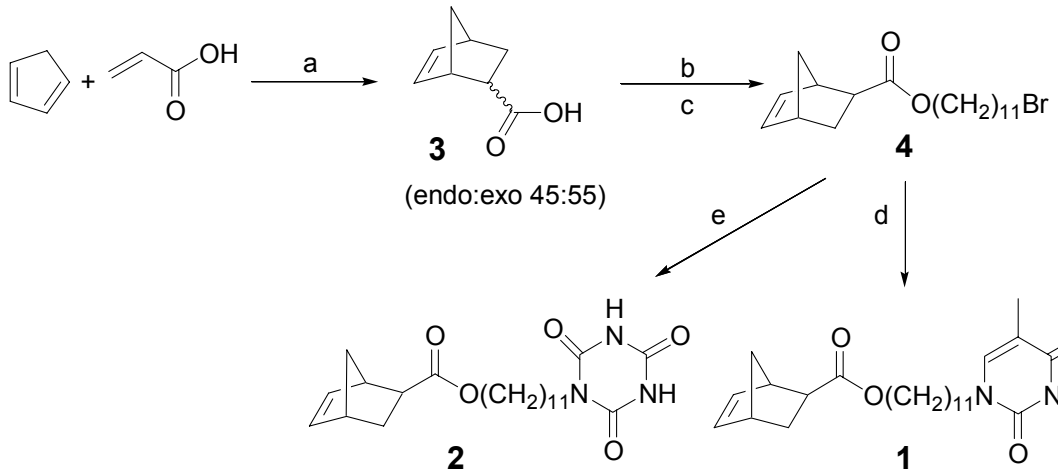
Figure 2.1. Fully hydrogen-bonded copolymer and the corresponding recognition units.

These recognition units were chosen because of their structural similarity (*i.e.* the acceptor-donor-acceptor moiety present in the thymine derivative is also present in the cyanuric acid derivative) and thus their possibility to display competitive interactions during the self-assembly process.

2.3 Monomer synthesis.

The monomers were synthesized as outlined in Scheme 2.1. Isomerically pure *exo*-norbornene carboxylic acid was synthesized from the endo:exo mixture by iodolactonaization using established literature procedures.[41-43] The *exo*-norbornene carboxylic acid was then functionalized with 11-bromoundecanol using DCC/DMAP to yield the corresponding norbornene bromide **4**.[40] Monomers **1** and **2** were formed in one step by reacting **4** with an excess of either thymine or cyanuric acid, respectively. Di-butylamido pyridine **5** was synthesized in one step from the acylation of diamino pyridine (recrystallized from chloroform) using butyl chloride. The octyl-ether isophthalic wedge receptor **6** was synthesized in close analogy to literature procedures[26, 29] after functionalizing the phenolic hydroxyl of dimethyl 5-hydroxy isophthalate with 1-bromo-octane via a Williamson ether synthesis.

Scheme 2.1. Synthesis of Monomers **1** and **2**.



Reagents and Conditions: (a) 180 °C, reflux eight hours, 70%; (b) 1. NaOH, H_2O, 2. KI, I_2, H_2O 44%; (c) DCC/DMAP, Br $(CH_2)_{11}OH$, 50 °C, 82%; (d) thymine, K_2CO_3, DMSO, rt, 53%; and (e) cyanuric acid, K_2CO_3, DMSO, rt. 36%.

2.4 Polymer synthesis and living characterization.

All monomers were subjected to ROMP using Grubbs' first generation initiator.[39] The polymerizations were carried out in 0.2 M solutions of reiterated tetrahydrofuran at room temperature with monomer to initiator ratios of 20:1-120:1. All polymerizations were monitored via ^{1}H NMR spectroscopy. A 50:1 monomer to initiator ratio of **2** polymerizes within less than five minutes while the ROMP of **1** (50:1 monomer to initiator ratio) is complete within an hour. Figure 2.2 shows the kinetic data for the ROMP of **1** (the detailed polymerization behavior of **2** has been reported before[26]).

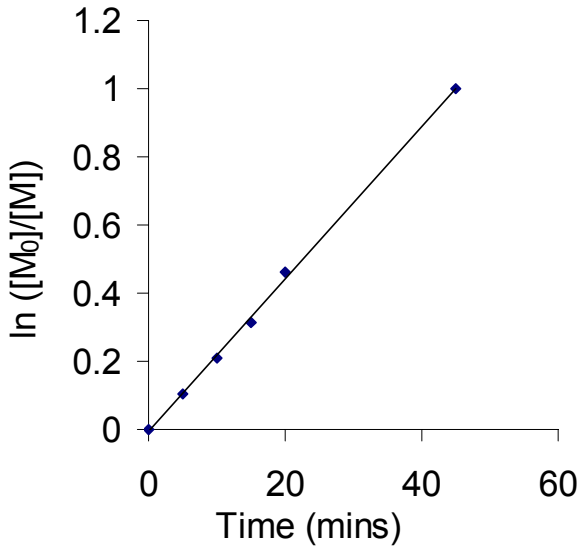


Figure 2.2 Kinetic data for the ROMP of **1**.

All polymers were purified and isolated by repeated precipitations into hexanes. The polymers were characterized by gel-permeation chromatography (GPC) and the obtained molecular weights and polydispersities are displayed in Table 2.1.

Table 2.1. Polymer Characterization Data for Polymers **1** and **2**.

	[M]:[I]	M_n (10^{-3})	M_w (10^{-3})	PDI
Poly-**1**	20	12.0	15.0	1.23
	40	20.0	29.5	1.46
	60	27.0	42.0	1.57
	80	33.0	55.0	1.66
	120	47.0	63.0	1.35
Poly-**2**	20	12.0	15.0	1.20
	40	21.0	29.0	1.26
	60	31.0	42.0	1.37
	80	45.0	66.5	1.49
	120	66.0	108.0	1.64

For both monomers we explored the living nature of the polymerization by investigating whether the stoichiometry was decisive in the resultant polymers. A linear relationship between M_n and the monomer to catalyst ratios was found in both cases (Figure 2.3A). To further characterize the living nature of the monomers we carried out homo-block copolymerizations in two steps. A 20:1 [M]:[I] ratio of the desired monomer (**1** or **2**) was polymerized to completion and allowed to sit for one hour. Subsequently, 100 equivalents of additional monomer were added. As shown in Figure 2.3B, a dramatic increase in the molecular weight of **1** was observed for the polymer after the addition of additional monomer. These results in conjunction with the stoichiometric

experiments clearly prove the living nature of **1**. While this dramatic increase during the block copolymerization experiment did not occur for polymers based on **2**, polymerization of **2** still displays a linear relationship between M_n and monomer to catalyst ratios. This data suggests but does not prove unequivocally the living nature of the ROMP of **2**.

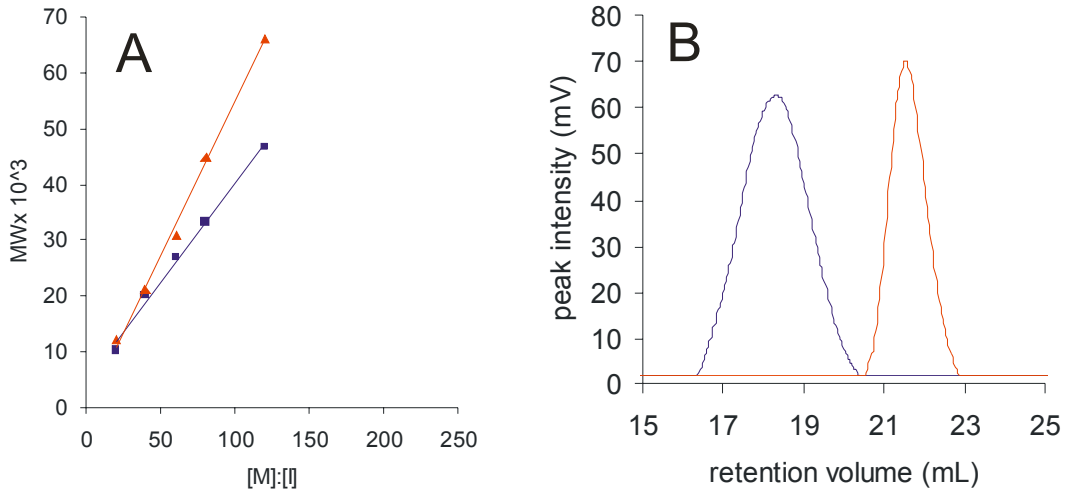


Figure 2.3 (A): Characterization of the living character of the ROMP of monomers **1** and **2**. (■) stoichiometric polymerization of **1**, (▲) stoichiometric polymerization of **2**. (B): GPC traces of polymers prepared using monomer **1**. (blue -) Polymer after complete conversion ([M]:[I] = 20:1, M_w = 1.5 x 10^4, M_n = 1.2 x 10^4, PDI= 1.23). (red -) Same polymer after standing for 0.5 hours followed by polymerization of 100 equiv ([M2]:[M1] = 100:1, [M]:[I] = 20:1, M_w = 1.1 x 10^5 , M_n = 7.2 x 10^4, PDI= 1.78) of additional monomer.

After establishing the living nature of the ROMP of **1** and **2**, we synthesized AB block copolymers starting with monomer **1** followed by **2**. A 50:1 [M]:[I] ratio of **1** was polymerized to completion. Subsequently, 50 equivalents of **2** were added and allowed polymerize to completion. Random copolymers were synthesized by polymerizing an equimolar solution of **1** and **2** (50 equivalents each) to completion. Both copolymers were characterized by GPC and ^{1}HNMR. Polymers were found to have molecular

weights between 1.0-7.0 x 10^4 versus poly(styrene) standards, with polydispersities ranging from 1.2-1.6 (Table 2.1).

2.5 Self-Assembly.

The pendant functional groups of our polymers have been shown throughout the literature to exhibit well-defined self-assembly behavior with their corresponding recognition units, diamino pyridine for **1** and isophthalic wedge for **2**.[13-23] [24-31] To address the question whether self-sorting occurs on polymers, *i.e*. if hydrogen-bonded recognition units on polymers containing two hydrogen-bonded moieties are able to find their complementary recognition units in the presence of each other, we carried out self-assembly studies in 15:85 dioxane:chloroform solutions. First we investigated the self-assembly of small molecules onto the monomers and the homopolymers of **1** and **2** by carrying out NMR spectroscopy titration experiments of the monomers and the individual homopolymers thereby establishing the hydrogen-bonding properties and measuring the association constants of **5** onto **1** and **6** onto **2** *without* the presence of competitive moieties. All association constants were determined by titration of the corresponding recognition unit (**5** or **6**) into a chloroform/dioxane solution of the polymer (**1** and **2**) and following the shift of the polymeric imide signals by ^{1}H NMR spectroscopy (Figures 2.4 and 2.5 and Table 2.2).

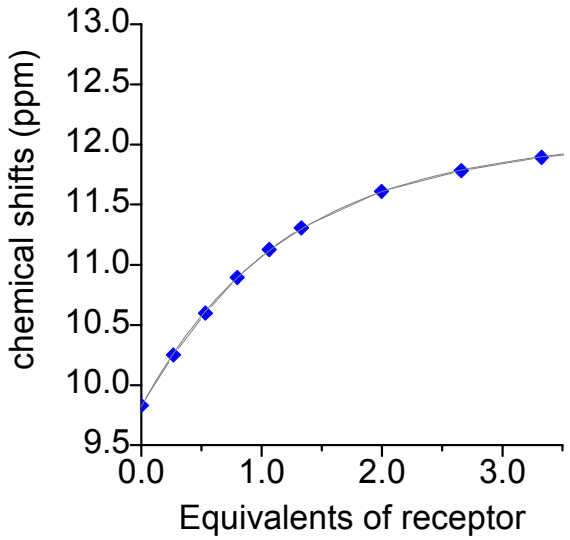


Figure 2.4. Chemical shifts of the imide protons of poly-**1** (◆) as a function of the equivalents of **5**.

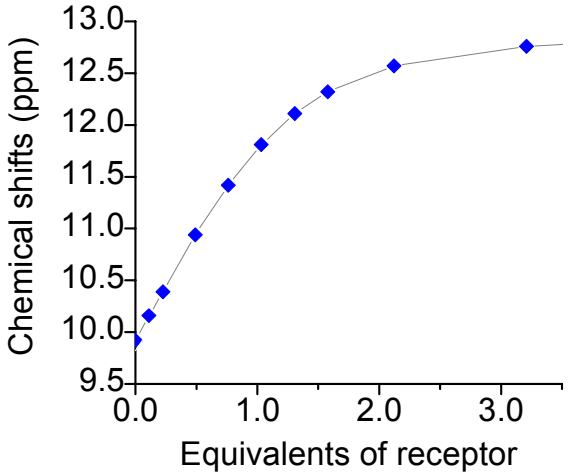


Figure 2.5. Chemical shifts of the imide protons of poly-**2** (◆) as a function of the equivalents of **6**.

Table 2.2. Association constants determined by ^{1}H NMR spectroscopy.[44]

Association constants of **1:5**	K_a [M^{-1}]
Monomer **1: 5**	1.0×10^2 (+/- 4)
Poly-**1 : 5**	1.0×10^2 (+/- 5)
50:50 block copoly. **1:2:5**	8.0×10^1 (+/- 8)
50:50 random copoly. **1:2:5**	1.0×10^2 (+/- 10)

Association constants of **2:6**	K_a [M^{-1}]
Monomer **2: 6**	3.0×10^2 (+/- 52)
Poly-**2 : 6**	3.0×10^2 (+/- 60)
50:50 block copoly. **1:2 : 6**	2.5×10^2 (+/- 108)
50:50 random copoly. **1:2: 6**	3.2×10^2 (+/- 134)

The association constants of the self-assembly steps of **5** onto **1** and **6** onto **2** were measured to be 1.0×10^2 and 3.0×10^2 M^{-1}, respectively. These association constants are very similar to the association constants between the monomers and their corresponding units suggesting that the bond strengths between the receptor units along the polymer and their small molecule recognition units are comparable to the bond strength of their monomeric analogs. It is important to note that these constants were measured in the presence of a competitive solvent (mixture of dioxane: chloroform) thereby reducing the association constant to reported values in the literature that were obtained in pure halogenated solvents.[13-23, 24-31] However, the use of this mixed solvent system was

necessary to tailor the solubility of both homopolymers and copolymers throughout all self-assembly experiments thereby allowing us to compare all data.

To prove if the concept of self-sorting in synthetic polymers is possible, we carried out titration experiments on both, block and random copolymers containing 50:50 mixtures of **1** and **2** using both recognition units in a one pot procedure (Figures 2.6 and 2.7).

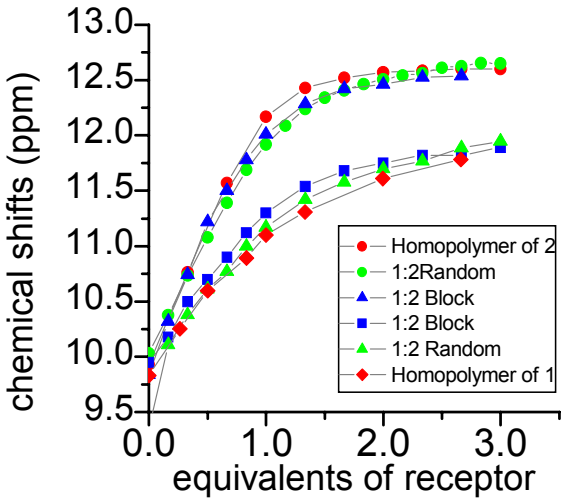


Figure 2.6. Self-sorting on polymers: NMR-titration curve of the addition of equimolar solutions of both recognition units at once: (●) shift of the imide protons of the cyanuric acid moieties of a cyanuric acid based homopolymers, (●) shift of the imide protons of the cyanuric acids of a 50:50 **1:2**-random copolymer, (▲) shift of the imide protons of the cyanuric acids of a 50:50 **1:2**-block copolymer, (■) shift of the imide protons of the thymines of a 50:50 **1:2**-block copolymer, (▲) shift of the imide protons of the thymines of a 50:50 **1:2**-random copolymer, and (◆) shift of the imide protons of the thymine moieties of thymine homopolymers.

Figure 2.7 shows the amide region (10.5 ppm – 13.5 ppm) of the ^{1}H NMR spectra of the homopolymers self-assembled with 2.8 equivalents of their corresponding units in a mixture of 15:85 dioxane-d_8:$CDCl_3$ followed by both, the block and random copolymers, assembled with 2.8 equivalents of both complementary units. The figure

clearly shows that the signals observed for the homopolymers (spectra A and B) are a superposition with those observed for the copolymers (spectra C and D). This superposition is evident that self-sorting of these mixed solutions does occur, *i.e.* each individual recognition unit finds it receptor molecule in the copolymer mixtures with the same fidelity as in the homopolymer solutions.

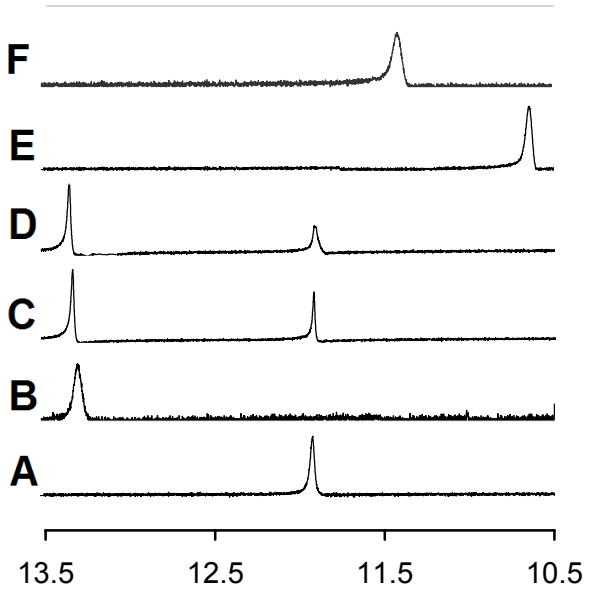


Figure 2.7. Self-sorting on polymers: Amide region of the ^{1}H NMR spectra of the polymers after the addition of 2.8 equivalents of recognition units (A) homopolymer (50 repeating units) of **1** after the addition of 2.8 equivalents of **5**, (B) homopolymer (50 repeating units) of **2** after the addition of 2.8 equivalents of **6**, (C) random copolymer of **1** and **2** after the addition of 2.8 equivalents of both **5** and **6**, (D) block copolymer of **1** and **2** after the addition of 2.8 equivalents of both **5** and **6**, **(**E**)** homopolymer (50 repeating units) of **2** after the addition of 2.8 equivalents of **5**, and **(**F**)** homopolymer (50 repeating units) of **1** after the addition of 2.8 equivalents of **6**.

We also determined the binding constants of both side-chain recognition units on the random and block copolymers. The association constants were measured to be 1.0 x 10^{2} and 3.2 x 10^{2} M^{-1} for the random copolymer and 6.0 x 10^{1} and 2.5 x 10^{2} M^{-1} for the block copolymer. These numbers are strikingly similar to their non-competitive

homopolymer analogs, which were measured to be 1.0 x 10^2 and 3.0 x 10^2 M^{-1}. It is important to note that the association constants for the random and block copolymers are the same within the error range of the measurements. Combining these results on the association constants measurements with the titration and NMR data clearly demonstrates that by simply selecting competitive recognition units that have well-defined self-assembly motifs in equimolar concentrations, it is possible to translate the concept of self-sorting into synthetic polymer chemistry.

With the previous result clearly demonstrating the principle of self-sorting on random and block copolymers, the question arises whether individual recognition units along the copolymers can be addressed by their complementary receptors in the presence of a second competitive recognition unit. To address this question, we investigated the copolymers by measuring the association constants using only one recognition unit at a time, *i.e.* single self-assembly experiments in the presence of a competitive receptor (Figure 2.8).

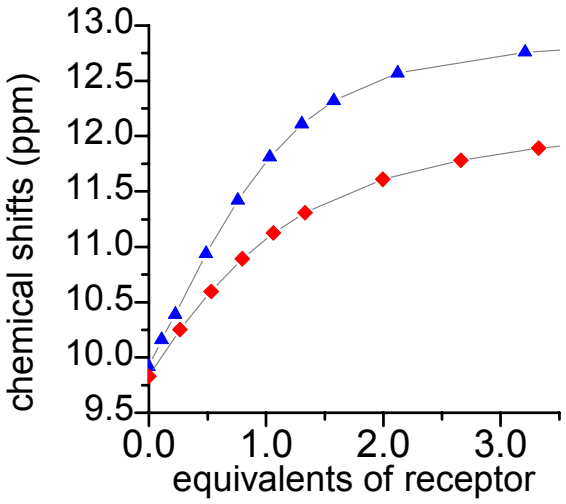


Figure 2.8. Chemical shifts of a 50:50 **1:2**-random copolymer stepwise titration with only one recognition unit at a time: (▲) shift of the imide protons of the cyanuric acid moieties with **6** and (◆) shift of the imide protons of the thymine moieties with **5** on the copolymer.

The binding constants were determined by a step-wise titration of the single recognition unit into a copolymer solution. The dynamic equilibrium of the hydrogen bonds is responsible for competition when a single side-chain's pairing nature is left unsatisfied. Due to the competitive nature of the monomers (when there is only one complementary receptor available for hydrogen-bonding) the association constants of the copolymers are slightly decreased. The stronger interaction of **2:6** shows less of a decrease from a K_a of 3.0 x 10^2 M^{-1} for the homopolymer to 2.5 x 10^2 M^{-1} for the copolymer systems, as opposed to that of the weaker interaction of **1:5** from 1.0 x 10^2 M^{-1} to 6.0 x 10^1 M^{-1}. This result demonstrates that a) competitive interactions take place along the copolymer backbones and b) by employing recognition units with stronger association constants (such as **2:6**) any interference from competitive moieties can be minimized.

Finally, we investigated if the hydrogen-bonding and self-sorting processes are truly dynamic processes. If the notion of a truly dynamic process holds, a stepwise self-assembly experiment onto the copolymers with both receptor molecules should yield fully self-sorted copolymers. Therefore, we carried out self-assembly experiments on the random and block 50:50 copolymers in a stepwise fashion using first one receptor (twelve equivalents) followed by the second one and *vice versa*. Figures 2.9 and 2.10 show the results of these experiments.

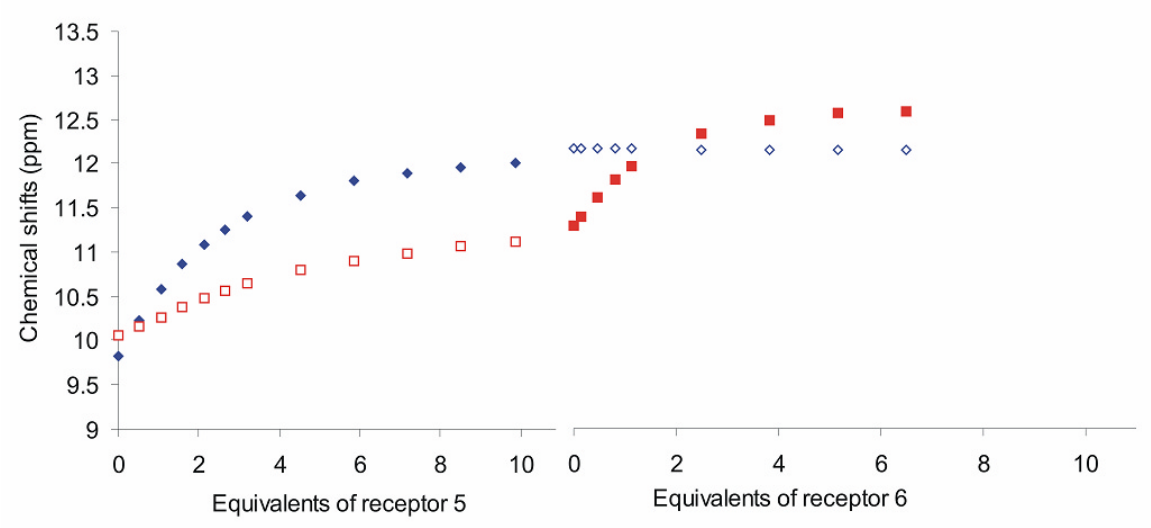


Figure 2.9. Chemical shifts of a 50:50 **1:2**-random copolymer stepwise titration (first addition of **5** followed by the addition of **6**): (◆) thymine imide proton shift associated with **5,** (◇) thymine imide proton shift associated with **6** after full assembly of **5** (equivalents are for a combination of **5** and **6**), (□) cyanuric acid imide proton shifts associated with the addition of **5**, followed by the addition of **6** (■).

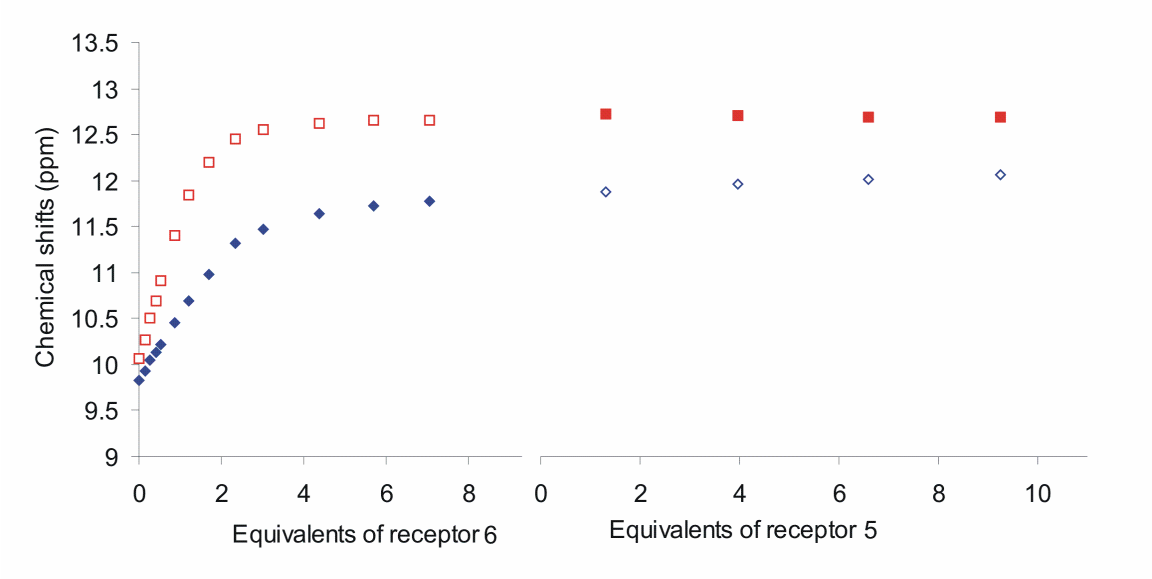


Figure 2.10. Chemical shifts of a 50:50 **1:2**-random copolymer stepwise titration, (first addition of **6** followed by the addition of **5)**: (◆) thymine imide proton shift associated with **6**, (◇) thymine imide proton shift associated with **5** after full assembly of **6** (equivalents are for a combination of **5** and **6**), (□) cyanuric acid imide proton shifts associated with the addition of **6**, followed by the addition of **5** (■).

In both cases, the titration curves of the first self-assembly step clearly showed the expected shifts of the imide protons of the targeted side-chain recognition unit along the copolymers. However, the non-targeted recognition unit also displayed some degree of hydrogen-bonding which is evident by the slow shifting of the imide protons of the non-targeted side-chain recognition unit. Nevertheless, when carrying out the second self-assembly titration, these weak non-specific hydrogen-bonding interactions between the first receptor unit and its non-complementary copolymer side-chain give way to specific hydrogen-bonding interaction between the second receptor and its targeted recognition unit as evident by the strong and selective titration curve. Furthermore, *NO* shifts of the imide protons of the first targeted self-assembly pair is observed, *i.e.* in Figures 2.9 and 2.10, the imide signals corresponding to **1** and **2**, respectively, do not change or increase further, however the signals associated with **2** or **1** show a subsequent increase. The final

placements of each of the imide signals of both **1** and **2** in Figures 9 and 10 are an exact superposition of the full titration of both of their corresponding homopolymers. Therefore, while the binding constants in a competitive environment (only one recognition unit) are decreased, when the competition is removed through the addition of a second recognition unit, self-sorting is again observed.

2.6 Conclusion.

In this chapter, I have demonstrated that self-sorting can be translated to synthetic side-chain functionalized polymers and occurs even in the presence of highly competitive recognition units. This was shown by designing, synthesizing (via ROMP) and self-assembling random and block copolymers containing both cyanuric acid and thymine-based moieties with their corresponding recognition units. The resulting copolymers can be viewed as 'universal polymer backbones' based solely on two competitive hydrogen-bonding recognition motifs. Selective functionalization of the resultant copolymers was accomplished via a one-step orthogonal self-assembly displaying self-sorting in a competitive environment. This methodology, that can be viewed on a very primitive level as a synthetic DNA analogue, has the potential to create a variety of complex, rapidly functionalizable, materials for use in areas such as material science, drug delivery, and biomimetic chemistry.

2.7 Experimental Section

All commercially available reagents and solvents were used without further purification. Dueterated solvents were distilled over calcium hydride and stored in the dark. Anhydrous dichloromethane and THF were dried via passage through copper oxide and

alumina columns under argon. Column chromatography was carried out on silica gel 60, 230 ± 400 mesh (Whatman). Gel-permeation chromatographies were carried out on polymer solutions in THF at 30 °C (column combination: 2x American Polymer Standards 10 μm particle size, linear mixed bed packing, flow rate 1 mL min^{-1}) with a Waters 1525 binary pump coupled to a Waters 2414 refractive index detector. Calibrations are based on poly(styrene) standards. NMR spectra were recorded on a Varian Mercury 300 spectrometer (^{1}H: 300 MHz, ^{13}C: 75 MHz). Chemical shifts are reported in ppm on the δ scale relative to the solvent signal. Electrospray ionization (ESI) mass spectra were obtained on a Micromass Quattro LC spectrometer, and fast atom bombardment (FAB) mass spectra on a VG Instruments 70SE spectrometer. Elemental analyses were performed by Atlantic Microlabs, Norcross, GA. Monomer **1**,[26] and recognition units **5**[17] and **6**[26, 29] were prepared as previously reported.

***Exo*-bicyclo [2.2.1] hept-5-ene-2-carboxylic acid-11-(3-methyl-4,6-trioxo-[1,5] diazinan-1-yl)-undecyl ester (1).**

To a stirred solution of **4** (4.0 g, 10.8 mmol)[26] and thymine (108 mmol) in DMSO (100 mL), K_2CO_3 (3.0 g, 22 mmol) was added. The reaction mixture was allowed to stir at room temperature for 60 hours, poured into a solution of $NaHSO_{3(aq)}$ (500 mL), extracted with a 1:1 mixture of diethyl ether/dichloromethane, and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the residue was purified by passage over silica (1:1 mixture EtOAc/hexanes). After drying on high vacuum, **1** was obtained as a white solid in 53% yields. ^{1}H NMR (300 MHz $CDCl_3$): δ = 9.33 (br s, 1H, NH), 6.96 (br s, 1H), 6.10 (m, 2H, CH=CH), 4.07 (t, 2H, *J* = 6.7 Hz, CH_2O), 3.88 (t, 2H, *J* = 7.5 Hz, CH_2N), 3.03 (m,1H), 2.91 (m, 1H), 2.22 (m, 1H), 1.91 (m, 1H), 1.90 (s, 3H),

1.69–1.49 (m, 5H), 1.41–1.24 (m, 16H). ^{13}C NMR (75 MHz $CDCl_3$): δ = 176.3, 164.5, 151.1, 140.6, 138.2, 135.9, 111.2, 64.9, 48.9, 46.9, 46.7, 43.5, 41.9, 30.64, 29.8, 29.5, 29.4, 29.0, 26.8, 26.3, 12.7. MS (EI): m/z (%) = 416.26601 (M^+, 416.26751 calcd.). Anal. calcd for $C_{24}H_{36}N_2O_4$: C, 69.10; H, 8.64; N, 6.70; Found: C, 68.75; H, 8.83; N, 6.64.

General Procedure for Polymerizations.

To a 0.2 M stirred solution of the target monomer in tetrahydrofuran, 0.006 mmol of ruthenium catalyst was added. The mixture was stirred at room temperature and the reaction progress was monitored by ^{1}H NMR spectroscopy until completion. After complete conversion, two drops of ethyl vinyl ether were added to terminate the reaction. The polymers were purified by precipitation into hexanes.

Polymer 1. ^{1}H NMR (300 MHz, 15:85 Dioxane-d_6:$CdCl_3$): δ = 9.8 (br s, 1H, NH), 6.90 (br s, 1H), 5.4-5.1 (m, 2H), 3.90 (br m, 2H), 3.60 (t, 2H, *J* = 5.5 Hz, CH_2N), 2.7-2.3 (br m, 5 H), 2.2-0.5 (br m, 23 H).

Copolymer 1:2.

^{1}H NMR (300 MHz, 15:85 Dioxane-d_6:$CdCl_3$): δ = 10.0 (br s, 2H, NH), 9.8 (br s, 1H, NH), 6.90 (br s, 2H), 5.4-5.1 (m, 4H), 3.90 (br m, 4H), 3.60 (t, 4H, *J* = 6.4 Hz, CH_2N), 2.7-2.3 (br m, 10 H), 2.2-0.5 (br m, 46 H).

Self-Assembly.

To a 0.04 M solution (15:85 dioxane:chloroform) of polymer, 2.8 equivalents of recognition unit (either **5**, **6**, or both) dissolved in 0.5 mL 15:85 dioxane:chloroform were added dropwise over a period of one minute at room temperature.

Titration Studies.

Association constants were measured by NMR spectroscopy titration studies of a 0.2 M solution (15:85 dioxane:chloroform) of the receptor molecules with a 0.04 M solution (based on recognition units) of the corresponding polymer, where the molarity is based on the number of recognition units. The chemical shifts of the imide protons on either the thymine or the cyanuric acid moieties were monitored by ^{1}HNMR spectroscopy. The NMR data was evaluated using the computer program ChemEquili.[44]

2.8 References

1. Pollino, J. M.; Stubbs, L. P.; Weck, M. W., One-Step Multifunctionalization of Random Copolymers Via Self-Assembly *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

2. Mukhopadhyay, P.; Wu, A. X.; Isaacs, L., Social Self-Sorting In Aqueous Solution *J. Org. Chem.* **2004**, *69*, 6157-6164.

3. Corbin, P. S.; Lawless, L. J.; Li, Z. T.; Ma, Y. G.; Witmer, M. J.; Zimmerman, S. C., Discrete And Polymeric Self-Assembled Dendrimers: Hydrogen Bond-Mediated Assembly With High Stability And High Fidelity *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 5099-5104.

4. Cai, M. M.; Shi, X. D.; Sidorov, V.; Fabris, D.; Lam, Y. F.; Davis, J. T., Cation-Directed Self-Assembly Of Lipophilic Nucleosides: The Cation's Central Role In The Structure And Dynamics Of A Hydrogen-Bonded Assembly *Tetrahedron* **2002**, *58*, 661-671.

5. Jolliffe, K. A.; Calama, M. C.; Fokkens, R.; Nibbering, N. M. M.; Timmerman, P.; Reinhoudt, D. N., Characterization Of Hydrogen-Bonded Supramolecular Assemblies By MALDI-TOF Mass Spectrometry After Ag+ Labeling *Angew. Chem. Int. Ed.* **1998**, *37*, 1247-1251.

6. Ma, Y. G.; Kolotuchin, S. V.; Zimmerman, S. C., Supramolecular Polymer Chemistry: Self-Assembling Dendrimers Using The DDA Center Dot AAD (GC-Like) Hydrogen Bonding Motif *J. Am. Chem. Soc.* **2002**, *124*, 13757-13769.

7. Wu, A. X.; Isaacs, L., Self-Sorting: The Exception Or The Rule? *J. Am. Chem. Soc.* **2003**, *125*, 4831-4835.

8. Wu, A. X.; Chakraborty, A.; Fettinger, J. C.; Flowers, R. A.; Isaacs, L., Molecular Clips That Undergo Heterochiral Aggregation And Self-Sorting *Angew. Chem. Int. Ed.* **2002**, *41*, 4028-4031.

9. Valkama, S.; Lehtonen, O.; Lappalainen, K.; Kosonen, H.; Castro, P.; Repo, T.; Torkkeli, M.; Serimaa, R.; Ten Brinke, G.; Ikkala, O., Multicomb Polymeric Supramolecules And Their Self-Organization: Combination Of Coordination And Ionic Interactions *Macromol. Rapid. Commun.* **2003**, *24*, 556-560.

10. Bazzi, H. S.; Bouffard, J.; Sleiman, H. F., Self-Complementary ABC Triblock Copolymers Via Ring-Opening Metathesis Polymerization *Macromolecules* **2003**, *36*, 7899-7902.

11. Ruokolainen, J.; Mäkinen, R.; Torkkeli, M.; Mäkelä, T.; Serimaa, R.; Ten Brinke, G.; Ikkala, O., Switching Supramolecular Polymeric Materials With Multiple Length Scales *Science* **1998**, *280*, 557-560.

12. Van Ekenstein, G. A.; Polushkin, E.; Nijland, H.; Ikkala, O.; Ten Brinke, G., Shear Alignment At Two Length Scales: Comb-Shaped Supramolecules Self-Organized As Cylinders-Within-Lamellar Hierarchy *Macromolecules* **2003**, *36*, 3684-3688.

13. Lehn, J.-M., *Supramolecular Chemistry*. Wiley-VCH: 1995.

14. Thibault, R. J.; Hotchkiss, P. J.; Gray, M.; Rotello, V. M., Thermally Reversible Formation Of Microspheres Through Non-Covalent Polymer Cross-Linking *J. Am. Chem. Soc.* **2003**, *125*, 11249-11252.

15. Ilhan, F.; Gray, M.; Rotello, V. M., Reversible Side Chain Modification Through Noncovalent Interactions. "Plug And Play" Polymers *Macromolecules* **2001**, *34*, 2597-2601.

16. Carroll, J. B.; Waddon, A. J.; Nakade, H.; Rotello, V. M., "Plug And Play" Polymers. Thermal And X-Ray Characterizations Of Noncovalently Grafted Polyhedral Oligomeric Silsesquioxane (POSS)-Polystyrene Nanocomposites *Macromolecules* **2003**, *36*, 6289-6291.

17. Stubbs, L. P.; Weck, M., Towards A Universal Polymer Backbone: Design And Synthesis Of Polymeric Scaffolds Containing Terminal Hydrogen-Bonding Recognition Motifs At Each Repeating Unit *Chem. Eur. J.* **2003**, *9*, 992-999.

18. Pranata, J.; Wierschke, S. G.; Jorgensen, W. L., Opls Potential Functions For Nucleotide Bases - Relative Association Constants Of Hydrogen-Bonded Base-Pairs In Chloroform *J. Am. Chem. Soc.* **1991**, *113*, 2810-2819.

19. Murray, T. J.; Zimmerman, S. C., New Triply Hydrogen-Bonded Complexes With Highly Variable Stabilities *J. Am. Chem. Soc.* **1992**, *114*, 4010-4011.

20. Jorgensen, W. L.; Pranata, J., Importance Of Secondary Interactions In Triply Hydrogen-Bonded Complexes - Guanine-Cytosine Vs Uracil-2,6-Diaminopyridine *J. Am. Chem. Soc.* **1990**, *112*, 2008-2010.

21. Kyogoku, Y.; Lord, R. C.; Rich, A., Effect Of Substituents On Hydrogen Bonding Of Adenine And Uracil Derivatives *Proc. Natl. Acad. Sci. U. S. A.* **1967**, *57*, 250-&.

22. Beijer, F. H.; Sijbesma, R. P.; Vekemans, J. A. J. M.; Meijer, E. W.; Kooijman, H.; Spek, A. L., Hydrogen-Bonded Complexes Of Diaminopyridines And Diaminotriazines: Opposite Effect Of Acylation On Complex Stabilities. [Erratum To Document Cited In CA125:194913] *J. Org. Chem.* **1996**, *61*, 9636.

23. Markees, D. G.; Dewey, V. C.; Kidder, G. W., Synthesis And Biological Activity Of Substituted 2,6-Diaminopyridines *J. Med. Chem.* **1968**, *11*, 126-&.

24. Berl, V.; Schmutz, M.; Krische, M. J.; Khoury, R. G.; Lehn, J.-M., Supramolecular Polymers Generated From Heterocomplementary Monomers Linked Through Multiple Hydrogen-Bonding Arrays - Formation, Characterization, And Properties *Chem. Eur. J.* **2002**, *8*, 1227-1244.

25. Binder, W. H.; Kunz, M. J.; Kluger, C.; Hayn, G.; Saf, R., Synthesis And Analysis Of Telechelic Polyisobutylenes For Hydrogen-Bonded Supramolecular Pseudo-Block Copolymers *Macromolecules* **2004**, *37*, 1749-1759.

26. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Cross-Linked And Functionalized 'Universal Polymer Backbones' Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

27. Chang, S. K.; Hamilton, A. D., Molecular Recognition Of Biologically Interesting Substrates - Synthesis Of An Artificial Receptor For Barbiturates Employing 6 Hydrogen-Bonds *J. Am. Chem. Soc.* **1988**, *110*, 1318-1319.

28. Chang, S. K.; Vanengen, D.; Fan, E.; Hamilton, A. D., Hydrogen-Bonding And Molecular Recognition - Synthetic, Complexation, And Structural Studies On Barbiturate Binding To An Artificial Receptor *J. Am. Chem. Soc.* **1991**, *113*, 7640-7645.

29. Berl, V.; Krische, M. J.; Huc, I.; Lehn, J.-M.; Schmutz, M., Template-Induced And Molecular Recognition Directed Hierarchical Generation Of Supramolecular Assemblies From Molecular Strands *Chem. Eur. J.* **2000**, *6*, 1938-1946.

30. Loeb, S. J.; Shimizu, G. K. H., Dimetallated Thioether Complexes As Building-Blocks For Organometallic Coordination Polymers And Aggregates *J. Chem. Soc. Chem. Commun.* **1993**, 1395-1397.

31. Binder, W. H.; Kluger, C., Combining Ring-Opening Metathesis Polymerization (ROMP) With Sharpless-Type "Click" Reactions: An Easy Method For The Preparation Of Side Chain Functionalized Poly(Oxynorbornenes) *Macromolecules* **2004**, *37*, 9321-9330.

32. Kool, E. T., Preorganization Of DNA: Design Principles For Improving Nucleic Acid Recognition By Synthetic Oligonucleotides *Chem. Rev.* **1997**, *97*, 1473-1487.

33. Gartner, Z. J.; Kanan, M. W.; Liu, D. R., Multistep Small-Molecule Synthesis Programmed By DNA Templates *J. Am. Chem. Soc.* **2002**, *124*, 10304-10306.

34. Calderone, C. T.; Puckett, J. W.; Gartner, Z. J.; Liu, D. R., Directing Otherwise Incompatible Reactions In A Single Solution By Using DNA-Templated Organic Synthesis *Angew. Chem. Int. Ed.* **2002**, *41*, 4104-4108.

35. Kanan, M. W.; Rozenman, M. M.; Sakurai, K.; Snyder, T. M.; Liu, D. R., Reaction Discovery Enabled By DNA-Templated Synthesis And In Vitro Selection *Nature* **2004**, *431*, 545-549.

36. Tecilla, P.; Jubian, V.; Hamilton, A. D., Synthetic Hydrogen-Bonding Receptors As Models Of Transacylase Enzymes *Tetrahedron* **1995**, *51*, 435-448.

37. Valenta, J. N.; Dixon, R. P.; Hamilton, A. D.; Weber, S. G., Enhanced Extraction Of Phenobarbital From Serum With A Designed Artificial Receptor *Anal. Chem.* **1994**, *66*, 2397-2403.

38. Tecilla, P.; Chang, S. K.; Hamilton, A. D., Transition-State Stabilization And Molecular Recognition - Acceleration Of Phosphoryl-Transfer Reactions By An Artificial Receptor *J. Am. Chem. Soc.* **1990**, *112*, 9586-9590.

39. Grubbs, R. H., *Handbook Of Metathesis*. Wiley-VCH: Wilheim, 2003.

40. Pollino, J. M.; Weck, M., Supramolecular Side-Chain Functionalized Polymers: Synthesis And Self-Assembly Behavior Of Polynorbornenes Bearing Pdii SCS Pincer Complexes *Synthesis* **2002**, *9*, 1277-1288.

41. Manning, D. D.; Strong, L. E.; Hu, X.; Beck, P. J.; Kiessling, L. L., Neoglycopolymer Inhibitors Of The Selectins *Tetrahedron* **1997**, *53*, 11937-11952.

42. Ver Nooy, C. D.; Rondestvedt, C. S., Formation Of Nortricyclene Derivatives By Bromination Of Exo-2,5-Methylene-1,2,5,6-Tetrahydrobenzoic Acids *J. Am. Chem. Soc.* **1955**, *77*, 3583 - 3586.

43. Roberts, J. D.; Trumbull, E. R.; Bennett, W.; Armstrong, R., The Reaction Of Norbornylene With N-Bromosuccinimide. Nortricyclene And Its Derivatives *J. Am. Chem. Soc.* **1950**, *72*, 3116-3124.

44. Solov'ev, V., In 6.1, C., Ed. 1996-1998.

CHAPTER 3

INFLUENCE OF SOLVENTS ON THE ORTHOGONALITY OF NONCOVALENTLY FUNCTIONALIZED TERPOLYMERS

3.1 Abstract

In this chapter the poly(norbornene) copolymers of chapter 2 are extended to terpolymers containing palladated sulfur-carbon-sulfur (SCS) pincer complexes, cyanuric acid, and thymine moieties in their side-chains. Functionalization of the terpolymers was achieved by self-assembling (i) the Hamilton wedge to the cyanuric acid receptor, (ii) diaminopyridine to the thymine receptor, and (iii) pyridine to the palladated pincer complexes. While all three noncovalent interactions are fully orthogonal to each other in dichloromethane, the employment of a dioxane/chloroform solvent mixture results in the quantitative disassembly of one of the hydrogen bonding recognition units (the Hamilton wedge:cyanuric acid pair) during the metal-coordination event. This disassembly is completely independent from the diaminopyridine:thymine hydrogen-bonding pair and allows for the selective removal of one of the side-chain functionalities. This removal occurs with a switch-type mechanism: as one functionality is put on (the pyridine), another one (the Hamilton-wedge receptor) is taken off quantitatively.

3.2 Introduction

Nature has provided us with some of the most elegant examples of smart materials. Smart materials can be defined as materials that have properties which can be tuned in a controlled fashion by external stimuli, such as stress, temperature, moisture, pH, electric and magnetic fields or by molecular switching.[1-5] One of Nature's most important examples of a biological smart material is skeletal muscle fibers. When

acetylcholine binds to the receptors on the muscle fibers, the ligand gated sodium ion channels in the cell membrane are opened. Sodium ions then enter the cell resulting in muscle contraction.

In order to mimic the elegance seen in Nature's responsive materials, it is nessecary to be able to both assemble and disassemble bound entities. One class of smart materials, supramolecular smart materials rely on the controlled and quantitative tuning of *assembly* and *disassembly* steps on the molecular level.[6] Stimulus induced disassembly has been employed throughout the literature for polymer supported synthesis, assisted drug delivery/release, to remove cleavable units in host-guest pairs and in tunable materials chemistry.[2-5, 7] In supramolecular chemistry, disassembly has been used as the key step in the modulation of noncovalent interactions, such as hydrogen bonding and the formation of pseudorotaxanes for a variety of applications including molecular latches, *i.e.* molecules that can hold macromolecular building blocks together but at the same time can be selectively unfastened on demand.[6, 8-11] Tunable control over supramolecular gels, *i.e.* the control of the viscosity of gels by tuning the assembly of cross-linking interactions, is yet another important use of self-assembly/disassembly interactions in material science.[12-14] While these later examples demonstrate the importance of reversible assemblies in tunable supramolecular materials, they all rely on the use of a single noncovalent interaction. This chapter expands the toolbox of tunable assemblies of noncovalent functionalization strategies to terpolymers containing three highly directive noncovalent interactions. Furthermore, this chapter presents metal salts as a new type of stimuli for the reversible tuning of hydrogen bonding. The recognition motifs presented can be tuned in two-steps by either controlling the polarity of the solvent

thus modulating the directed self-assembly or a switch-type mechanism that can completely remove one self-assembly motif while simultaneously incorporating a second one.

The research presented in this chapter is based on terpolymers containing three distinct molecular recognition receptors. The Weck group recently communicated the noncovalent functionalization of terpolymers to form supramolecular functionalized materials.[15] In particular, we reported the orthogonal functionalization of terpolymers using a combination of hydrogen-bonding, metal-coordination, and pseudorotaxane formation.[14] This chapter extends these studies to two distinct hydrogen-bonding pairs and metal coordination. It demonstrates that the noncovalent functionalization strategies are fully orthogonal to each other in halogenated solvents (Figure 3.1A) while one can selectively and quantitatively remove, or disassemble, one hydrogen-bonding interaction during the metal-coordination step in a chloroform:dioxane mixture (Figure 3.1B). This removal occurs selectively and fully independent from the third recognition pair.

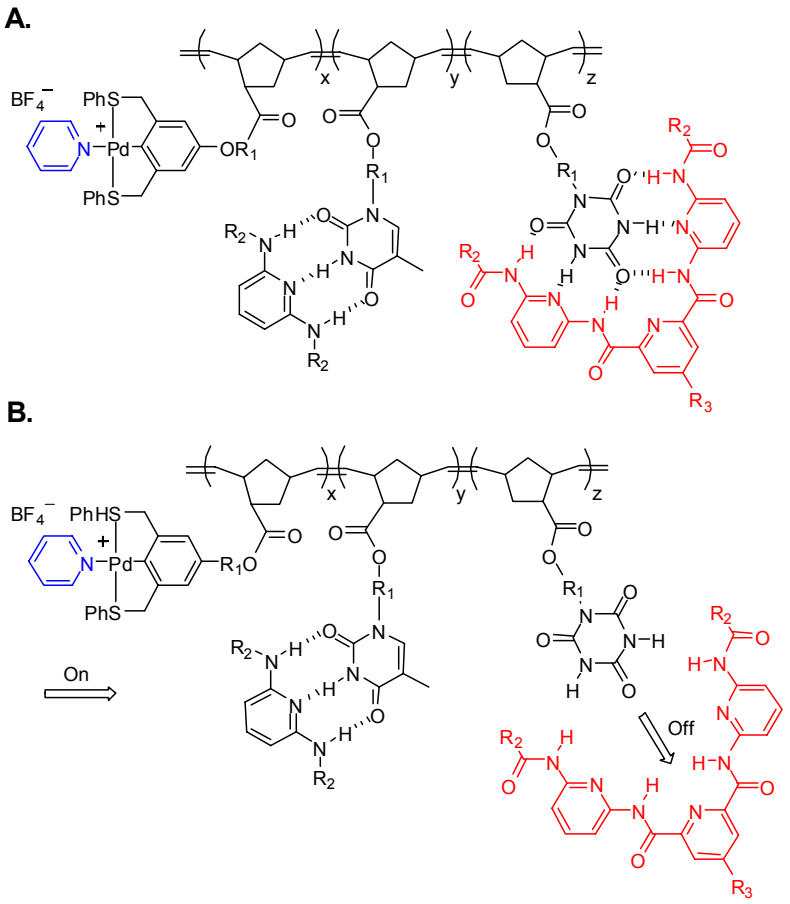


Figure 3.1. Schematic representation of a solvent dependant noncovalently functionalized triblock copolymer. (A) Fully functionalized terpolymer in dichloromethane. (B) Selective self-assembly/disassembly in a 85:15 mixture of chloroform:dioxane. Upon metal-coordination of the pincer ligand to the pyridine (on), the cyanuric acid:wedge hydrogen-bonding interaction is broken (off). This is independent of the third interaction: the hydrogen-bonding between diamidopyridine and thymine. (R_1= -$(CH_2)_{11}$-, R_2= -$COCH_2CH_2CH_3$, R_3= -$O(CH_2)_7CH_3$)

3.3 Research Design

The terpolymer presented here is based on norbornenes that can be polymerized using ruthenium initiated ring-opening metathesis polymerization (ROMP). Each monomer contains a terminal recognition site along the side-chains: monomer **1** is a metal complex that can be functionalized via coordination chemistry, monomer **2** is a

hydrogen-bonding moiety that is capable of undergoing three hydrogen bonds, and monomer **3** is a hydrogen bonding moiety which can undergo six hydrogen bonds. Monomers **1**-**3** as well as homopolymers based on **1**, **2**, or **3** have been shown previously (as discussed in both chapters 1 and 2) to undergo self-assembly with their complementary recognition units (**4**-**6**) (Figure 3.2).[16, 17] Terpolymers based on **1**-**3** are designed to allow for side-chain functionalization by (i) self-assembling the Hamilton wedge **6**[18] onto the cyanuric acid receptors of **3**, (ii) self-assembling diaminopyridine **5** onto the thymine receptors along **2**, and (iii) coordinating pyridines **4** to the palladated pincer complexes along **1**.

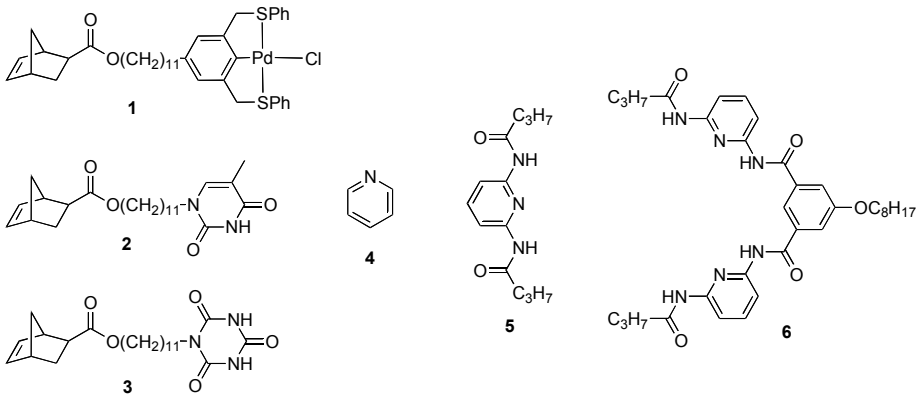


Figure 3.2. Monomers and complementary functional units employed in this study.

The metal coordinating unit employed is based on a sulfur-carbon-sulfur (SCS) palladated pincer complex.[17, 19-21] The Weck group and others have demonstrated that such complexes can be coordinated quantitatively to pyridines, nitriles and phosphines.[12, 15, 17, 19-25] The hydrogen bonding motifs are: the six hydrogen-bonding motif is based on cyanuric acid, which is able to assemble to its complementary receptor, the Hamilton wedge, via a strong six point ADA-DAD hydrogen bond association.[12, 16, 18, 26-31] and the

three hydrogen-bonding receptor moiety is based on functionalized thymines and were studied in detail in chapter 2.

Chapter 2 reported the synthesis, polymerization and detailed self-assembly behavior of random and block copolymers consisting of two of these monomers.[16] Furthermore, chapter 2 demonstrated that both hydrogen-bonding receptors along a polymer backbone (**2** and **3**) are orthogonal to each other when their target receptors (**5** and **6**) are present by demonstrating the concept of self-sorting (*i.e.* the recognition of two competitive recognition pairs along a polymer backbone with high fidelity).[16] Similarly, Joel Pollino in the Weck group has proven the orthogonal self-assembly behavior of copolymers consisting of monomers **1** and **2** using metal-coordination and hydrogen-bonding as noncovalent functionalizations.[17] In summary, the previous studies suggest that all three noncovalent interactions are highly orthogonal to each other and that no competitive interactions exist between hydrogen-bonding and metal-coordination.

3.4 Monomer Self-Assembly Studies and Solvent Dependence

The complete orthogonality of all three recognition pairs has not been shown before. In order to gain a detailed understanding of all the components of a synthetic toolbox, the orthogonality of the Pd-SCS complex based metal-coordination and the hydrogen-bonding between cyanuric acid and the Hamilton wedge needs to be demonstrated. Therefore, I initially investigated the self-assembly behavior of mixtures of monomers **1** and **3** with recognition motifs **4** and **6** in dichloromethane and in a chloroform:dioxane (85:15) mixtures. The self-assembly behavior of the monomers with their respective complementary recognition units can be determined by monitoring characteristic changes in chemical shifts using ^{1}H NMR spectroscopy. Figure 3.3A-C

displays a ^{1}H NMR spectroscopy experiment using dichloromethane as solvent demonstrating the selectivity of monomers **1** and **3** for their complementary units **4** and **6** respectively in this solvent.

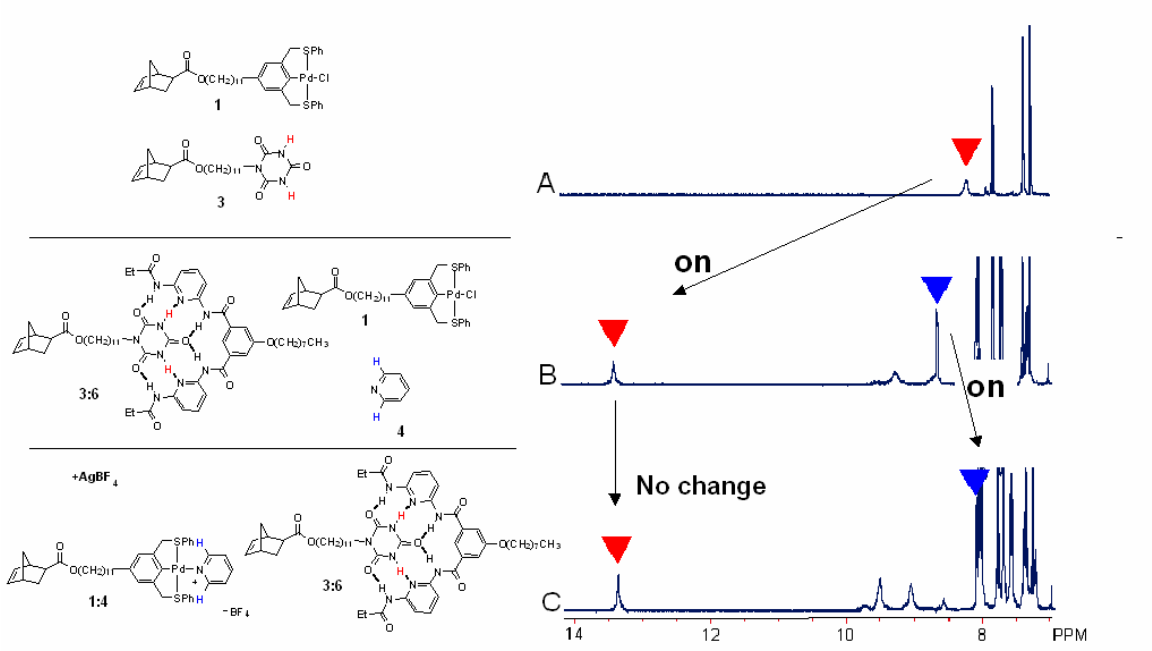


Figure 3.3. ^{1}HNMR spectra of the functionalization of the pincer and cyanuric acid monomers in dichloromethane. Signals corresponding to (▲) the cyanuric acid imide protons of **3** and (▲) the α-pyridyl protons of **4**. (A) Monomers **1** and **3** without the addition of any recognition units, (B) addition of 1 equivalent of both, the Hamilton wedge receptor **6** and **4**, and (C) addition of $AgBF_4$ to the mixture of (B).

Figure 3.3A shows the ^{1}H NMR spectrum of an equimolar solution of monomers **1** and **3** before the addition of any complementary recognition units. One equivalent of pyridine was then added (not shown). No changes in the ^{1}H NMR spectrum were observed upon the addition of pyridine. Figure 3.3B shows the subsequent addition of five equivalents of the Hamilton Wedge **6** to the mixture of **1**, **3**, and **4**. The addition of **6** resulted in the characteristic downfield shift of the imide protons of cyanuric acid from 8.2 to 13.4 ppm indicating strong hydrogen bonding between **3** and **6**. Silver tetrafluoroborate was then added to the reaction mixture to remove the chlorine ligand

from the palladium center of **1** thereby activating the metal complex for coordination. After the addition, the characteristic upfield shift of the α-pyridyl protons of **4** from 8.58 to 8.00 ppm was observed (Figure 3.3C) demonstrating coordination of **4** to the palladium center of **1**. During the coordination step, the signal corresponding to the hydrogen-bonded imide protons of the cyanuric acid moiety at 13.4 ppm remain unaffected. Integrations indicate that the remaining signal at 8.5 ppm is attributed to the imide protons of the assembled Hamilton wedge and not to uncoordinated pyridine. These results confirm the selectivity of each recognition receptor on monomers **1** and **3** for its respective recognition motif. Furthermore, titration experiments monitoring the downfield shift of the imide proton of the cyanuric acid moiety of **3** as a function of the addition of **6** allowed us to calculate an association constant (K_a) of 1 x 10^4 M^{-1} between **3** and **6** which is consistent with the literature.[18, 26, 28, 29, 31]

After demonstrating the orthogonality of all monomers in dichloromethane, we started to investigate the orthogonality of the monomers in a chloroform:dioxane solvent mixture (85:15) since the terpolymers presented in this contribution were not soluble in pure halogenated solvents. We have never investigated before the combination of hydrogen bonding and metal coordination in such a solvent mixture. In analogy to above, we studied the self-assembly behavior of **1** and **3** before and after the addition of their complementary receptors by ^{1}H NMR spectroscopy. Figure 3.4 shows this NMR spectroscopy experiment.

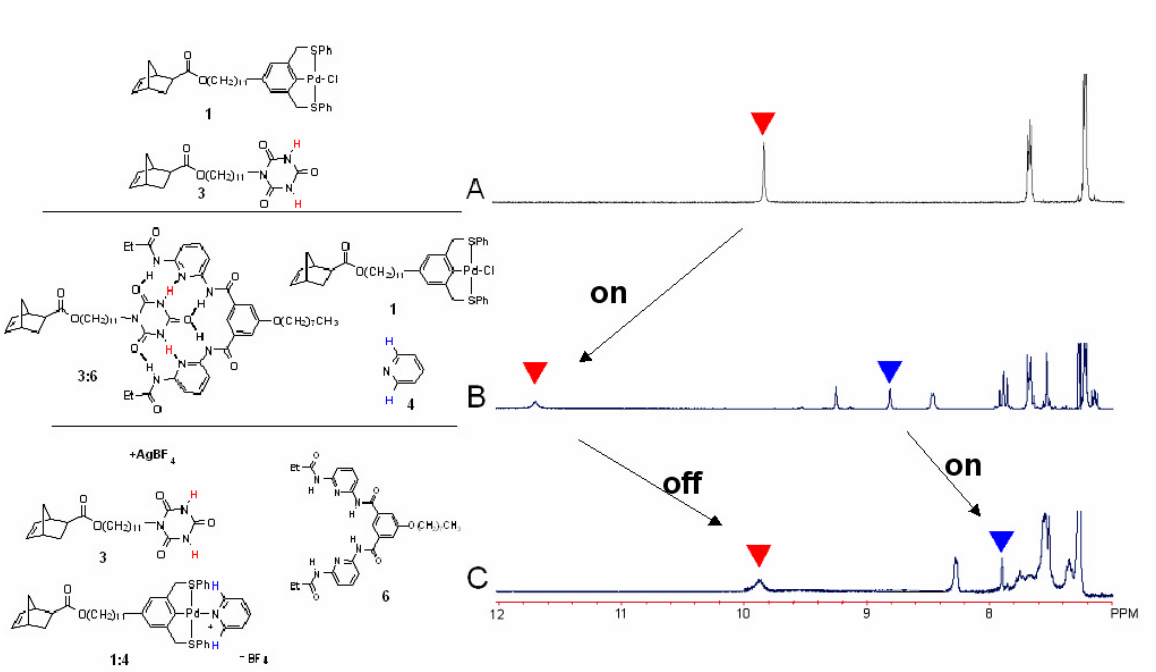


Figure 3.4. ^{1}H NMR spectra of the coordination of the pincer and cyanuric acid monomers in a 85:15 chloroform:dioxane solvent mixture. Signals corresponding to (▲) the cyanuric acid imide protons of **3** and (▲) the α-pyridyl protons of **4**. (A) Monomers **1** and **3** without the addition of any recognition units, (B) addition of 1 equivalent of both, the Hamilton wedge receptor **6** and **4**, and (C) addition of $AgBF_4$ to the mixture of (B).

Figure 3.4A displays the ^{1}H NMR spectrum of an equimolar solution of monomers **1** and **3**. We then functionalized **3** with **6** in the presence of one equivalent of both **1** and **4** (Figure 3.4B). The typical downfield shift of the imide protons of **3** from 9.8 ppm to 11.8 ppm characteristic of the hydrogen-bonding between **3**:**6** was observed.[16] Due to the competitive nature of the co-solvent dioxane, the hydrogen bonding interaction is weaker in comparison to pure dichloromethane. Upon the addition of silver tetrafluoroborate to remove the chlorine ligand from the palladium center and to activate the palladium center, we observed two simultaneous shifts: i) the expected upfield shift the of the α-pyridyl protons of the pincer ligands from 8.60 to 8.00 ppm and ii) an upfield shift of the imide protons of the cyanuric acid moiety from 11.8 back to 9.8 ppm (Figure 3.4C), *i.e.* a quantitative disassembly of the hydrogen-bonding interaction between the

cyanuric acid and the wedge during the coordination event was observed. This was unexpected since there have been no negative or destructive interactions reported in the literature between the metal-coordination of pincer complexes and hydrogen-bonding interactions. It is important to note that no interruption of the hydrogen-bonding was observed when adding **4** to a mixture of **1**, **3**, and **6**. Only after the addition of $AgBF_4$ did I observe a disruption of the hydrogen bonding, indicating that the pincer complex activation step is crucial for the disassembly of the hydrogen-bonding interaction between **3** and **6**.

We also investigated the reverse reaction: first coordinating pyridine to the pincer complex followed by addition of **6**. While I was able to observe a shift of the imide protons of **3** after the addition of **6**, the binding constant was significantly reduced (200 M^{-1}). We hypothesize that, despite purification by centrifugation and filtration, some silver chloride salts are still present in the reaction mixture preventing strong hydrogen bonding between **3** and **6**.

Since the disassembly has only been observed in this mixed solvent system I carried out a series of controls to determine if this disassembly step is solvent, ion, or metal dependent. First, I investigated the role of the solvent that is used to solubilize $AgBF_4$. $AgBF_4$ is typically added as a solution in nitromethane, acetonitrile or water. The addition of 50 equivalents (to the pincer moiety) of either nitromethane or acetonitrile to an equimolar solution of **1**, **3**, **4** and **6** (in 85:15 chloroform:dioxane) resulted in only negligible shifts in the ^1H NMR spectrum of the cyanuric acid imide protons that were within the error range (<0.1 ppm) suggesting that the disassembly step is not nitromethane or acetonitrile dependent.

Also the anion does not play a crucial role in the disassembly mechanism. Addition of an excess of NH_4BF_4 (the same anion present as in $AgBF_4$) showed no significant shifts in the ^1H NMR spectrum of the hydrogen bonded complex between **3** and **6**. Quantitative shifting was only observed when $AgBF_4$ was used during the pyridine ligand exchange on the pincer. This is independent of the mode of adding the $AgBF_4$, *i.e.* dissolved in nitromethane, acetonitrile, or added as a solid.

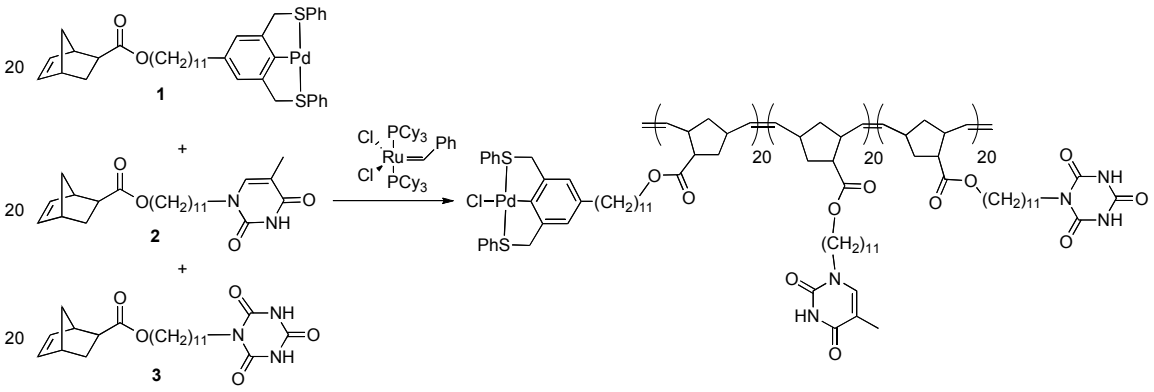
AgCl does not dissociate in a chloroform:dioxane solution, and did not dissolve, however, the addition of AgCl also showed no shifts of the ^1H NMR spectrum of the hydrogen bonded complex between **3** and **6.** We believe the key to the disassembly is in the formation of the **free silver ions** immediately resulting from the pyridine ligand exchange. A variety of silver salts have NO effect on the assembly of 3:6 when there is no pincer moiety and pyridine present. Silver salts do not normally dissociate in organic solvents, however during a pincer ligand exchange, silver ions briefly exist before forming the expected AgCl precipitate. We hypothesize that the nitrogens along **6** are able to coordinate to the free silver ions created in the solution during the ligand exchange. When activating palladium pincer complexes with $AgBF_4$, we always observed a precipitate (AgCl). However in the presence of **6**, no precipitate was visible, strengthening our hypothesis. We attribute the disassembly in this solvent system to the reduced binding affinity of **3**:**6** (K_a = 10^2 in the mixed solvent versus 10^5 in dichloromethane).

3.5 Polymer Synthesis, Characterizations and Self-Assemblies

Terpolymerizations were carried out using Grubbs' first-generation initiator in tetrahydrofuran at room temperature.[32] The terpolymers were synthesized as a block

copolymer using a 20:20:20:1 **1**:**2**:**3**:initiator ratio according to Scheme 3.1. We have proven before that monomers **1** and **2** polymerize in a living fashion using Grubbs' first generation initiator.[24, 16] Therefore we employed **1** and **2** for the first and second block respectively. The copolymerizations were complete within one hour and terminated through the addition of ethyl-vinyl-ether. Purifications were carried out by repeated precipitations into hexanes. The molecular weights of the resulting polymers were determined via gel-permeation chromatography (GPC) in THF using poly(styrene) standards. GPC traces of all terpolymers displayed monomodal distributions with low polydispersities (PDI's of 1.30, M_n= 2.9 x 10^4, M_w= 2.3 x 10^4).

Scheme 3.1. Terpolymer synthesis.



After the complete synthesis and characterization of all terpolymers, we investigated whether the hydrogen bonding pair **3** and **6** also disassembles in the terpolymers during the coordination event. Again, the self-assembly behavior of the terpolymers was characterized by monitoring the characteristic shift of the α-pyridyl protons of **4** and the imide protons of both **5** and **6** by ^{1}H NMR spectroscopy. First, we carried out titration studies to investigate any changes of the binding constants of the

hydrogen bonding moieties during any self-assembly steps beginning with the addition of both hydrogen-bonding receptors (first **5** then **6**) to the terpolymer followed by the metal-coordination step (Figure 3.5).

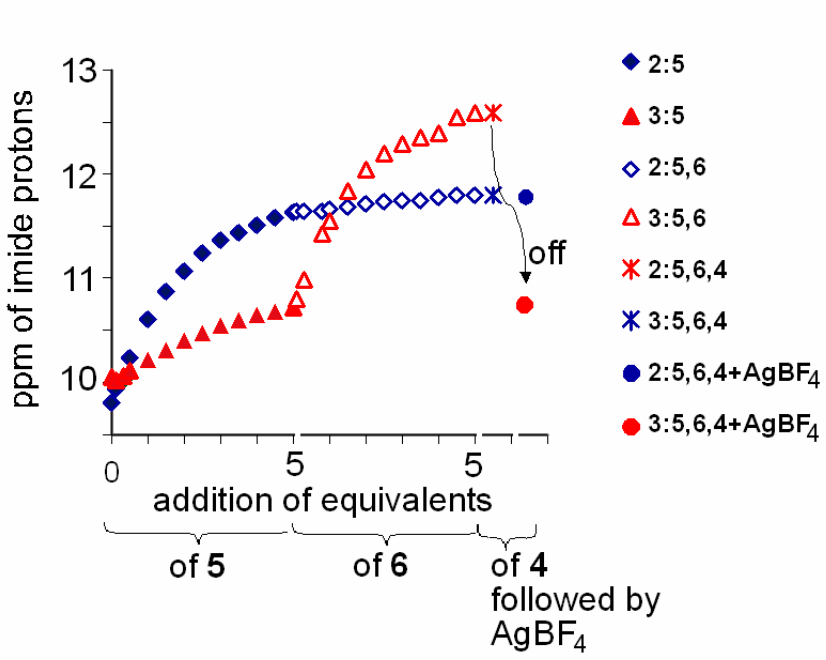


Figure 3.5. Chemical shifts of a stepwise titration experiment of a **1:2:3** triblock copolymer, in a 1:1:1 molar ratio. First addition of **5** followed by **6** and finally a mixture of **4** and $AgBF_4$. Shifts of the (♦) thymine imide protons when adding **5**, (◊) thymine imide protons when adding **6**, (▲) cyanuric acid imide protons when adding **5**, (Δ) cyanuric acid imide protons when adding **6**, (*) thymine imide proton shifts after the addition of **4**, **5**, and **6**, (*) cyanuric acid imide protons after the addition of **4**, **5**, and **6**, (●) thymine imide protons after the addition of all three recognition units and $AgBF_4$ and finally (●) cyanuric acid imide protons after the addition of all three recognition units and $AgBF_4$.

The titration of **5** and **6** onto the thymine and cyanuric acid recognition sites along the polymer backbone showed no changes in the presence of the third pincer block from previously reported self-assembly studies.[16] Our previous studies have shown that a competitive interaction exists between **3** and **5** when there is no Hamilton wedge (**6**) present, *i.e.* the dynamic equilibrium of the hydrogen-bonds is responsible for the competition when only a single side-chain's pairing nature is left unsatisfied.[16] This is

evident in the titration curve of the cyanuric acid **3** imide proton. The addition of five equivalents of **5** results in a downfield shift of the cyanuric acid imide protons from 9.8 to 10.6 ppm (a **3:5** interaction). The subsequent addition of the wedge receptor **6** causes a further downfield shift of the cyanuric acid imide protons to 11.6 ppm, which is due to the formation of the stronger **3:6** recognition pair. There are no observable changes in the ^{1}H NMR spectrum of the mixture of the terpolymer, **5** and **6** when adding **4**. However, upon the activation of the palladium center using $AgBF_4$, the cyanuric acid imide signals in the ^{1}H NMR spectrum shift back to 10.6 ppm, *i.e.* the hydrogen-bonding interaction of **3**:**6** disassembles. This shift is analogous to the one observed in the monomer studies. The imide proton signal of **3** in the ^{1}H NMR spectrum does not shift completely back to its pre-assembled position at 9.8 ppm. Instead, a signal at 10.6 ppm is observed. This position is attributed to the **3:5** interaction which is still present in the system (because the competition required for self-sorting is removed).[16] While this disassembly between **3** and **6** occurs, no changes in the hydrogen-bonding between **2**:**5** (and **3:5**) were observed, *i.e.* the hydrogen bonding between **2**:**5** is independent of the coordination event.

Figure 3.6 shows the NMR characterization of the one-pot functionalization/ defunctionalization of the triblock copolymer. Again, the characteristic shifts of the α-pyridyl protons of **4** and the imide protons of both **2** and **3** were monitored by ^{1}H NMR spectroscopy. The imide signals of both **2** and **3** show the characteristic shifts from 9.8 to 11.0 ppm for the **2**:**5** interaction and from 10.0 to 12.0 ppm for the **3**:**6** interaction. Upon the addition of $AgBF_4$, the imide signals associated with the **3**:**6** interaction shows the expected upfield shift from 12.0 ppm to 10.4 ppm which is analogous to the terpolymer

titration experiment and the monomer studies. As expected, no effect on the **2:5** interaction is observed, as the imide signal associated with the thymine imine protons remains at 11.0 ppm and does not move.

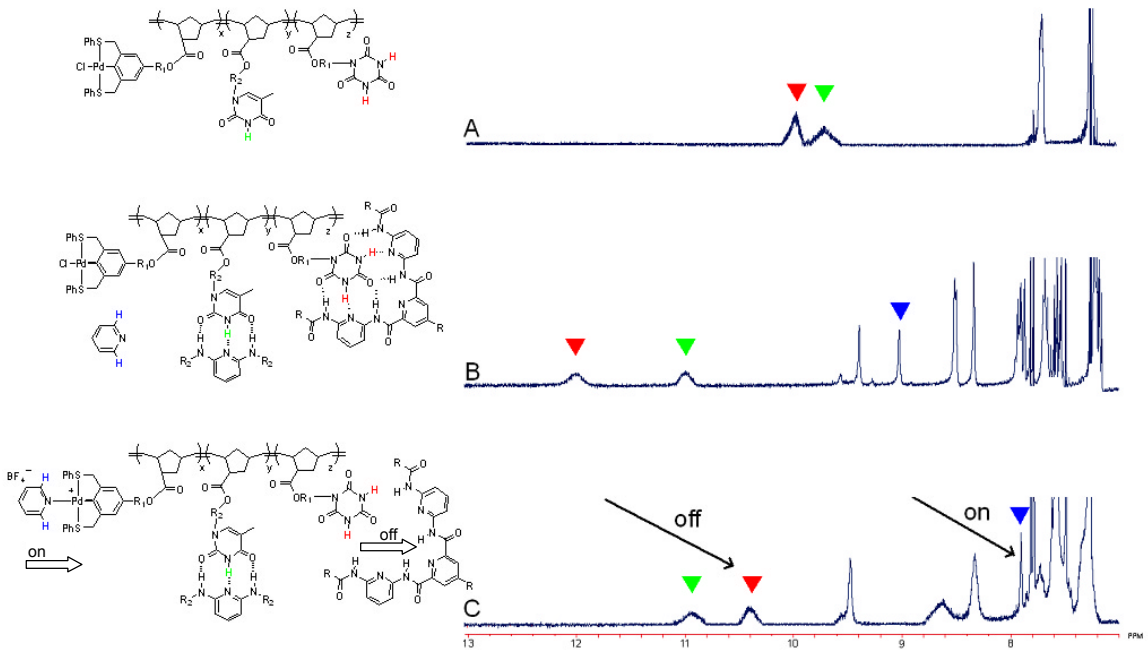


Figure 3.6. One-pot ^{1}H NMR spectra of the simultaneous assembly/disassembly of the functionalized block terpolymer following the shifts in the ^{1}H NMR spectrum of (▲) α-pyridyl protons, (▲) cyanuric acid imide protons, and (▲) thymine imide protons. (A) ABC triblock copolymer before the addition of any recognition units, (B) the triblock copolymer after the addition of one equivalent of **4**, **5**, and **6**, and finally (C) triblock copolymer after the addition of $AgBF_4$.

3.6 Conclusion

This chapter presented a switch-type mechanism for noncovalently functionalized copolymers. The recognition motifs presented in this chapter can be tuned in two-ways by either changing the polarity of the solvent thus tuning the association constants or by the addition of a silver salt (causing a switch type mechanism) that completely removes one self-assembly motif while simultaneously incorporating a second self-assembly motif. Based on the choice of solvent we can promote or prevent this switch type mechanism. Noncovalent functionalization revealed that one specific hydrogen-bonded

assembly could be controlled by solvent choice during the metal coordination of a Pd-Pincer unit. This tunable on-off mechanism occurs independently of other hydrogen-bonding moieties already assembled onto the terpolymers. This allows for the tuning of functional group assembly (or disassembly) in the presence of other recognition motifs on a single terpolymer. We envision these tunable bioinspired interactions could be used for smart materials with applications in drug delivery, the tuning of nanostructure formations, in and tunable optical materials.

3.7 Experimental

Reagents were purchased either from Acros Organics, Aldrich or Strem Chemicals and used without further purification. Monomers and recognition units, **1**-**6**, were synthesized according to published procedures.[16, 19, 24, 31] ^{1}H-NMR and ^{13}C-NMR spectra (300 MHz ^{1}H NMR, 75 MHz ^{13}C NMR) were taken using a Varian Mercury Vx 300 spectrometer. All spectra are referenced to residual proton solvent. Abbreviations used include broad singlet (br s) and broad unresolved multiplet (br m). Gel-permeation chromatography (GPC) analyses were carried out using a Shimadzu pump and a Shimadzu UV detector with tetrahydrofuran (THF) or dichloromethane as the eluant and a set of American Polymer Standards columns (100, 1,000, 100,000 Å linear mixed bed). The flow rate used for all the measurements was 1 mL/min. All GPC data are reported versus poly(styrene) standards. M_w, M_n and PDI represent weight average molecular weight, number average molecular weight and the polydispersity index respectively.

Block Copolymerizations.

To a 0.2 M stirred solution of **1** in THF, 0.006 mmol of the ruthenium initiator was added. The mixture was stirred at room temperature while the reaction progress was

monitored by ^{1}H NMR spectroscopy. After complete conversion, a 0.2 M solution of **2** in THF was added and the polymerization continued. Upon complete conversion of **2**, a 0.2 M solution of **3** in THF was added. After complete conversion of all the monomers, two drops of ethyl vinyl ether were added to terminate the reaction. The polymers were purified by repeated precipitations into hexanes. ^{1}H NMR (300 MHz, 15:85 dioxane-d_8:$CDCl_3$): δ = 10.0 (br s, 2H, NH), 9.8 (br s, 1H, NH), 6.90 (br s, 2H), 5.4-5.1 (m, 4H), 3.90 (br m, 4H), 3.60 (t, 4H, J = 6.4 Hz, CH_2N), 2.7-2.3 (br m, 10 H), 2.2-0.5 (br m, 46 H). ^{13}C NMR (75 MHz, 15:85 dioxane-d_8:$CDCl_3$): δ = 174.0, 156.7, 151.6, 150.3, 149.9, 148.8, 133.5, 132.7, 131.9, 131.0, 129.6, 108.9, 67.7, 64.0, 50.8, 49.8, 49.2, 47.5, 41.7, 38.3, 37.0, 35.9, 35.2, 34.6, 31.6, 29.2, 28.8, 28.6, 28.2, 27.7, 26.7, 25.8, 22.8, 22.3, 14.1.

Titration Studies.

Association constants were measured by NMR titration of a 0.2 M solution (15:85 dioxane: chloroform) of the receptor molecules with a 0.04 M solution (based on recognition units) of the corresponding polymer. All molarities are based on the number of recognition units. The chemical shifts of the imide protons on either the thymine or the cyanuric acid moieties were monitored by ^{1}H NMR spectroscopy. The NMR data was evaluated using the computer program ChemEquili.[33]

Metal Coordination.

Pyridine (0.10 mmol) was added to a solution of the target polymer (0.10 mmol) in either dichloromethane or an 85:15 $CHCl_3$:dioxane solution (10 mL) and stirred at room temperature for five minutes. An excess of $AgBF_4$ (0.194 mL of a 5.13 M stock solution, 1.00 mmol) was added to the 1:1 mixture of pyridine to palladated pincer

complex. The mixture was stirred for an additional ten minutes and then filtered to provide the self-assembled terpolymers in quantitative yields.

3.8 References

1. Ball, C. P.; Barrett, A. G. M.; Poitout, L. F.; Smith, M. L.; Thorn, Z. E., Polymer Backbone Disassembly: Polymerisable Templates And Vanishing Supports In High Loading Parallel Synthesis *Chem. Commun.* **1998**, *6*, 2453-2454.

2. Mcgrath, D. V., Dendrimer Disassembly As A New Paradigm For The Application Of Dendritic Structures *Mol. Pharm.* **2005**, *2*, 253-263.

3. Cooke, G.; Rotello, V. M., Methods Of Modulating Hydrogen Bonded Interactions In Synthetic Host-Guest Systems *Chem. Soc. Rev.* **2002**, 75-286.

4. Hofmeier, H.; Schubert, U. S., Combination Of Othogonal Supramolecular Interactions In Polymeric Architectures *Chem. Commun.* **2005**, 2423-2432.

5. Kataoka, K.; Harada, A.; Nagasaki, Y., Block Copolymer Micelles For Drug Delivery: Design, Characterization And Biological Significance *Adv. Drug Deliv. Rev.* **2001**, *47*, 113-131.

6. Wan, Y.; Mitkin, O.; Barnhurst, L.; Kurchan, A.; Kutateladze, A., Molecular Assembly And Disassembly: Novel Photolabile Molecular Hosts *Org. Lett.* **2000**, *2*, 3817-3819.

7. Ball, C. P.; Barrett, A. G. M.; Poitout, L. F.; Smith, M. L.; Thorn, Z. E., Polymer Backbone Disassembly: Polymerisable Templates And Vanishing Supports In High Loading Parallel Synthesis *Chem. Commun.* **1998**, *6*, 2453-2454.

8. Kim, K., Mechanically Interlocked Molecules Incorporating Cucurbituril And Their Supramolecular Assemblies *Chem. Soc. Rev.* **2002**, *31*, 96-107.

9. Balzani, V.; Credi, A.; Venturi, M., Controlled Disassembling Of Self-Assembling Systems:Toward Artificial Molecular-Level Devices And Machines *PNAS* **2002**, *99*, 4814-4817.

10. Brinke, G. T.; Ikkala, O., Smart Materials Based On Self-Assembled Hydrogen-Bonded Comb-Shaped Supramolecules *Chem. Rec.* **2004**, *4*, 219-230.

11. Cooke, G.; Garety, J. F.; Hewage, S. G.; Jordan, B. J.; Rabani, G.; Rotello, V. M.; Woisel, P., Tunable Side-Chain Supramolecular Polymer *Org. Lett.* **2007**, ASAP.

12. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Crosslinked And Functionalized Universal Polymer Backbones Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly. *Tetrahedron* **2004**, *60*, 7205-7215.

13. Nair, K. P.; Breedveld, V.; Weck, M., Tunable Thermo-Reversible Polymer Networks By Multifunctional Hydrogen Bonding Self-Assembly. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **2007**, *48*, 46-347.

14. Cao, R.; Gu, Z.; Hsu, L.; Patterson, G. D.; Armitage, B., Synthesis And Characterization Of Thermoreversible Biopolymer Microgels Based On Hydrogen Bonded Nucleobase Pairing *J. Am. Chem. Soc.* **2003**, *125*, 10250-10256.

15. South, C. R.; Leung, K. C.-F.; Lanari, D.; Stoddart, J. F.; Weck, M., Noncovalent Side-Chain Functionalization Of Terpolymers *Macromolecules* **2006**, *39*, 3738-3744.

16. Burd, C.; Weck, M., Self-Sorting In Polymers *Macromolecules* **2005**, *38*, 7225-7230.

17. Pollino, J. M.; Stubbs, L. P.; Weck, M., One-Step Multifunctionalization Of Random Copolymers Via Self-Assembly. *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

18. Chang, S. K.; Hamilton, A. D., *J. Am. Chem. Soc.* **1988**, *110*, 1318.

19. Pollino, J. M.; Stubbs, L. P.; Weck, M., Living ROMP Of Exo-Norbornene Esters Possessing Pdii SCS Pincer Complexes Or Diaminopyridines. *Macromolecules* **2003**, *36*, 2230-2234.

20. Albrecht, M.; Lutz, M.; Schreurs, A. M. M.; Lutz, E. T. H.; Spek, A. L.; Koten., G. V., Self-Assembled Organoplatinum(II) Supermolecules As Crystalline, SO2 Gas-Triggered Switches *J. Chem. Soc., Dalton* **2000**, *21*,3797-3804.

21. Albrecht, M.; Van Koten, G., Platinum Group Organometallics Based On Pincer Complexes: Sensors, Switches, And Catalysts *Angew. Chem., Int. Ed.* **2001**, *40*, 3750-3781.

22. South, C. R.; Higley, M. N.; Leung, K. C.-F.; Lanari, D.; Nelson, A.; Grubbs, R. H.; Stoddart, J. F.; Weck, M., Self-Assembly With Block Copolymers Through Metal Coordination Of SCS-Pdii Pincer Complexes And Pseudorotaxane Formation. *Chem. Eur. J.* **2006**, *12*, 3789-3797.

23. Pollino, J. M.; Weck, M., Non-Covalent Side-Chain Polymers: Design Principles, Functionalization Strategies, And Perspectives *Chem. Soc. Rev.* **2005**, *34*, 1078.

24. Pollino, J. M.; Weck, M., Supramolecular Side-Chain Functionalized Polymers: Synthesis And Self-Assembly Behavior Of Polynorbornenes Bearing Pdii SCS Pincer Complexes. *Synthesis* **2002**, *9*, 1277-1285.

25. Nair, K. P.; Pollino, J. M.; Weck, M., Noncovalently Functionalized Block Copolymers Possessing Both Hydrogen Bonding And Metal Coordination Centers *Macromolecules* **2006**, *39*, 931-940.

26. Chang, S. K.; Van Engen, D.; Fan, E.; Hamilton, A. D., Hydrogen-Bonding And Molecular Recognition - Synthetic, Complexation, And Structural Studies On Barbiturate Binding To An Artificial Receptor *J. Am. Chem. Soc.* **1991**, *113*, 7640-7645.

27. Chang, S. K.; Hamilton, A. D., Molecular Recognition Of Biologically Interesting Substrates - Synthesis Of An Artificial Receptor For Barbiturates Employing 6 Hydrogen-Bonds *J. Am. Chem. Soc.* **1988**, *110*, 1318-1319.

28. Binder, W. H.; Kunz, M. J.; Kluger, C.; Hayn, G.; Saf, R., Synthesis And Analysis Of Telechelic Polyisobutylenes For Hydrogen-Bonded Supramolecular Pseudo-Block Copolymers *Macromolecules* **2004**, *37*, 1749-1759.

29. Binder, W. H.; Kluger, C., Combining Ring-Opening Metathesis Polymerization (ROMP) With Sharpless-Type "Click" Reactions: An Easy Method For The Preparation Of Side Chain Functionalized Poly(Oxynorbornenes) *Macromolecules* **2004**, *37*, 9321-9330.

30. Berl, V.; Schmutz, M.; Krische, M. J.; Khoury, R. G.; Lehn, J.-M., Supramolecular Polymers Generated From Heterocomplementary Monomers Linked Through Multiple Hydrogen-Bonding Arrays - Formation, Characterization, And Properties *Chem.-Eur. J.* **2002**, *8*, 1227-1244.

31. Berl, V.; Krische, M. J.; Huc, I.; Lehn, J.-M.; Schmutz, M., Template-Induced And Molecular Recognition Directed Hierarchical Generation Of Supramolecular Assemblies From Molecular Strands *Chem. Eur. J.* **2000**, *6*, 1938-1947.

32. Grubbs, R. H., *Handbook Of Metathesis;* . Wiley-VCH:: Weinheim, , 2003.

33. Solov'ev, V., In 6.1, C., Ed. 1996-1998.

CHAPTER 4

ORTHOGONALLY SELF-ASSEMBLED MULTIFUNCTIONAL BLOCK COPOLYMERS

4.1 Abstract

Using ring-opening metathesis polymerization (ROMP) of side-chain functionalized norbornene and mono-functional chain-terminators (CT), homopolymers were synthesized which contain sites for main- and side-chain self-assembly, and when combined the homopolymers created an AB type block copolymer system. Several distinct pathways for self-assembly of the AB type block copolymer were studied to find if assembling the side-chain affects the backbone assembly and vice versa. The self-assembly motifs were found to be orthogonal to one another showing similar association constants regardless of assembly pathway.

4.2 Introduction

One of the key features of nature's biomaterials machinery is orthogonal multi-step self-assembly events.[1, 2] Such self-assembly events, which occur on multiple length scales using a variety of noncovalent interactions and bond strengths, are integral components to nature's design and synthesis of biomaterials and their function. Examples include the synthesis and function of proteins and enzymes as well as the replication of RNA and DNA. For example, the folding of peptide sequences into well-defined secondary structures is based on noncovalent molecular interactions between individual amino acids while the formation of proteins requires subsequent self-assembly events to yield the final highly complex machinery capable of performing the protein's

complex function. This is just one example where the utilization of a cascade of orthogonal multi-step self-assembly events is vital to the formation of the biological machinery. Such complex self-assembly events are unrivaled by synthetic chemists yet.

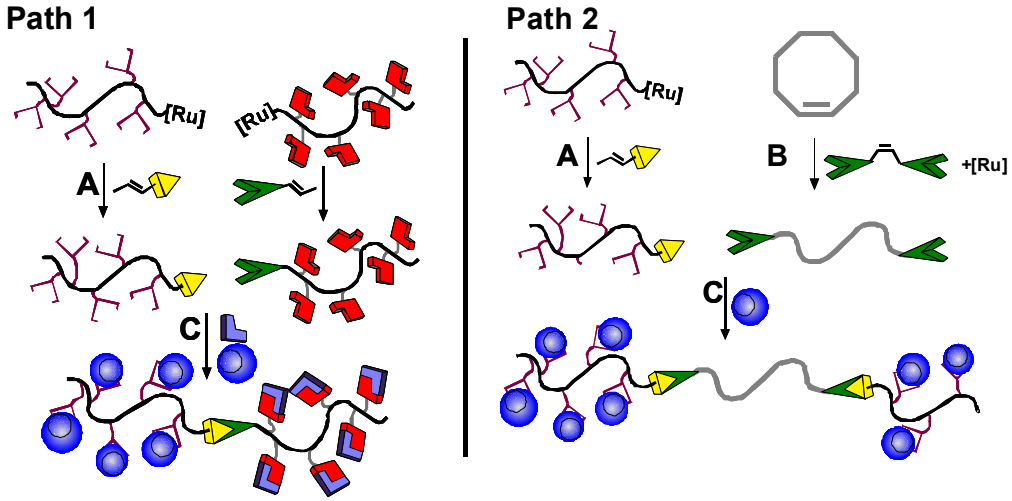
Over the past two decades, scientists have reported a variety of attempts that are starting to mimic nature's ingenious engineering.[3-11] One strategy that mimics nature's self-assembly complexity on a very basic level is the use of supramolecular polymers.[12-17] This research thrust has led to the development of polymers with both side-chain and main-chain self-assembly sites.[14, 16, 18-30] These materials can either be functionalized (via side-chain assembly) or fabricated into block copolymers (via main-chain assembly strategies).[14, 16, 18-30] However, neither of these two approaches allows for the utilization of sequential self-assembly events on multiple length scales. The combination of side- and main-chain self-assembly strategies to bring synthetic materials a step closer towards the realization of the multi-level self-assembly complexity seen in biological systems, has not been reported. In this manuscript, we describe the realization of this goal through the synthesis of highly functionalized and complex polymeric materials by utilizing for the first time *both* side- and main-chain self-assembly sites.

4.3 Research Design

Our research design is based on side-chain functionalized norbornenes that are polymerized via ring-opening metathesis polymerization (ROMP)[31] in the presence of either a functional chain-terminator (CT)[32, 33] to create single terminal end group-functionalized polymers or a difuctional chain-transfer agent (CTA)[34-36] for the creation of telechelic polymers, *i.e.* polymers that are end functionalized on both the terminal and proximal ends. Each monomer, CT and CTA contains one (or in the case of the CTA,

two) discrete and orthogonal terminal recognition units.[34-36] After ROMP, the resulting telechelic polymers can be self-assembled into block copolymers using hydrogen bonding. The copolymer formation using noncovalent chemistry can be either preceded or succeeded by additional self-assembly steps via hydrogen bonding or metal coordination to functionalize the polymers along the side-chains (Scheme 4.1).

Scheme 4.1. Cartoon depicting the cascade self-assembly strategy towards fully functionalized block copolymers.



Conditions. Path 1: Formation of AB block copolymer: A) addition of CT to form an end-functionalized polymer followed by main-chain assembly and C) subsequent side-chain functionalization of the polymer. Path 2: Formation of ABA functionalized block copolymer: A) addition of a CT to form end-functionalized polymer, B) polymerization in presence of a CTA to form a telechelic polymer and finally C) side-chain functionalization of the resulting block copolymer.

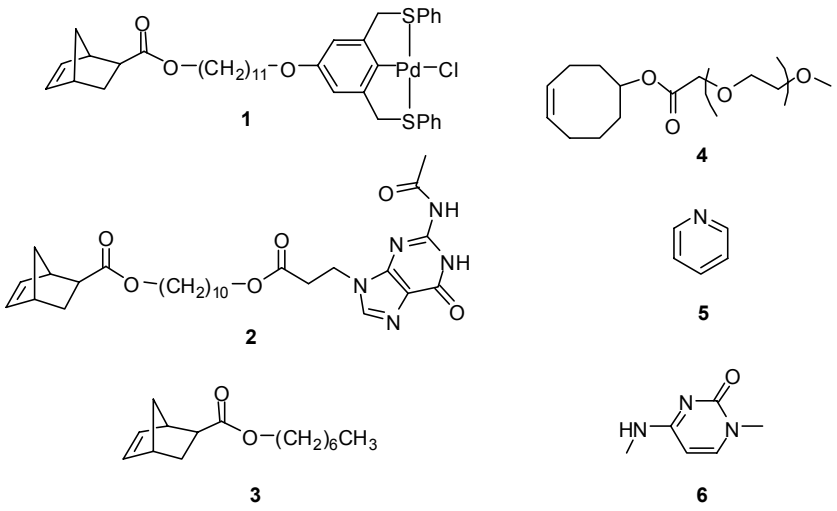
4.4 Polymer Synthesis and Characterization

In order to realize our cascade self-assembly strategy towards functionalized block copolymers, we employed monomers that contain three important features: 1) a polymerizable group, norbornene, which is known to undergo ROMP, often under living conditions,[31] 2) an alkyl spacer that allows the self-assembly motif to be isolated from

the polymer backbone after polymerization, and 3) the molecular recognition group that will undergo the selective self-assembly.

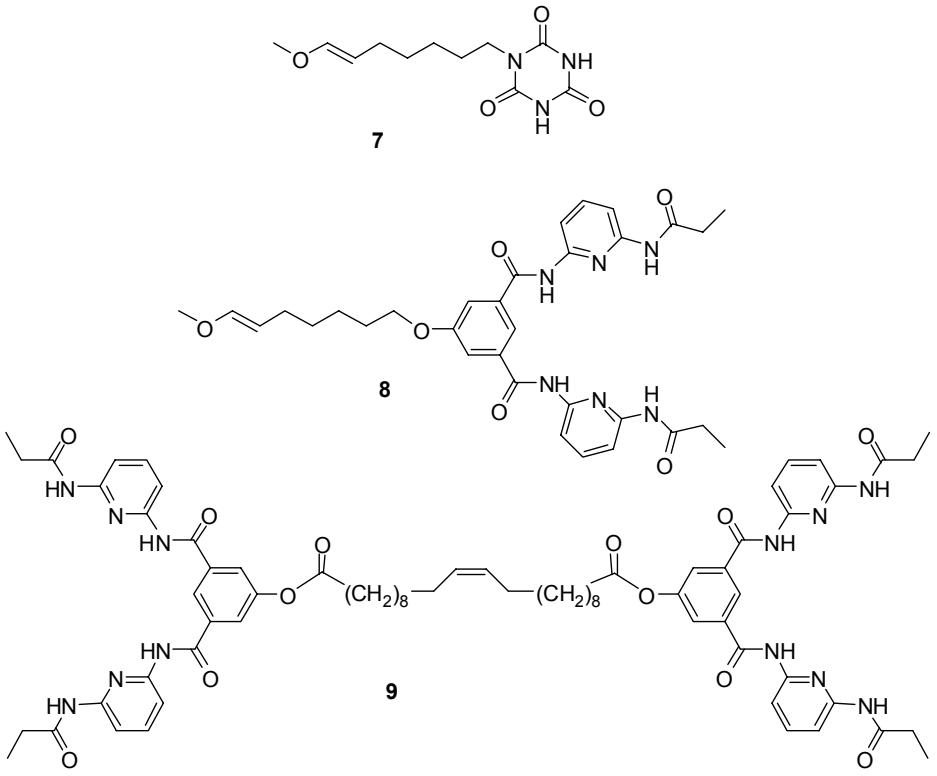
Figure 4.1 describes the norbornene monomers **1**-**3** that were utilized to fabricate the poly(norbornene) backbone as well as the complementary recognition motifs **5** and **6** for the metal-coordination and hydrogen bonding side-chains along **1** and **2**, respectively. The hydrogen bonding moiety on **2** is a guanine derivative, which has a donor-donor-acceptor (DDA) hydrogen bonding motif[37] that can hydrogen bond to cytosine derivatives such as **6**. The hydrogen bonding between guanine and cytosine (**2:6**) has an association constant of approximately 10^4 M^{-1} in $CDCl_3$ as reported in the literature.[38] The recognition unit on **1** is a palladated SCS pincer complex which has been shown to form assemblies with pyridine (**5**), phosphine and nitrile derivatives.[26, 27, 39-45] The metal-coordination between metallated pincer complexes and pyridine (**1:5**) has been shown to form strong and easily characterizable assemblies in a variety of solvents. [26, 27, 39-46] Monomer **4**, a PEG-functionalized cyclooctadiene, was chosen as the backbone of the middle block for the ABA polymers.

Figure 4.1. Norbornene based monomers **1** and **2** with functional groups for side-chain self-assembly, norbornene monomer **3** which will serve as diluting monomers, and the complementary recognition units **5** and **6**.



Complex copolymers can be created by employing chain-transfer agents (CTAs) and chain terminating units (CTs) in combination with ROMP and self-assembly. Chain-terminating agents (CTs) terminate a ROMP by transferring the desired functional group to the terminal ends of the polymer chain while rendering the ruthenium catalyst inactive towards ROMP.[47] All CTs used in this study are based on cyanuric acid (**7**) or bis-isophthalamide (also often called 'Hamilton wedge') (**8**) (Figure 4.2).[48-52] The chain-transfer agent (CTA) (**9**) is designed to terminate one polymer chain while starting a second chain[34-36] thereby introducing self-assembly motifs to the end-groups of the terminated and started polymer chains. CTA **9** is also based on the Hamilton wedge (Chart 4.2). The self-assembly between the Hamilton wedge and cyanuric acid is known to form strong hydrogen bonds with association constants in polymeric system around 10^4 M^{-1} in $CDCl_3$,[21, 36, 51-55] making this the recognition pair of choice for the hydrogen bonding-based main-chain supramolecular polymer self-assembly.

Figure 4.2. End-functionalized CTs **7** and **8** and difuntional CTA **9**.



Monomers **1**, **2** and **3**, CTs **7** and **8**, and CTA **9** were synthesized either as reported in the literature or in close analogy to literature procedures.[26, 33, 36, 37, 51, 56-60] With the functionalized monomers, CTs, and CTA in hand, the ring-opening metathesis polymerizations were carried out to synthesize the building blocks for our functionalized block copolymer study based on cascade self-assembly steps. All norbornene polymerizations were carried to completion in THF with monomer to initiator ratios of 20 to 1 and were terminated by the addition of the desired chain-terminator **7** or **8**, which removes the ruthenium catalyst from the polymer and replaces it with the functional portion of the chain-terminator. This results in the formation of end-group functionalized poly(norbornene)s that contain a single terminal recognition motif. The side products are

the ruthenium complex **13**. The synthesis of **poly-A** from monomer **1** and CT **7** is shown in Scheme 4.2 as an example for the formation of a mono-telechelic polymer. **Poly-A** contains the pincer moiety along the side-chains of the repeating units and a single cyanuric acid moiety at one terminus. The other mono-telechelic polymer, obtained from the polymerization of **2** with CT **8** (**poly-B**) had limited solubility in halogenated solvents. Therefore, we copolymerized **2** with a spacer monomer (**3**), in a 5:1 ratio, and terminated the polymerization with **8** resulting in a polymer that was readily soluble in chloroform and could be characterized by Isothermal Titration Calorimetry (ITC) and ^{1}H NMR spectroscopy. To synthesize the dual end-functionalized (or telechelic) polymer (**poly-B'**), we polymerized the cyclooctene monomer (**4**) in the presence of CTA **9** in close analogy to the literature.[36, 58-60] Polymers **poly-A**, **B**, **B'** were characterized by both NMR spectroscopy and GPC. The GPC characterization data of all polymers are shown in Table 4.1

Scheme 4.2. Synthesis of the end-functionalized homopolymer **poly-A**

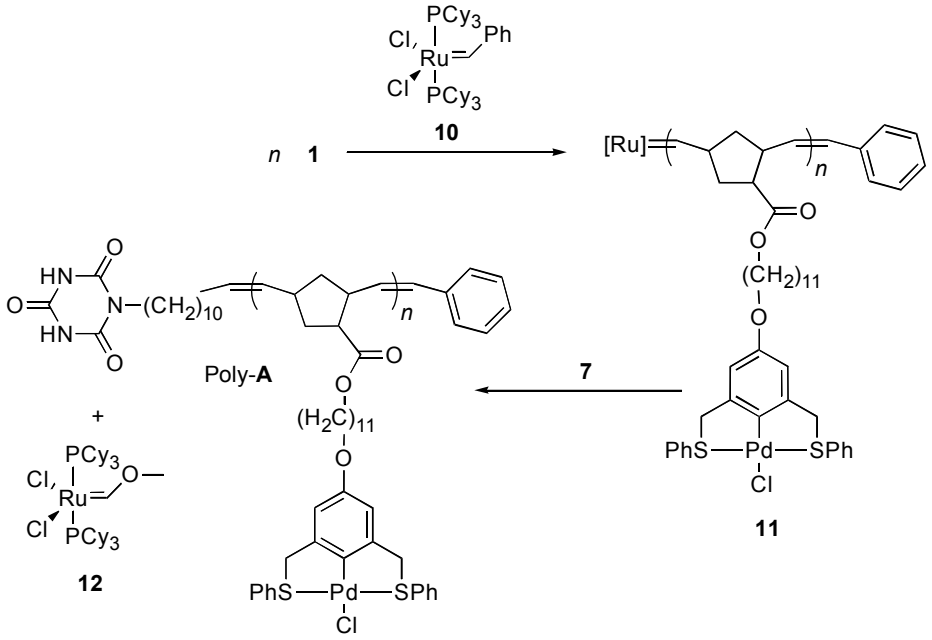


Table 4.1. Gel-permeation chromatography characterization of polymers **Poly-A**, **B**, and **B'**.

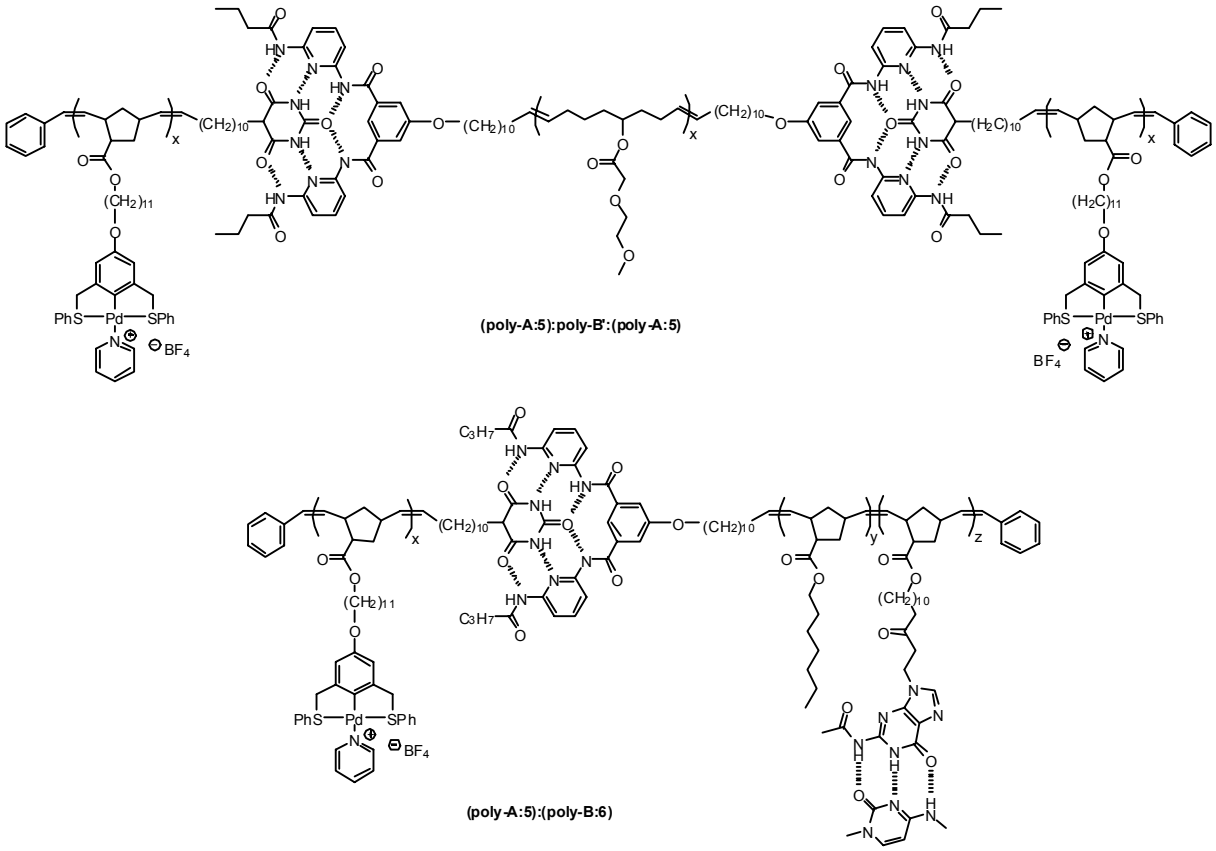
Monomer	CT/CTA	Polymer	M_n (10^{-3})[a]	M_w (10^{-3})[a]	PDI[a]
1	**7**	**Poly-A**	3.3	2.6	1.29
2 and **3**	**8**	**Poly-B**	1.25	1.05	1.19
4	**9**	**Poly-B'**	35.5	12.5	2.82

[a]Determined by gel-permeation chromatography in THF. Reported relative to monodispersed poly(styrene) standards.

4.5 Competitive Binding Studies

A detailed study of the competitive nature of the hydrogen-bonding systems is required to assess all self-assemblies. A series of ^{1}H-NMR spectroscopy experiments were conducted to ascertain the orthogonal nature of the self-assembly motifs along all polymers and to determine the dissociation constant, K_d, and/or association constant, K_a, of each hydrogen bonding recognition pair. These findings are summarized in Table 4.2. In each case, a 0.005 M solution in $CDCl_3$ of species A was titrated with 0.1 mL aliquots of a 0.010 M solution in $CDCl_3$ of species B. Characteristic signals in the ^{1}H-NMR spectrum of A were monitored for changes upon the addition of B and were analyzed using Chem-Equili to determine K_d or K_a values.[61] The K_a of CTs **7** and **8** with guanine **2** were found to be negligible (40 M^{-1}<) when compared to the association constants of the complementary pair (10^4 M^{-1}). In summary, the K_a for the non-complementary interactions, *i.e.* those interactions that are not between complementary pairs, were all found to be negligible. Based on the results of these competitive binding studies, we expect that the non-complimentary interactions of the hydrogen bonding self-assembly sites will not significantly effect overall block copolymer formation nor side-chain self-assembly.

Figure 4.3. Fully functionalized AB'A (top) and AB (bottom) block copolymers.



4.6. Triblock AB'A Copolymer Formation and Side-Chain Self-Assembly

After establishing that all hydrogen bonding motifs are orthogonal to each other and that all dimerization constants are negligible, we studied the formation of functionalized AB'A triblock copolymers via a combination of main-chain and side-chain self-assembly (Figure 4.3, top). For these studies, we used **Poly-A** for the two A blocks and **Poly-B'** for the middle block. The two self-assembly steps that are needed for the synthesis of the fully functionalized AB'A triblock copolymers are metal coordination along the pincer complexes of the side-chains of the two A blocks and hydrogen bonding between the Hamilton Wedge receptors along the terminal ends of block B' and the cyanuric acid ends of the A blocks. Combinations of ITC and ^{1}H NMR spectroscopy

titration techniques were used to study the self-assemblies. As reported before in the literature, we were not able to measure the K_a value for the metal coordination step, *i.e.* coordination of pyridine, **5**, to the palladium pincer complex, via ITC as its strength is above the upper sensitivity level of the instrument.[62] Therefore, ^{1}H NMR spectroscopy was used to determine the quantitative side-chain interactions via metal coordination. In contrast to the characterization of the side-chain recognition event, the analogous ^{1}H NMR experiments for the main-chain hydrogen bonding self-assembly step could not be carried out practically due to the lower concentration of the end-functionalized units along the polymers. Therefore, we relied on ITC to study the main-chain interactions. The concentrations of the polymers for all ITC experiments were determined by the concentration of the end unit (*i.e.* for **poly-B'** each functional terminus was treated independently).[63]

First, we investigated the main-chain self-assembly between **Poly-A** and **Poly-B'** using hydrogen bonding, followed by the side-chain self-assembly along the two **Poly-A** blocks using metal coordination. During a typical ITC experiment to characterize the hydrogen bonding between the two polymer blocks to synthesize the supramolecular block copolymer, a 5 mM solution of **poly-A** in $CHCl_3$ was titrated into a 0.5 mM $CHCl_3$ solution of **poly-B'**. The association constant (K_a) for the hydrogen bonding was determined to be $1.55 \times 10^4 \pm 15\%$ M^{-1} which is in close analogy to association constants measured before for this system.[38]

After the completion of the block copolymer formation, we coordinated **5** onto the side-chains of the **poly-A:poly-B'** block copolymer via the addition of $AgBF_4$ and pyridine. The $AgBF_4$ removes the labile chlorine from Pd-pincer moieties of **poly-A** and

allows **5** to immediately coordinate to the palladium. We followed this second self-assembly event via ^{1}H NMR spectroscopy. We observed the characteristic upfield shift of the α-pyridyl protons of the Pd-Pincer moieties along the **poly-A** side- chains from 8.58 ppm to 8.00 ppm[26, 27] demonstrating quantitative coordination of **5** to the palladium centers of the **poly-A** block.

We also investigated the reverse self-assembly strategy: the coordination of **5** onto **poly-A** followed by the main-chain formation via hydrogen bonding of the functionalized **poly-A** block to **poly-B'**, *i.e.* we first functionalized the polymer side-chain (characterized by ^{1}H NMR spectroscopy) followed by the formation of the triblock copolymer (characterized by ITC). The K_a of the main-chain self-assembly event was found to be 1.34 x 10^4 ± 10% M^{-1} which is equivalent within experimental error to the association constant for the main-chain formation using the first pathway (or strategy). This demonstrates that the functionalization of the side-chain before or after backbone self-assembly has no significant effect on the K_a of the backbone and therefore on the formation of the block copolymer. The functionalization of the side-chains was again monitored by shifts in the ^{1}H-NMR spectrum of the palladated pincer complexes along the side-chain of **poly-A** and of **5** after combining a one to one mixture of the two species and adding one equivalent of $AgBF_4$ to the mixture. The ^{1}H-NMR spectrum after the addition of $AgBF_4$ shows diagnostic upfield shifts of the protons on the pincer ligand from 7.8 ppm to 7.6 ppm and the α-pyridyl proton signals shift from 8.5 ppm to 8.0 ppm. These shifts are identical for the AB'A block system regardless whether the coordination step was carried out before or after the backbone formation. In both cases the assembly was quantitative and immediate.

Table 4.2. Association Constants for the AB'A Self-Assembly System in $CHCl_3$.

First Assembly	Second Assembly	K_a [M^{-1}]
7•9	N/A	3.66 x 10^4 ± 8%
Poly-A•9	N/A	1.43 x 10^4 ± 10%
Poly-B'•7	NA	1.93 x 10^4 ± 23%
Poly-A•5	**(Poly-A•5)•9**	1.28 x 10^4 ± 11%
Poly-A• Poly-B'	**(Poly-A• Poly-B')•5**	1.55 x 10^4 ± 15%
Poly-A•5	**(Poly-A•5)• Poly-B'**	1.34 x 10^4 ± 10%

4.7. Diblock AB Copolymer Formation and Side-Chain Self-Assembly

The formation and functionalization of the AB block copolymer system was studied in close analogy to the ABA system using a similar combination of ^{1}H-NMR spectroscopy and ITC techniques (Chart 4.3, bottom). We studied five distinct self-assembly combinations of **poly-A** and **poly-B**, and their complementary side-chain recognition units **5** and **6**. The five distinct self-assembly pathways studied are: (A) the hydrogen-bonding based self-assembly of the AB backbone formed by combining **poly-A** and **poly-B** followed by hydrogen bonding based side-chain functionalization with **6**, and finally the side-chain functionalization via the metal-coordination with **5**. (B) The second pathway studied the formation of backbone **poly-A•poly-B**, followed by the side-chain functionalization via metal-coordination with **5** and thirdly the side-chain functionalization with **6**. (C) The third pathway examined the side-chain hydrogen bonding functionalization first, followed by the block copolymer formation and then the metal-coordination functionalization of the side-chain of **poly-A**. (D) In the fourth pathway, the side-chains of the homopolymers **poly-A** and **poly-B** are assembled first

and then the block copolymer is formed via self-assembly. (E) For the final pathway the quantitative self-assembly of metal-coordinated homopolymer **poly-A•5** was titrated into polymer **poly-B** to form the target block copolymer followed by the side-chain functionalization of the resulting block copolymer with **6**.

The results for the K_a of hydrogen-bonding event of the main-chain for each of the five pathways are summarized in Table 4.4. The detailed ^{1}H-NMR studies yielded important insights into the system. Comparing the first two pathways we found the coordination of **poly-B** with **6** to be complete for both systems. This was determined by the observance of same shifts of the imide peaks of the guanine with the addition of cytosine as seen in Figure 4.1. These results demonstrate that the side-chain functionalization steps do not interfere with each other in the presence of the diblock copolymer. When analyzing the third, fourth and fifth pathways, we observed the imide peak shifting for the side-chain functionalizations with the addition of 0.5, 1, and 3 equivalents of cytosine (i.e. that the peaks shift from the initial 8.7 ppm to 9.5 ppm to 9.9 ppm to 10.4 ppm as shown in Figure 4.1. Regardless of the path chosen the shift from 8.7 ppm to 9.5 ppm to 10.4 ppm for the same stoichiometries was observed. All side chain-binding events were found to be complete via the above described ^{1}H NMR spectroscopy analysis. For all pathways, quantitative metal-coordination was also observed.

Table 4.3. Association Constants for the AB Self-Assembly System in $CHCl_3$.

First Assembly	Second Assembly	Third Assembly	K_a [M^{-1}] of backbone
Poly-A•Poly-B	**(Poly-A•Poly-B)•6**	**((Poly-A• Poly-B)•6)•5**	$1.22 \times 10^4 \pm 10\%$
Poly-A•Poly-B	**(Poly-A•Poly-B)•5**	**((Poly-A• Poly-B)•5)•6**	$1.25 \times 10^4 \pm 8\%$
Poly-A•5	**(Poly-A•5)• Poly-B**	**((Poly-A•5)• Poly-B)•6**	$1.32 \times 10^4 \pm 10\%$
Poly-A•5	**Poly-B•6**	**(Poly-A•5) • (Poly-B•6)**	$1.17 \times 10^4 \pm 10\%$
Poly-B•6	**(Poly-B•6)•Poly-A**	**((Poly-B•6)• Poly-A)•5**	$1.24 \times 10^4 \pm 10\%$

For each of the five pathways, the K_a of the main-chain assembly was monitored via ITC experiments. For the ITC experiments, a 5 mM solution of **poly-A** (functionalized or non-functionalized) in $CHCl_3$ was titrated into a 0.5 mM $CHCl_3$ solution of **poly-B** (functionalized or non-functionalized). Triplicate ITC curves were obtained and averaged for the association constants displayed in Table 4.4. As can be seen, the association constants for all five pathways are around 1.2×10^4 and are identical within the experimental error indicating that the block copolymer formation is independent of the side-chain functionalization steps as well as any recognition units along the polymer side-chains.

To determine the K_a of the hydrogen bonding of the side-chains of **poly-B** with **6**, the imide signals of the guanine side-chains were monitored for change during addition of **6** using ^{1}H NMR spectroscopy. For ease of characterization, the complete titration experiment was carried out with the homopolymer as well as with the self-assembled block copolymer. The two titration curves are shown in Figure 4.1. The association constant for both curves was calculated to be 1×10^4 M^{-1}. As can be seen visually, the two curves are virtually identical which is further substantiated by the calculated association constants. These results indicate that the side-chain functionalization via

hydrogen bonding of **poly-B** with **6** is independent of the presence of the **poly-A** block and that the self-assembly events along the side-chain occur with equivalent association constants. The side-chain functionalizations for the other pathways appear to be of equivalent strength, which was determined by correlating the shift of the imide signals of the guanine upon addition of 0.5, 1 and 3 equivalents of the cytosine derivative (**6**) to those in the complete titration curves shown in Figure 4.4.

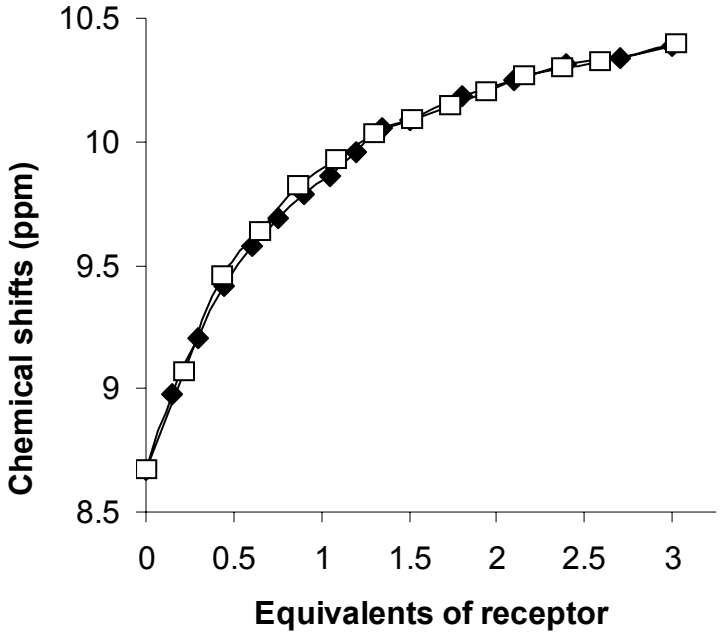


Figure 4.4. Chemical shifts of the imide protons of **poly-B** as a function of the equivalents of **6**. (◆) **poly-B** hydrogen bonded to **6,** (□) **((Poly-A• Poly-B)•5)** hydrogen bonded to **6**

The side-chain functionalization via the metal-coordination of polymer **poly-A** with **5** was characterized as described above for the ABA triblock copolymer.

Overall the study of the AB block copolymer system showed that the diblock copolymer formation is independent of any side-chain functionalization and can be

carried out before or after the functionalization step. The same holds true for the hydrogen bonding based and metal-coordination based side-chain functionalization steps.

4.8. Conclusion

In conclusion, homopolymers containing one or two functional end-group(s) were synthesized by ROMP through the addition of a functional CT or CTA. These homopolymers were combined in a variety of pathways to form AB and ABA type block copolymers containing functionalized side-chains. The orthogonal nature of all side- and main-chain self-assembly events was demonstrated by ^{1}H-NMR spectroscopy and isothermal titration calorimetry. These polymers which mimic natural systems with their multiple functionalities are the first block copolymer systems reported combining both side- and main-chain self-assembly. This system provides a method for the control over the architecture of the block copolymers that is similar to that found in living systems.

4.9 Experimental

General methods: All reagents were purchased either from Acros Organic, TCI or Aldrich. All chemicals were reagent grade and used without further purification. Et_3N, $CHCl_3$, and cyclooctene were distilled from CaH_2. CH_2Cl_2 was dried via passage through Cu_2O and alumina columns. NMR spectra were recorded on a Varian Mercury spectrometer (300 MHz). Chemical shifts are reported in parts per million (ppm), using residual solvent as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, b = broad), coupling constant and integration. Mass spectral analysis was provided by the Georgia Tech Mass Spectrometry Facility.

The synthesis of 10-hydroxydecyl bicyclo[2.2.1]hept-5-ene-2-carboxylate, (E)-12-bromo-1-methoxydodec-1-ene, (Z)-tetracos-12-enedioic acid, monomers **1**, **3**, **4** and recognition unit **6** have been published elsewhere.

9-(3-(2-acetamido-6-oxo-1H-purin-9(6H)-yl)propanoyloxy)nonyl bicyclo[2.2.1]hept-5-ene-2-carboxylate (2)

A solution of 10-hydroxydecyl bicyclo[2.2.1]hept-5-ene-2-carboxylate (0.446g, 1.51 mmol) and Et_3N (3.7 mL) were combined in $CHCl_3$ (100 mL) and cooled to 0°C. Acryol chloride (1.23 mL, 15.1 mmol) was added slowly, and the reaction was allowed to stir overnight. The solution was poured into MeOH (200 mL) and the solid was filtered. The organic layer was removed and the solid purified by column chromoatography (silica hexane/ethyl acetate 3 to 1) to provide 10-(acryloyloxy)decyl bicyclo[2.2.1]hept-5-ene-2-carboxylate as a white solid (20% yield). 10-(acryloyloxy)decyl bicyclo[2.2.1]hept-5-ene-2-carboxylate (0.100 g, 0.287 mmol) was dissolved in DMSO (25 mL). *N*-(6-Oxo-6,9-dihydro-1H-purin-2-yl)-acetamide (0.554g, 2.87mmol) was added followed by a catalytic amount of *t*-BuOK (0.3 mL, 1.0 M solution in THF). The solution was heated to 60 C and stirred for 24 hours. The DMSO was removed at 60 C and ethyl acetate was added (50 mL). The solid is filtered and the organic layer is removed. The resulting solid is purified by column chromatography (THF:hexane 4 to 1) to yield a white solid (0.108 g, 70% yield)**.** ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.37 (mb, 15H), 1.57 (m, 5H), 1.91 (m, 1H), 2.21 (m, 1 H), 2.36 (s, 3H), 2.83 (t, 2H), 2.92 (m, 1 H), 3.03 (m, 1 H), 3.63 (t, 2H), 4.07 (t, 2H), 4.31 (t, 2H), 6.12 (m, 2H), 7.74 (s, 1H), 8.67 (s, 1H), 11.97 (s, 1H)**.** ^{13}C NMR (300 MHz, $CDCl_3$) δ = 24.4, 25.9, 26.0, 28.6, 28.7, 28.8, 29.2, 29.5, 30.5, 34.3, 41.7, 43.2, 46.6, 46.7, 63.2, 64.9, 120.7, 136.3, 138.5, 140.5, 148.3, 149.3, 155.5, 171.1,

174.2, 175.8. MS (ESI): *m/z* (%) = 542.4 (542.3 M^+ calculated). Elemental Analysis calculated for $C_{27}H_{37}N_5O_6$: C 61.46, H 7.07, N 13.27, found: C 61.48, H 7.09, N 13.31

(E)-1-(7-methoxyhept-6-enyl)-1,3,5-triazinane-2,4,6-trione (7)

Cyanuric acid (0.92g, 7.1 mmol), bromoalkyl enol ether (0.31g, 1.88 mmol) and potassium carbonate (0.31g, 2.2 mmol) were mixed in anhydrous DMSO and stirred at 80 ˚C for 15h. Reaction mixture was then poured in water and product was extracted in diethyl ether. Organic layer was washed several times with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue obtained was washed with a mixture of hexanes:dichloromethane (80:20) to get a white solid that was isolated by centrifugation. Yield: 0.23g (48%). ^{1}H NMR (300 MHz, Acetone-d_6,) δ = 1.37-1.4 (m, 4H), 1.62-1.67 (m, 2H), 1.95-2.07 (m, 2H), 3.49 (s, 1.5H), 3.57 (s, 1.5H), 3.8 (t, 2H, *J* = 7Hz), 4.32 (dt, 0.4H, *J* = 8.4, 6.3Hz), 4.74 (dt, 0.6H, *J* = 12.9, 6.9 Hz), 5.95 (dt, 0.4H, *J* = 6.3, 1.5 Hz), 6.34 (d, 0.6H, *J* = 12Hz), 10.2 (br s, 2H) ppm; ^{13}C NMR (75 MHz, Acetone-d_6) δ = 24.76, 27.08, 27.35, 28.65, 28.76, 28.83, 42.15, 56.30, 59.98, 103.44, 106.96, 147.84, 148.62, 150.91 ppm**;** EI-MS *m/z* 255.1 (M^+, 8%), 71.1 (100%), HRMS Calcd.: 255.1219 for $C_{11}H_{17}N_3O_4$, Found: 255.1218 (20%)

(E)-5-(7-methoxyhept-6-enyloxy)-N1,N3-bis(6-propionamidopyridin-2-yl)isophthalamide (8)

A mixture of 5-hydroxy-N^1,N^3-bis(6-propionamidopyridin-2-yl)isophthalamide (0.24g, 0.48 mmol), bromopentyl enol ether (0.1g, 0.48 mmol) and potassium carbonate (0.2g, 1.44 mmol) in dimethyl formamide was stirred at 90 ˚C for 12h and then quenched by addition of water. Product was extracted in ethyl acetate and organic layer was washed with brine, dried over anhydrous Na_2SO_4 and solvent was evaporated in a rotavapor. The

crude product was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 65:35) to obtain a viscous solid that was further purified by precipitation from acetone into hexanes to get a white solid. Yield: 0.19g (63%).

^{1}H NMR (300 MHz, $CDCl_3$,) δ = 0.99 (t, 6H, *J* = 7.2 Hz), 1.39-1.45 (m, 4H), 1.81-1.71 (m, 6H), 1.90-2.10 (m, 2H), 2.36 (t, 4H, *J* = 7.5Hz), 3.51 (s, 2H), 3.58 (s, 1H), 4.06 (t, 2H, *J* = 6.3 Hz), 4.34 (dd, 0.4H, *J* = 7.2, 6.3 Hz), 4.73 (td, 0.6H, *J* = 12.9, 7.2 Hz), 5.89 (td, 0.4H, *J* = 4.8, 1.5 Hz), 6.3 (d, 0.6H, *J* = 12.6 Hz), 7.6 (s, 2H), 7.72 (br s, 2H), 7.76 (t, 2H, *J* = 8 Hz), 7.94-8.04 (m, 5H), 8.4 (br s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$,) δ = 13.71, 18.75, 23.67, 25.24, 28.83, 30.35, 39.52, 55.91, 68.68, 109.61, 110.07, 117.12, 135.83, 140.88, 146.27, 149.22, 149.72, 159.89, 164.44, 171.81 ppm; EI-MS *m/z* 630.0 (M^+, 28%), 109.1 (100%), HRMS Calcd.: 630.3165 for $C_{34}H_{42}N_6O_6$, Found: 630.3172 (14%).

(E)-5-(12-methoxydodec-11-enyloxy)-N1,N3-bis(6-propionamidopyridin-2-yl)isophthalamide (5)

(Z)-tetracos-12-enedioic acid (0.245 g, 0.665 mmol) and 5-hydroxy-N^1,N^3-bis(6-propionamidopyridin-2-yl)isophthalamide (0.836 g, 1.622 mmol) were combined in dry THF (60 mL). DCC (0.346 g, 1.662 mmol) and DMAP (0.020 g, 0.1662 mmol) were added to the solution. The mixture was refluxed over night. The THF was removed and the resulting solid was purified by column chromatography (ethyl acetate: CH_2Cl_2 3 to 1) to yield a white solid (0.775 g, 87% yield)**.** ^{1}H-NMR (300 MHz, $CDCl_3$) δ = 1.01 (t, 6H), 1.28 (mb, 24H), 1.68 (m, 4H), 1.79 (m, 4H), 2.39 (t, 4 H), 3.66 (t, 4H), 3.88 (t, 4H), 5.33 (dd, *J* = 4.9 Hz, 2H), 7.15 (s, 2H), 7.74 (t, 2H), 7.88 (s, 2H), 8.01 (t, 4H), 8.31 (sb, 4H), 8.83 (sb, 4H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 14.4, 19.3, 26.1, 27.5, 29.5, 29.6, 29.7,

29.9, 30.1, 32.9, 33.1, 38.8, 63.4, 71.5, 109.9, 111.4, 118.7, 130.1, 136.6, 140.6, 150.7, 151.2, 159.0, 165.5, 172.6. MS (ESI): *m/z* (%) = 1342.5 (1342.6 M^+ calculated). Elemental Analysis calculated for $C_{74}H_{92}N_{12}O_{12}$: C 66.25, H 6.91, N 12.53, found C 66.31, H 6.92, N 12.49

General polymerization method for norbornene based polymers: 0.006 mmol of monomer is dissolved in 2 mL CH_2Cl_2, 0.0006 mmol of Grubbs First Generation Catalyst in solution is added to the reaction and stirred for 2 hours under argon. 0.012 mmol of CT is added and stirred for another 2 hours. The polymer is precipitated into cold MeOH and collected via filtration.

General polymerization method for substituted cyclooctene based polymer: General polymerization procedure: CTA **9** (100 mg) was placed in a dried three-necked round-bottomed flask and $CHCl_3$ (5 mL) was added. The corresponding amount of monomer ([monomer]/[CTA]= 20) was added, followed by the addition of the grubs third generation catalyst([9]/[catalyst]=500) in $CHCl_3$. The solution was stirred for 72 h at room temperature, and then precipitated in cold MeOH (10 mL) to yield the desired polymer. Polymers were collected by filtration and dried.

Table 4.3. Association constants for competitive binding

Species A	Species B	K_d [M^{-1}]	Species A	Species B	K_a [M^{-1}]
2	**2**	<5 ± 1	**2**	**8**	40±10
Poly-B	**Poly-B**	< 1	**2**	**7**	35±10
1	**1**	< 1	**Poly-B**	**2**	3 ± 1
			1	**7**	<1
			1	**8**	<1

Table 4.4. position of amine proton of **2** with 0, 1, and 3 aliquot addition of **6**

	+0 equiv of **6**	+1 equiv of **6**	+3 equiv of **6**
2•6	8.63 ppm	9.88 ppm	10.38 ppm
Poly-B'•6	8.63 ppm	9.92 ppm	10.40 ppm
(Poly-A• Poly-B') •6	8.63 ppm	9.90 ppm	10.39 ppm
(Poly-A•5•Poly-B') •6	8.63 ppm	9.93 ppm	10.39 ppm

4.10 References

1. Carlise, J.; Weck, M., Functional Materials Via Multiple Noncovalent Interactions. In *Functional Organic Materials*, Müller, T. J. J.; Bunz, U. H. F., Eds. 2007; Pp 261-292.

2. Vendruscolo, M.; Zurdo, J.; Macphee, C. E.; Dobson, C. M., Protein Folding And Misfolding: A Paradigm Of Self-Assembly And Regulation In Complex Biological Systems *Philos. Trans. Royal Soc. London Series A-Math. Phys. Eng. Sci.* **2003**, *361*, 1205-1222.

3. Ma, P. X., Biomimetic Materials For Tissue Engineering *Adv. Drug Deliv. Rev.* **2008**, *60*, 184-198.

4. Kokkoli, E.; Mardilovich, A.; Wedekind, A.; Rexeisen, E. L.; Garg, A.; Craig, J. A., Self-Assembly And Applications Of Biomimetic And Bioactive Peptide-Amphiphiles *Soft Mat.* **2006**, *2*, 1015-1024.

5. Mecke, A.; Dittrich, C.; Meier, W., Biomimetic Membranes Designed From Amphiphilic Block Copolymers *Soft Mat.* **2006**, *2*, 751-759.

6. Lahann, J., Reactive Polymer Coatings For Biomimetic Surface Engineering *Chem. Eng. Commun.* **2006**, *193*, 1457-1468.

7. Yoshida, R., Design Of Functional Polymer Gels And Their Application To Biomimetic Materials *Curr. Org. Chem.* **2005**, *9*, 1617-1641.

8. Knoblauch, M.; Peters, W. S., Biomimetic Actuators: Where Technology And Cell Biology Merge *Cell. Mol. Life Sci.* **2004**, *61*, 2497-2509.

9. Drotleff, S.; Lungwitz, U.; Breunig, M.; Dennis, A.; Blunk, T.; Tessmar, J.; Gopferich, A., Biomimetic Polymers In Pharmaceutical And Biomedical Sciences *Eur. J. Pharm. Biopharm.* **2004**, *58*, 385-407.

10. Estroff, L. A.; Hamilton, A. D., At The Interface Of Organic And Inorganic Chemistry: Bioinspired Synthesis Of Composite Materials *Chem. Mater.* **2001**, *13*, 3227-3235.

11. Binder, W. H., Polymeric Ordering By H-Bonds. Mimicking Nature By Smart Building Blocks *Monatshefte Fur Chemie* **2005**, *136*, 1-19.

12. Friese, V. A.; Kurth, D. G., Soluble Dynamic Coordination Polymers As A Paradigm For Materials Science *Coord. Chem. Rev.* **2008**, *252*, 199-211.

13. Davis, J. T.; Spada, G. P., Supramolecular Architectures Generated By Self-Assembly Of Guanosine Derivatives *Chem. Soc. Rev.* **2007**, *36*, 296-313.

14. South, C. R.; Burd, C.; Weck, M., Modular And Dynamic Functionalization Of Polymeric Scaffolds *Acc. Chem. Res.* **2007**, *40*, 63-74.

15. Sivakova, S.; Rowan, S. J., Nudeobases As Supramolecular Motifs *Chem. Soc. Rev.* **2005**, *34*, 9-21.

16. Gerhardt, W.; Crne, M.; Weck, M., Multifunctionalization Of Synthetic Polymer Systems Through Self-Assembly *Chem. Eur. J.* **2004**, *10*, 6212-6221.

17. Joseph R. Carlisle, M. W., Functional Materials Via Multiple Noncovalent Interactions. In *Functional Organic Materials*, Prof. Dr. Thomas J. J. Müller, P. D. U. H. F. B., Ed. 2007; Pp 261-292.

18. Ky Hirschberg, J. H. K.; Beijer, F. H.; Van Aert, H. A.; Magusin, P. C. M. M.; Sijbesma, R. P.; Meijer, E. W., Supramolecular Polymers From Linear Telechelic Siloxanes With Quadruple-Hydrogen-Bonded Units *Macromolecules* **1999**, *32*, 2696-2705.

19. Hirschberg, J. H. K. K.; Beijer, F. H.; Van Aert, H. A.; Magusin, P. C. M. M.; Sijbesma, R. P.; Meijer, E. W., Supramolecular Polymers From Linear Telechelic Siloxanes With Quadruple-Hydrogen-Bonded Units *Macromolecules* **1999**, *32*, 2696-2705.

20. Folmer, B. J. B.; Sijbesma, R. P.; Versteegen, R. M.; Van Der Rijt, J. A. J.; Meijer, E. W., Supramolecular Polymer Materials: Chain Extension Of Telechelic Polymers Using A Reactive Hydrogen-Bonding Synthon *Adv. Mater.* **2000**, *12*, 874-878.

21. Binder, W. H.; Kunz, M. J.; Kluger, C.; Hayn, G.; Saf, R., Synthesis And Analysis Of Telechelic Polyisobutylenes For Hydrogen-Bonded Supramolecular Pseudo-Block Copolymers *Macromolecules* **2004**, *37*, 1749-1759.

22. Hofmeier, H.; Hoogenboom, R.; Wouters, M. E. L.; Schubert, U. S., High Molecular Weight Supramolecular Polymers Containing Both Terpyridine Metal Complexes And Ureidopyrimidinone Quadruple Hydrogen-Bonding Units In The Main Chain *J. Am. Chem. Soc.* **2005**, *127*, 2913-2921.

23. Carlise, J. R.; Weck, M., Side Chain Funcitonalized Polymers Containing Bipyridine Coordination Sites *J. Poly. Sci., Part A: Polym. Chem.* **2004**, *42*, 2973-2984.

24. Cho, B.-K.; Choi, M.-G.; Zin, W.-C.; Lee, M., Supramolecular Nanostructures From Side Chain Rod-Coil Polymer Self-Assembly *Macromolecules* **2002**, *35*, 4845-4848.

25. Ilhan, F.; Gray, M.; Rotello, V. M., Reversible Side Chain Modification Through Noncovalent Interactions. "Plug And Play" Polymers *Macromolecules* **2001**, *34*, 2597-2601.

26. Pollino, J. M.; Weck, M., Supramolecular Side-Chain Functionalized Polymers: Synthesis And Self-Assembly Behavior Of Polynorbornenes Bearing Pdii SCS Pincer Complexes *Synthesis* **2002**, *9*, 1277-1288.

27. Pollino, J. M.; Stubbs, L. P.; Weck, M. W., One-Step Multifunctionalization Of Random Copolymers Via Self-Assembly *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

28. Stubbs, L. P.; Weck, M., A Polymeric Scaffold For The Self-Assembly Of Receptors Through Hydrogen Bonding *Chem. Eur. J.* **2003**, *9*, 992-999.

29. Binder, W. H.; Zirbs, R., Supramolecular Polymers And Networks With Hydrogen Bonds In The Main- And Side-Chain. In *Hydro. Bond. Polym.*, 2007; Vol. 207, Pp 1-78.

30. Farnik, D.; Kluger, C.; Kunz, M. J.; Machl, D.; Petraru, L.; Binder, W. H., Synthesis And Self Assembly Of Hydrogen-Bonded Supramolecular Polymers *Macromol. Symp.* **2004**, *217*, 247-266.

31. Grubbs, R. H., *Handbook Of Metathesis*. Wiley-VCH: Wilheim, 2003.

32. Owen, R. M.; Gestwicki, J. E.; Young, T.; Kiessling, L. L., Synthesis And Applications Of End-Labeled Neoglycopolymers *Org. Lett.* **2002**, *4*, 2293 - 2296.

33. Chen, B. Z.; Metera, K.; Sleiman, H. F., Biotin-Terminated Ruthenium Bipyridine Ring-Opening Metathesis Polymerization Copolymers: Synthesis And Self-Assembly With Streptavidin *Macromolecules* **2005**, *38*, 1084-1090.

34. Hillmyer, M. A.; Grubbs, R. H., Chain Transfer In The Ring-Opening Metathesis Polymerization Of Cyclooctadiene Using Discrete Metal Alkylidenes *Macromolecules* **1995**, *28*, 8662-8667.

35. Gibson, V. C.; Okada, T., Synthesis Of End-Functionalized Polynorbornenes And Polynorbornanes Via Metathesis: Novel Macromonomers For Polycondensation Reactions *Macromolecules* **2000**, *33*, 655-656.

36. Higley, M. N.; Pollino, J. M.; Hollembeak, E.; Weck, M., A Modular Approach Toward Block Copolymers *Chem. Eur. J.* **2005**, *11*, 2946-2953.

37. Davies, R. G.; Gibson, V. C.; Hursthouse, M. B.; Light, M. E.; Marshall, E. L.; North, M.; Robson, D. A.; Thompson, I.; White, A. J. P.; Williams, D. J.; Williams, P. J.,

Synthesis Of Nucleic-Acid Base Containing Norbornene Derivatives As Monomers For ROMP *J. Chem. Soc., Perkin Trans. 1* **2001**, 3365-3381.

38. Jorgensen, W. L.; Pranata, J., Importance Of Secondary Interactions In Triply Hydrogen-Bonded Complexes - Guanine-Cytosine Vs Uracil-2,6-Diaminopyridine *J. Am. Chem. Soc.* **1990**, *112*, 2008-2010.

39. Gerhardt, W. W.; Zucchero, A. J.; Wilson, J. N.; South, C. R.; Bunz, U. H. F.; Weck, M., Supramolecular Cruciforms *Chem. Commun.* **2006**, 2141-2143.

40. Nair, K. P.; Pollino, J. M.; Weck, M., Noncovalently Functionalized Block Copolymers Possessing Both Hydrogen Bonding And Metal Coordination Centers *Macromolecules* **2006**, *39*, 931-940.

41. South, C. R.; Higley, M. N.; Leung, K. C.-F.; Lanari, D.; Nelson, A.; Grubbs, R. H.; Stoddart, J. F.; Weck, M., Self-Assembly With Block Copolymers Through Metal Coordination Of SCS-Pdii Pincer Complexes And Pseudorotaxane Formation. *Chem. Eur. J.* **2006**, *12*, 3789-3797.

42. Albrecht, M.; Van Koten, G., Platinum Group Organometallics Based On Pincer Complexes: Sensors, Switches, And Catalysts *Angew. Chem. Int. Ed.* **2001**, *40*, 3750 - 3781.

43. Pollino, J. M.; Stubbs, L. P.; Weck, M., Living ROMP Of Exo-Norbornene Esters Possessing Pdii SCS Pincer Complexes Or Diaminopyridines *Macromolecules* **2003**, *36*, 2230-2234.

44. Huck, W. T. S.; Prins, L. J.; Fokkens, R. H.; Nibbering, N. M. M.; Van Veggel, F. C. J. M.; Reinhoudt, D. N., Convergent And Divergent Noncovalent Synthesis Of Metallodendrimers *J. Am. Chem. Soc.* **1998**, *120*, 6240-6246.

45. Huck, W. T. S.; Veggel, F. C. J. M. V.; Kropman, B. L.; Blank, D. H. A.; Keim, E. G.; Smithers, M. M. A.; Reinhoudt, D. N., Large Self-Assembled Organopalladium Spheres *J. Am. Chem. Soc.* **1995**, *117*, 8293-8294.

46. Suijkerbuijk, B.; Lutz, M.; Spek, A. L.; Van Koten, G.; Gebbink, R., Pincer-Porphyrin Hybrids *Org. Let.* **2004**, *6*, 3023-3026.

47. Gordon, E. J.; Gestwicki, J. E.; Strong, L. E.; Kiessling, L. L., Synthesis Of End-Labeled Multivalent Ligands For Exploring Cell-Surface-Receptor–Ligand Interactions *Chem. Biol.* **2000**, *7*, 9-16.

48. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Cross-Linked And Functionalized 'Universal Polymer Backbones' Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

49. Dirksen, A.; Hahn, U.; Schwanke, F.; Nieger, M.; Reek, J. N. H.; Voegtle, F.; De Cola, L., Multiple Recognition Of Barbiturate Guests By Hamilton-Receptor-Functionalized Dendrimers *Chem. Eur. J.* **2004**, *10*, 2036-2047.

50. Berl, V.; Schmutz, M.; Krische, M. J.; Khoury, R. G.; Lehn, J.-M., Supramolecular Polymers Generated From Heterocomplementary Monomers Linked Through Multiple Hydrogen-Bonding Arrays-Formation, Characterization, And Properties *Chem. Eur. J.* **2002**, *8*, 1227-1244.

51. Burd, C.; Weck, M., Self-Sorting In Polymers *Macromolecules* **2005**, *38*, 7225-7230.

52. Burd, C.; Weck, M., Solvent Influence On The Orthogonality Of Noncovalently Functionalized Terpolymers *J. Polym. Sci. A, Polym. Chem.* **2008**, *46*, 1936-1944.

53. Binder, W. H.; Kluger, C., Combining Ring-Opening Metathesis Polymerization (ROMP) With Sharpless-Type "Click" Reactions: An Easy Method For The Preparation Of Side Chain Functionalized Poly(Oxynorbornenes) *Macromolecules* **2004**, *37*, 9321-9330.

54. Berl, V.; Krische, M. J.; Huc, I.; Lehn, J.-M.; Schmutz, M., Template-Induced And Molecular Recognition Directed Hierarchical Generation Of Supramolecular Assemblies From Molecular Strands *Chem. Eur. J.* **2000**, *6*, 1938-1946.

55. South, C.; Burd, C.; Weck, M., Modular And Dynamic Functionalization Of Polymeric Scaffolds *Acc. Chem. Res.* **2007**, *40*, 63-74.

56. Kunz, M. J.; Hayn, G.; Saf, R.; Binder, W. H., Hydrogen-Bonded Supramolecular Poly(Ether Ketone)S *J. Polym. Sci. A, Polym. Chem.* **2004**, *42*, 661-674.

57. Binder, W. H.; Kunz, M. J.; Ingolic, E., Supramolecular Poly(Ether Ketone)-Polyisobutylene Pseudo-Block Copolymers *J. Polym. Sci. A, Polym. Chem.*, **2004**, *42*, 162-172.

58. Bielawski, C. W.; Benitez, D.; Grubbs, R. H., An "Endless" Route To Cyclic Polymers *Science* **2002**, *297*, 2041-2044.

59. Morita, T.; Maughon, B. R.; Bielawski, C. W.; Grubbs, R. H., A Ring-Opening Metathesis Polymerization (ROMP) Approach To Carboxyl- And Amino-Terminated Telechelic Poly(Butadiene)S *Macromolecules* **2000**, *33*, 6621-6623.

60. Bielawski, C. W.; Grubbs, R. H., Increasing The Initiation Efficiency Of Ruthenium-Based Ring-Opening Metathesis Initiators: Effect Of Excess Phosphine *Macromolecules* **2001**, *34*, 8838-8840.

61. Solov'ev, V., In 6.1, C., Ed. 1996-1998.

62. South, C. R.; Leung, K. C. F.; Lanari, D.; Stoddart, J. F.; Weck, M., Noncovalent Side-Chain Functionalization Of Terpolymers *Macromolecules* **2006**, *39*, 3738-3744.

63. The single-site binding constant for a ligand X binding to The single site association constants are calculated using the thermodynamic parameters obtained from ITC measurementsa polymer is given by the equation Ka = [unfilled sites]/([filled sites][X]).

CHAPTER 5

SUPRAMOLECULAR POLYMERS AND THE TOOLBOX CONCEPT: TODAY AND TOMORROW

5.1 Abstract

While this thesis describes the development of an understanding of the interactions that play in the noncovalent toolbox when used in supramolecular polymeric systems, the exciting applications and potential impact of these systems have yet to be realized. This chapter reviews the current status of the synthetic toolbox and it's role in supramolecular chemistry and suggests the next logical extensions of the concepts presented in this thesis. A broad look at the potential applications of these systems is also explored.

5.2 Current status of the synthetic toolbox

Frederic Menger, wrote that "Progress in the field of self-assembly requires, in addition to clever *a priori* design, the investigation of thoughtfully selected synthetic compounds".[1] At the commencement of this thesis, the interactions that occur between the recognition elements commonly used in the Weck group for supramolecular chemistry were mostly unknown. Furthermore, there were only a mere handful of examples of supramolecular assemblies based on two distinct recognition motifs reported in the literature.[2-8] In order to carefully select synthetic compounds for supramolecular self-assembled materials, a through understanding of interactions between distinct recognition motifs (both competitive and non-competitive) needed to be developed. Over the past five years, I have taken a collection of known synthetic supramolecular motifs

and developed them into a well-defined toolbox from which the individual components interactions with each other are well understood (Figure 5.1).

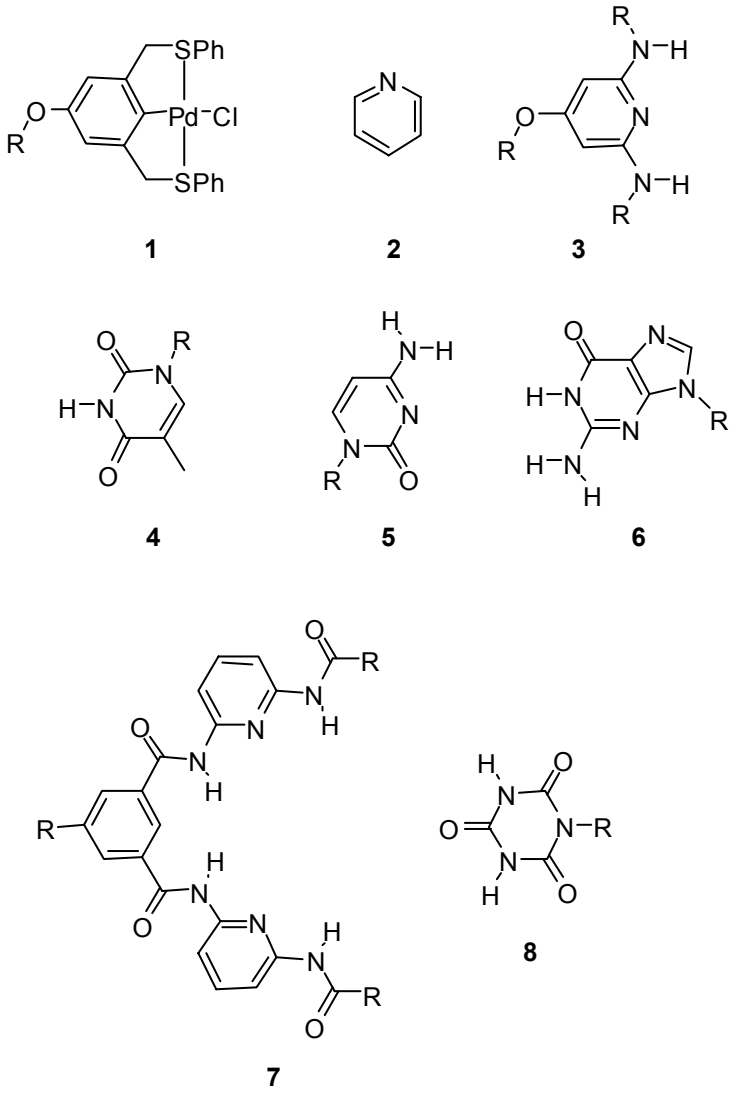


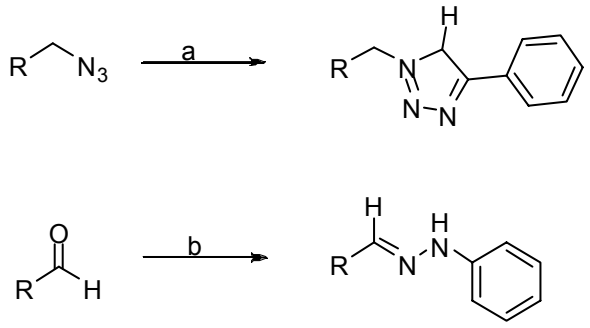
Figure 5.1 Toolbox of noncovalent interactions studied.

In particular, I have determined the specific interactions that occur in between derivatives of pincer complexes (**1**), pyridine (**2**), diamidopyridine (**3**), thymine (**4**), cytosine (**5**), guanine (**6**), Hamilton-wedge (**7**), and cyanuric acid (**8**) in a variety of solvents and solvent mixtures. My studies allow one to choose from any of these

recognition pairs to specifically tailor a material with known competitive interactions and binding strengths. At the beginning of the work presented here, the only pair of studied interactions present in my toolbox were those studied by Pollino between the metal coordination moieties **1** and **2**, and the hydrogen bonding moieties **3** and **4**.[2] The research presented in chapter 2, develops the self-sorting interactions of two sets of complementary pairs of hydrogen bonding units **3** and **4**, and **7** and **8**.[9] The science reported in chapter 3 combines the work of Pollino and chapter 2 by studying the interactions of metal coordination moieties **1** and **2,** and hydrogen bonding units **3** and **4**, and **7** and **8.** These studies resulted in very unexpected phenomena that were extremely solvent dependent.[10] Relying on the lessons learned in chapters 2 and 3, chapter 4 studied the competitive and non-competitive interactions of the entire toolbox, functional moieties **1**-**8**. The knowledge derived from this toolbox and presented in chapters 2, 3, and 4, allows for the careful selection of compounds for cleverly designed self-assembly materials inspired by Nature.

Throughout the course of my studies, a plethora of research has spawned from the idea of multi-component supramolecular assemblies.[11-22] Many groups have studied competitive interactions of supramolecular assemblies in combinatorial libraries.[23-29] The obvious next step in the development of the toolbox would be to add even more recognition motifs. In the Weck lab, Si Kung Yang has studied a variety of covalent coupling transformations of azide and ketone side-chain functionalized polymers based on 1,3-dipolar cycloadditions and hydrazone formations (scheme 5.1).[30]

Scheme 5.1 Covalent functionalization strategies



Reagents and Conditions (a) phenyl acetylene, $CuSO_4 \cdot 5H_2O$, sodium ascorbate, THF, 65° C, 5h; (b) phenylhydrazine, THF, 65° C, 2 h.

Many other groups have studied the effects of ionic assemblies on hydrogen bonding in natural materials.[14, 31-33] Kamlesh Nair, in the Weck group has studied the interactions of hydrogen-bonding and coulombic interactions along a poly(norbornene) backbone (Figure 5.2).[34] He found that these interactions occur independently when used in conjunction with the diamidopyridine: thymine (**3**:**4**) interaction.

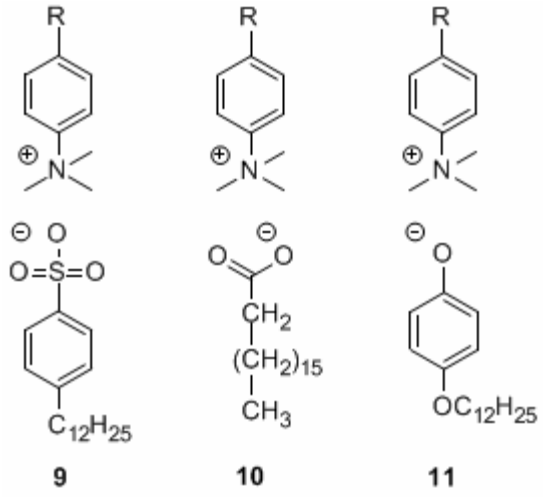


Figure 5.2 Coulombic interactions used by Nair. Coulombic self-assembly between a quaternary ammonium group and (**9**) sodium dodecyl sulfonate, (**10**) sodium stearate (**11**) sodium dodecyloxy phenolate.

While a part of this thesis concerns the development of the noncovalent

synthetic toolbox, a major thrust of this research has been the use of the toolbox components combined with the development of new supramolecular polymer chemistry methodologies. At the commencement of this thesis there were no accounts of synthetic block copolymers containing two-different hydrogen-bonding moieties in the side-chains (chapter 2), nor block terpolymers containing two different hydrogen bonding moieties and a metal coordination complex (chapter 3). In addition there were no accounts of AB and ABA block copolymers composed of noncovalent functionalities in both the main and side-chains (chapter 4). Throughout the course of my studies, a plethora of research has spawned from the idea of multi-component supramolecular assemblies,[11-22] side-chain supramolecular polymer functionalization,[35-41] and main-chain block copolymer formation.[35, 40, 42-48]

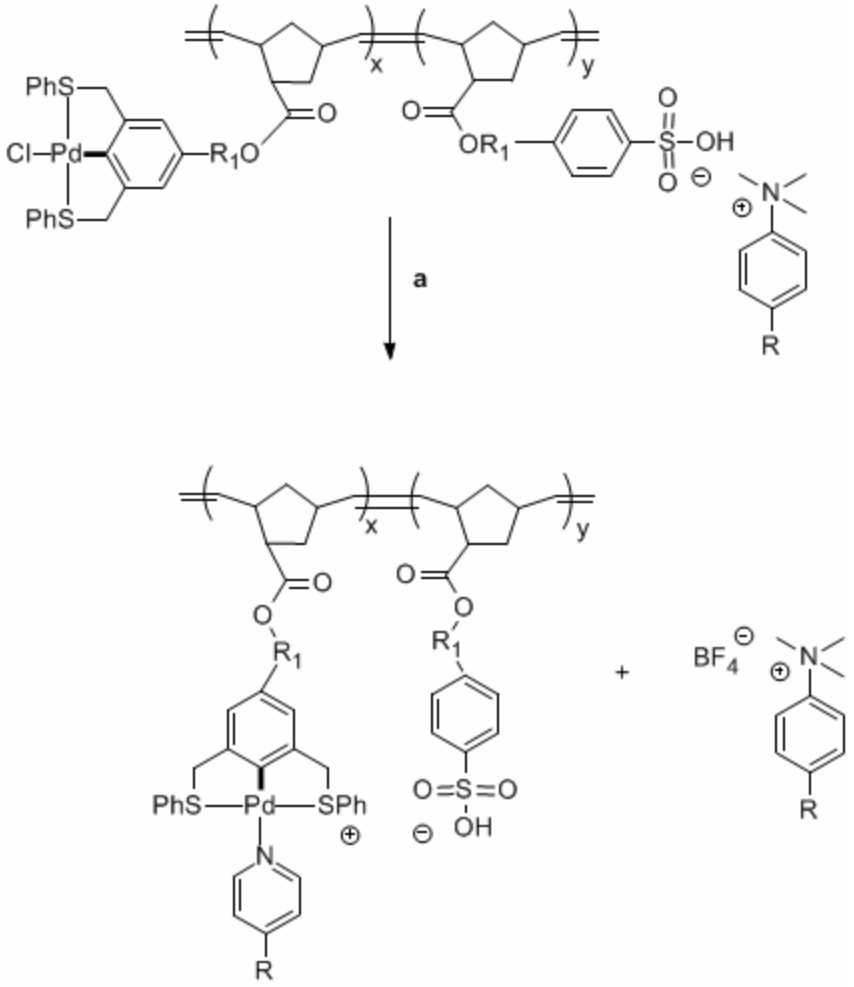
5.3 Future perspectives for supramolecular chemistry and the synthetic toolbox

The next generation of the synthetic toolbox for functionalized polymers will also be extended to include other noncovalent functionalities such as ionic interactions, π-π stacking and hydrophobic interactions. For example, a number of groups have begun studying the effects of ionic assemblies on hydrogen bonding in natural materials.[31-33] Still yet other scientists have used the idea of metal coordination with π-π stacking to form very small conductive nanowires on silicon chips.[49]

Preliminary studies of the combinations of Kamlesh Nair's columbic interactions[34] and the pincer complex:pyridine (**1**:**2**) coordination indicate interesting effects (Scheme 5.2). Upon the coordination of the pincer ligand via the addition of $AgBF_4$, the signals of the ^1H NMR spectra correlating to the coulombic interactions are shifted. I hypothesize that the tetrafluoroborate anion is displacing the anion assembled

to the cationic monomer moiety, this could be manipulated to induce a change in polymer morphology with the addition of an analyte (Scheme 5.2). Other groups have also studied displacement reactions of the counterions of pincer complexes and these studies also support this hypothesis.[50-53] While further studies are needed to determine the exact mechanism of this displacement, this exchange could also be further exploited to develop a material that can act as a molecular switch or for targeted delivery of a substance such as a drug. In figure 5.2, upon complexation of the pincer ligand, the quaternary amine cation is released. This phenomenon could be combined with the work presented in chapter 3 to develop a two-switch system capable of releasing multiple molecules on demand. Furthermore, employing this mechanism would allow for a second functionality to switch to the already functionalized coordinated pincer bringing two functionalities together in a single side-chain in a switch-type mechanism.

Scheme 5.2 Switchable folding polymer containing metal-coordination and coulombic interactions. Upon coordination of the pincer ligand with pyridine, the anions switch causing a change in the morphology and the release of the quaternary amine cation.



Reagents and Conditions (a) Pyridine, $AgBF_4$, Nitromethane.

The interactions of the noncovalent functionalities studied in the noncovalent toolbox I have developed have not been studied in conjunction with Yang's[30] covalent transformations previously discussed. One can clearly see that a combination of rapidly coupled covalent and noncovalent functionalities can be used to create unique tunable properties. Materials that can be rapidly functionalized via both covalent and

noncovalent chemistry can have a variety of applications such as targeted drug delivery, molecular machines and as tunable polymers for electroptical materials.

Still yet to be explored further is the combination of more than one metal coordination moiety. Bipyridine and terpyridine metal complexes have been used for a variety of applications ranging from uses in biological sensors, to hydrogen storage to photophysical devices.[54-65] These systems have yet to be studied in combination with all of the components described in my toolbox.

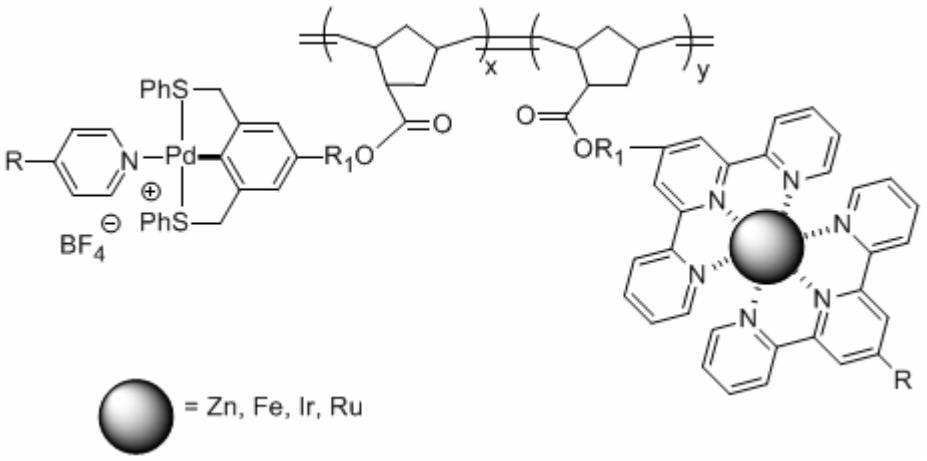


Figure 5.3 Fully functionalized block copolymer based on two different metal coordination moieties

With the fully designed toolbox in hand and the polymer methodologies presented here, a particular polymeric material can be designed according to the intended application. For example, a photophysical electronic device would require the choice of more stable interactions and would benefit from metal coordination and the covalent coupling interactions, *i.e*. the material must be thermally stable and a weak hydrogen-bonding would be a poor choice due to heat instability. On the other hand, a system used for drug delivery, may require the components to come apart when subjected to a particular environment and would benefit from hydrogen bonding interactions.

The next generation of work in this area will move towards applying the components in the toolbox with polymer science to form materials with real life applications. There are a number of applications that can benefit from the combination of the supramolecular toolbox and polymer chemistry. These applications range from developing polymers with specific morphologies[35, 66-72] and properties[73] to drug delivery[19, 74,75, 76] and biologically engineering artifical proteins and tissues.[77]

5.4 Conclusion

Albeit, depending on the application, the use of multiple types of interactions in a single material can be useful. The further development of this toolbox would enhance both the applicability and versatility of the universal polymer backbone (UPB) concept[78] and the development of biomimetic materials. Moreover, in order for biology and medicine to progress, we must develop a complete understanding of how Nature's components are assembled. This will only happen when we have mastered the phenomenon of noncovalent interactions. The work that was presented here is one step closer to mastering this phenomenon.

5.5 References

1. Menger, F. M., Supramolecular Chemistry And Self-Assembly *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 4818-4822.

2. Pollino, J. M.; Stubbs, L. P.; Weck, M. W., One-Step Multifunctionalization Of Random Copolymers Via Self-Assembly *J. Am. Chem. Soc.* **2004**, *126*, 563-567.

3. Ikkala, O.; Ten Brinke, G., Hierarchical Self-Assembly In Polymeric Complexes: Towards Functional Materials *Chem. Comm.* **2004**, 2131-2137.

4. Valkama, S.; Lehtonen, O.; Lappalainen, K.; Kosonen, H.; Castro, P.; Repo, T.; Torkkeli, M.; Serimaa, R.; Ten Brinke, G.; Ikkala, O., Multicomb Polymeric

Supramolecules And Their Self-Organization: Combination Of Coordination And Ionic Interactions *Macromol. Rapid. Commun.* **2003**, *24*, 556-560.

5. Huck, W. T. S.; Hulst, R.; Timmerman, P.; Veggel, F. C. J. M. V.; Reinhoudt, D. N., Noncovalent Synthesis Of Nanostructures: Combining Coordination Chemistry And Hydrogen Bonding *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1006-1008.

6. Liu, D. R.; Schultz, P. G., Generating New Molecular Function: A Lesson From Nature *Angew. Chem. Int. Ed.* **1999**, *38*, 36-54.

7. Peng, Z.; Gharavi, A. R.; Yu, L., Synthesis And Characterization Of Photorefractive Polymers Containing Transition Metal Complexes As Photosensitizer *J. Am. Chem. Soc.* **1997**, *119*, 4622 - 4632.

8. Fyfe, M. C. T. S., J. F, Interwoven Supramolecular Arrays Via The Noncovalent Polymerization Of Pseudorotaxanes. *Coord. Chem. Rev.* **1999**, *183*, 139-155.

9. Burd, C.; Weck, M., Self-Sorting In Polymers *Macromolecules* **2005**, *38*, 7225.

10. Burd, C.; Weck, M., Solvent Influence On The Orthogonality Of Noncovalently Functionalized Terpolymers *J. Poly. Sci., Part A: Polym. Chem.* **2008**, *46*, 1936-1944.

11. Yang, Y. L.; Wang, C., Multi-Component Supramolecular Assembly Structures Studied By Scanning Tunnelling Microscopy *Int. J. Nano.* **2007**, *4*, 4-20.

12. Lutz, J. F.; Borner, H. G., Modern Trends In Polymer Bioconjugates Design *Prog. Poly. Sci.* **2008**, *33*, 1-39.

13. Colquhoun, H. M.; Zhu, Z.; Cardin, C. J.; Gan, Y.; Drew, M. G. B., Sterically Controlled Recognition Of Macromolecular Sequence Information By Molecular Tweezers *J. Am. Chem. Soc.* **2007**, *129*, 16163-16174.

14. Mather, B. D.; Baker, M. B.; Beyer, F. L.; Green, M. D.; Berg, M. A. G.; Long, T. E., Multiple Hydrogen Bonding For The Noncovalent Attachment Of Ionic Functionality In Triblock Copolymers *Macromolecules* **2007**, *40*, 4396-4398.

15. Chakrabarti, S.; Mukhopadhyay, P.; Lin, S.; Isaacs, L., Reconfigurable Four-Component Molecular Switch Based On Ph-Controlled Guest Swapping *Org. Lett.* **2007**, *9*, 2349-2352.

16. Ishihara, Y.; Bazzi, H. S.; Toader, V.; Godin, F.; Sleiman, H. F., Molecule-Responsive Block Copolymer Micelles *Chem. Eur. J.* **2007**, *13*, 4560-4570.

17. Hirst, A. R.; Huang, B. Q.; Castelletto, V.; Hamley, I. W.; Smith, D. K., Self-Organisation In The Assembly Of Gels From Mixtures Of Different Dendritic Peptide Building Blocks *Chem. Eur. J.* **2007**, *13*, 2180-2188.

18. Tang, H. D.; Radosz, M.; Shen, Y. Q., Synthesis And Self-Assembly Of Thymine-And Adenine-Containing Homopolymers And Diblock Copolymers *J. Poly. Sci., Part A: Polym. Chem.* **2006**, *44*, 5995-6006.

19. Lutz, J. F.; Pfeifer, S.; Chanana, M.; Thunemann, A. F.; Bienert, R., H-Bonding-Directed Self-Assembly Of Synthetic Copolymers Containing Nucleobases: Organization And Colloidal Fusion In A Noncompetitive Solvent *Langmuir* **2006**, *22*, 7411-7415.

20. South, C. R.; Leung, K. C. F.; Lanari, D.; Stoddart, J. F.; Weck, M., Noncovalent Side-Chain Functionalization Of Terpolymers *Macromolecules* **2006**, *39*, 3738-3744.

21. Nair, K. P.; Pollino, J. M.; Weck, M., Noncovalently Functionalized Block Copolymers Possessing Both Hydrogen Bonding And Metal Coordination Centers *Macromolecules* **2006**, *39*, 931-940.

22. Binder, W. H.; Bernstorff, S.; Kluger, C.; Petraru, L.; Kunz, M. J., Tunable Materials From Hydrogen-Bonded Pseudo Block Copolymers *Adv. Mat.* **2005**, *17*, 2824-+.

23. Corbett, P. T.; Sanders, J. K. M.; Otto, S., Competition Between Receptors In Dynamic Combinatorial Libraries: Amplification Of The Fittest? *J. Am. Chem. Soc.* **2005**, *127*, 9390-9392.

24. Ladame, S., Dynamic Combinatorial Chemistry: On The Road To Fulfilling The Promise *Org. Bio. Chem.* **2008**, *6*, 219-226.

25. Greig, L. M.; Slawin, A. M. Z.; Smith, M. H.; Philp, D., The Dynamic Covalent Chemistry Of Mono- And Bifunctional Boroxoaromatics *Tetrahedron* **2007**, *63*, 2391-2403.

26. Schmuck, C.; Wich, P., Combinatorial Receptor Finding - Large And Random Vs. Small And Focused Libraries *New J. Chem.* **2006**, *30*, 1377-1385.

27. Bennes, R. M.; Philp, D., Probing Selectivity In Recognition-Mediated Dynamic Covalent Processes *Org. Lett.* **2006**, *8*, 3651-3654.

28. De Bruin, B.; Hauwert, P.; Reek, J. N. H., Dynamic Combinatorial Chemistry: The Unexpected Choice Of Receptors By Guest Molecules *Angew. Chem. Int. Ed.* **2006**, *45*, 2660-2663.

29. Saur, B.; Scopelliti, R.; Severin, K., Utilization Of Self-Sorting Processes To Generate Dynamic Combinatorial Libraries With New Network Topologies *Chem. Eur. J.* **2006**, *12*, 1058-1066.

30. Yang, S. K.; Weck, M., Modular Covalent Multifunctionalization Of Copolymers *Macromolecules* **2008**, *41*, 346-351.

31. Evan-Salem, T.; Frish, L.; Van Leeuwen, F. W. B.; Reinhoudt, D. N.; Verboom, W.; Kaucher, M. S.; Davis, J. T.; Cohen, Y., Self-Assembled Ionophores From Isoguanosine: Diffusion NMR Spectroscopy Clarifies Cation's And Anion's Influence On Supramolecular Structure *Chem. Eur. J.* **2007**, *13*, 1969-1977.

32. Lehn, J. M., From Supramolecular Chemistry Towards Constitutional Dynamic Chemistry And Adaptive Chemistry *Chem. Soc. Rev.* **2007**, *36*, 151-160.

33. Ma, L.; Iezzi, M.; Kaucher, M. S.; Lam, Y. F.; Davis, J. T., Cation Exchange In Lipophilic G-Quadruplexes: Not All Ion Binding Sites Are Equal *J. Am. Chem. Soc.* **2006**, *128*, 15269-15277.

34. Nair, K. P.; Weck, M., Noncovalently Functionalized Poly(Norbornene)S Possessing Both Hydrogen Bonding And Coulombic Interactions *Macromolecules* **2007**, *40*, 211-219.

35. Ten Brinke, G.; Ruokolainen, J.; Ikkala, O., Supramolecular Materials Based On Hydrogen-Bonded Polymers. In *Hydrogen Bonded Polymers*, 2007; Vol. 207, Pp 113-177.

36. Weck, M., Side-Chain Functionalized Supramolecular Polymers *Polym. Int.* **2007**, *56*, 453-460.

37. Cooke, G.; Garety, J. F.; Hewage, S. G.; Jordan, B. J.; Rabani, G.; Rotello, V. M.; Woisel, P., Tuneable Side-Chain Supramolecular Polymer *Org. Lett.* **2007**, *9*, 481-484.

38. South, C. R.; Burd, C.; Weck, M., Modular And Dynamic Functionalization Of Polymeric Scaffolds *Acc. Chem. Res,* **2007**, *40*, 63-74.

39. Barbera, J.; Gimeno, N.; Pintre, I.; Ros, M. B.; Serrano, J. L., Self-Assembled Bent-Core Side-Chain Liquid Crystalline Polymers *Chem. Commun.* **2006**, 1212-1214.

40. Pfister, A.; Fraser, C. L., Synthesis And Unexpected Reactivity Of Iron Tris(Bipyridine) Complexes With Poly(Ethylene Glycol) Macroligands *Biomacromolecules* **2006**, *7*, 459-468.

41. Pollino, J. M.; Weck, M., Non-Covalent Side-Chain Polymers: Design Principles, Functionalization Strategies, And Perspectives (Vol 34, Pg 193, 2005) *Chem. Soc. Rev.* **2005**, *34*, 1078-1078.

42. Shimizu, L. S., Perspectives On Main-Chain Hydrogen Bonded Supramolecular Polymers *Polym. Int.* **2007**, *56*, 444-452.

43. Hoogenboom, R.; Fournier, D.; Schubert, U. S., Asymmetrical Supramolecular Interactions As Basis For Complex Responsive Macromolecular Architectures *Chem. Commun.* **2008**, 155-162.

44. Wilson, A. J., Non-Covalent Polymer Assembly Using Arrays Of Hydrogen-Bonds *Soft Matter* **2007**, *3*, 409-425.

45. Park, T.; Zimmerman, S. C., A Supramolecular Multi-Block Copolymer With A High Propensity For Alternation *J. Am. Chem. Soc.* **2006**, *128*, 13986-13987.

46. Ott, C.; Lohmeijer, B. G. G.; Wouters, D.; Schubert, U. S., Terpyridine-Terminated Homo And Diblock Copolymer LEGO Units By Nitroxide-Mediated Radical Polymerization *Macromol. Chem. Phys.* **2006**, *207*, 1439-1449.

47. Scherman, O. A.; Ligthart, G.; Ohkawa, H.; Sijbesma, R. P.; Meijer, E. W., Olefin Metathesis And Quadruple Hydrogen Bonding: A Powerful Combination In Multistep Supramolecular Synthesis *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 11850-11855.

48. Sivakova, S.; Bohnsack, D. A.; Mackay, M. E.; Suwanmala, P.; Rowan, S. J., Utilization Of A Combination Of Weak Hydrogen-Bonding Interactions And Phase Segregation To Yield Highly Thermosensitive Supramolecular Polymers *J. Am. Chem. Soc.* **2005**, *127*, 18202-18211.

49. Chai, J.; Wang, D.; Fan, X. N.; Buriak, J. M., Assembly Of Aligned Linear Metallic Patterns On Silicon *Nature Nanotech.* **2007**, *2*, 500-506.

50. Ruokolainen, J.; Mäkinen, R.; Torkkeli, M.; Mäkelä, T.; Serimaa, R.; Tenbrinke, G.; Ikkala, O., Switching Supramolecular Polymeric Materials With Multiple Length Scales *Science* **1998**, *280*, 557-560.

51. Valkama, S.; Lehtonen, O.; Lappalainen, K.; Kosonen, H.; Castro, P.; Repo, T.; Torkkeli, M.; Serimaa, R.; Ten Brinke, G.; Leskela, M.; Ikkala, O., Multicomb Polymeric Supramolecules And Their Self-Organization: Combination Of Coordination And Ionic Interactions *Macromol. R. Commun.* **2003**, *24*, 556-560.

52. Van De Coevering, R.; Alfers, A. P.; Meeldijk, J. D.; Martinez-Viviente, E.; Pregosin, P. S.; Gebbink, R.; Van Koten, G., Ionic Core-Shell Dendrimers With An Octacationic Core As Noncovalent Supports For Homogeneous Catalysts *J. Am. Chem. Soc.* **2006**, *128*, 12700-12713.

53. Van De Coevering, R.; Kuil, M.; Alfers, A. P.; Visser, T.; Lutz, M.; Spek, A. L.; Gebbink, R.; Van Koten, G., Organometallic Zwitterions: Arylpalladium(II) (Pincer) Complexes With A Tethered Sulfato Group As Para-Substituent *Organometallics* **2005**, *24*, 6147-6158.

54. Dong, T. Y.; Huang, C. L.; Chen, C. P.; Lin, M. C., Molecular Self-Assembled Monolayers Of Ruthenium(II)-Terpyridine Dithiol Complex On Gold Electrode And Nanoparticles *J. Organomet. Chem.* **2007**, *692*, 5147-5155.

55. Lo, K. K. W.; Tsang, K. H. K.; Sze, K. S.; Chung, C. K.; Lee, T. K. M.; Zhang, K. Y.; Hui, W. K.; Li, C. K.; Lau, J. S. Y.; Ng, D. C. M.; Zhu, N., Non-Covalent Binding

Of Luminescent Transition Metal Polypyridine Complexes To Avidin, Indole-Binding Proteins And Estrogen Receptors *Coord. Chem. Rev.* **2007**, *251*, 2292-2310.

56. Wong, K. M. C.; Yam, V. W. W., Luminescence Platinum(II) Terpyridyl Complexes - From Fundamental Studies To Sensory Functions *Coord. Chem. Rev.* **2007**, *251*, 2477-2488.

57. Baranoff, E.; Barigelletti, F.; Bonnet, S.; Collin, J. P.; Flamigni, L.; Mobian, P.; Sauvage, J. P., From Photoinduced Charge Separation To Light-Driven Molecular Machines. In *Photofunctional Transition Metals Complexes*, 2007; Vol. 123, Pp 41-78.

58. Kume, S.; Nishihara, H., Metal-Based Photoswitches Derived From Photoisomerization. In *Photofunctional Transition Metals Complexes*, 2007; Vol. 123, Pp 79-112.

59. Fukuzumi, S., Bioinspired Energy Conversion Systems For Hydrogen Production And Storage *Eur. J. Inorg. Chem.* **2008**, 1351-1362.

60. Lo, K. K. W.; Lee, T. K. M.; Lau, J. S. Y.; Poon, W. L.; Cheng, S. H., Luminescent Biological Probes Derived From Ruthenium(II) Estradiol Polypyridine Complexes *Inorg. Chem.* **2008**, *47*, 200-208.

61. Collinson, M. M., Electrochemistry: An Important Tool To Study And Create New Sol-Gel-Derived Materials *Acc. Chem. Res.* **2007**, *40*, 777-783.

62. Marin, V.; Holder, E.; Hoogenboom, R.; Schubert, U. S., Functional Ruthenium(II)- And Iridium(III)-Containing Polymers For Potential Electro-Optical Applications *Chem. Soc. Rev.* **2007**, *36*, 618-635.

63. De Cola, L.; Belser, P.; Von Zelewsky, A.; Vogtle, F., Design, Synthesis And Photophysics Of Ruthenium And Osmium Complexes Through 20 Years Of Collaboration *Inorg. Chim. Acta* **2007**, *360*, 775-784.

64. Ma, D. L.; Che, C. M.; Siu, F. M.; Yang, M. S.; Wong, K. Y., DNA Binding And Cytotoxicity Of Ruthenium(II) And Rhenium(I) Complexes Of 2-Amino-4-Phenylamino-6-(2-Pyridyl)-1,3,5-Triazine *Inorg. Chem.* **2007**, *46*, 740-749.

65. Belbakra, A.; Goeb, S.; De Nicola, A.; Ziessel, R.; Sabatini, C.; Barbieri, A.; Barigelletti, F., Spectroscopic And Redox Properties Of Novel D(6)-Complexes Engineered From All Z-Ethenylthiophene-Bipyridine Ligands *Inorg. Chem.* **2007**, *46*, 839-847.

66. Valkama, S.; Nykanen, A.; Kosonen, H.; Ramani, R.; Tuomisto, F.; Engelhardt, P.; Ten Brinke, G.; Ikkala, O.; Ruokolainen, J., Hierarchical Porosity In Self-Assemhled Polymers: Post-Modification Of Block Copolymer-Phenolic Resin Complexes Hy Pyrolysis Allows The Control Of Micro- And Mesoporosity *Adv. Func. Mat.* **2007**, *17*, 183-190.

67. Valkama, S.; Ruotsalainen, T.; Nykanen, A.; Laiho, A.; Kosonen, H.; Ten Brinke, G.; Ikkala, O.; Ruokolainen, J., Self-Assembled Structures In Diblock Copolymers With Hydrogen-Bonded Amphiphilic Plasticizing Compounds *Macromolecules* **2006**, *39*, 9327-9336.

68. Chen, S. L.; Song, B.; Wang, Z. Q.; Zhang, X., Self-Organization Of Bolaamphiphile Bearing Biphenyl Mesogen And Aspartic-Acid Headgroups *J. Phys. Chem. C* **2008**, *112*, 3308-3313.

69. Wan, Y.; Sho, Y.; Zhao, D., Supramolecular Aggregates As Templates: Ordered Mesoporous Polymers And Carbons *Chem. Mater.* **2008**, *20*, 932-945.

70. Huang, C. I.; Chen, C. M., Hierarchical Structure-Within-Structure Morphologies In A(2)-Star-(B-Alt-C) Molecules *Chemphyschem* **2007**, *8*, 2588-2594.

71. Runge, M. B.; Bowden, N. B., Synthesis Of High Molecular Weight Comb Block Copolymers And Their Assembly Into Ordered Morphologies In The Solid State *J. Am. Chem. Soc.* **2007**, *129*, 10551-10560.

72. Sallenave, X.; Bazuin, C. G., Interplay Of Ionic, Hydrogen-Bonding, And Polar Interactions In Liquid Crystalline Complexes Of A Pyridylpyridinium Polyamphiphile With (Azo)Phenol-Functionalized Molecules *Macromolecules* **2007**, *40*, 5326-5336.

73. Mather, B. D.; Baker, M. B.; Beyer, F. L.; Berg, M. A. G.; Green, M. D.; Long, T. E., Supramolecular Triblock Copolymers Containing Complementary Nucleobase Molecular Recognition *Macromolecules* **2007**, *40*, 6834-6845.

74. Lutz, J. F.; Thunemann, A. F.; Nehring, R., Preparation By Controlled Radical Polymerization And Self-Assembly Via Base-Recognition Of Synthetic Polymers Bearing Complementary Nucleobases *J. Poly. Sci., Part A: Polym. Chem.* **2005**, *43*, 4805-4818.

75. Jin, Y. G.; Xin, R.; Ai, P.; Chen, D. W., Self-Assembled Drug Delivery Systems 2. Cholesteryl Derivatives Of Antiviral Nucleoside Analogues: Synthesis, Properties And The Vesicle Formation *Int. J. Pharm.* **2008**, *350*, 330-337.

76. Jin, Y. G.; Tong, L.; Ai, P.; Li, M.; Hou, X. P., Self-Assembled Drug Delivery Systems - 1. Properties And In Vitro/In Vivo Behavior Of Acyclovir Self-Assembled Nanoparticles (SAN) *Int. J. Pharm.* **2006**, *309*, 199-207.

77. Roland, J. T.; Guan, Z. B., Synthesis And Single-Molecule Studies Of A Well-Defined Biomimetic Modular Multidomain Polymer Using A Peptidomimetic Beta-Sheet Module *J. Am. Chem. Soc.* **2004**, *126*, 14328-14329.

78. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Cross-Linked And Functionalized 'Universal Polymer Backbones' Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

APPENDIX A.

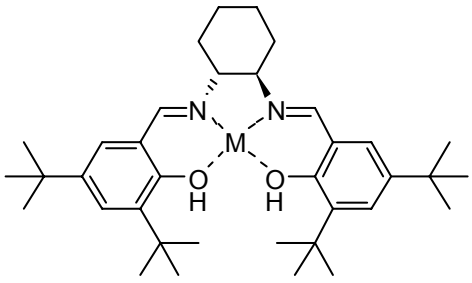
POLYMER SUPPORTED COBALT SALEN CATALYSTS

A1. Abstract

This appendix illustrates a practical one-pot synthesis of enantiopure unsymmetrical salen ligands is described, using a 1:1:1 molar ratio of a chiral diamine and two different salicylaldehydes. The new synthetic protocol can readily be performed in good yields (60–85%) on the multigram scale with good tolerance toward various functional groups. The pure unsymmetric salen ligands were then esterfied with norbornene-exo-acid to form salen-functionalized norbornenes.

A.2 Introduction

Metal complexes of chiral salen ligands are among the most versatile ligands used today.[1-9] The name salen is a contraction for salicylic aldehyde and ethylene diamine, which are the precursors that form the ligand via a schiff base reaction. Figure A1 shows an example of a typical salen ligand.



(M=metal)

Figure A1. Structure of the most widely active and selective metal-salen complex (Jacobsen type).

Enantioselective catalysts based on salen catalysts were first introduced in the 1990's by Jacobsen and Katsuki for the asymmetric epoxidation of unfunctionalized olefins.[1, 10, 11] Metallated salen-complex based catalysts have been successful for a variety of organic enantioselective transformations. These include asymmetric transformations[1, 3, 12] including ring-opening of epoxides,[13-17] hydrolytic kinetic resolution of terminal epoxides,[18-26] Hetero-Diels-Alder reactions,[27, 28] Pictet Spengler reactions,[29] and hydrocyanations.[30-33] In the past twenty years, a wide variety of different salen ligands have been studied for a wide variety of organic transformations.[34, 35] However, the metal-salen complexes originally proposed by Jacobsen are still the most widely used.[3] Catalysts based on the Jacobsen structure (Figure A1) are considered the most effective for the broadest range of substrates catalytic reactions.

One important use for chiral compounds such as those formed via salen catalysis reactions is in the pharmaceutical industry as intermediates for the synthesis of many drugs. For example, it has been made clear that enantiomerically pure drugs have many advantages such as fewer side effects and greater potency over racemic drug mixtures.[36] However, in order to utilize these catalysts better methods for removal of the metal species and reusability need to be developed. One strategy for achieving this goal is to use supported analogs of these salen complexes. [1, 37-42]

Over the past decade, basic design principles to yield the most active supported metal-salen species have been developed. These principles are primarily based on studies by Canali, Sherrington, Seebach and Laibinis.[17, 43, 44] These design principles include that (i) an optimized supported salen system should mimic the original chiral salen structure as closely as possible, (ii) the salen ligand should only have a single attachment to the

support to allow free access to the metal center, (iii) for epoxidation catalysts with Mn-salen species, the catalyst loading should be sufficiently low to maximize site-isolation of the catalytic centers and thus minimize the formation of catalytic inactive *oxo*-bridged dimers,[45, 46] (iv) the morphology of the supports should ensure free accessibility to all active sites and (v) that carbon-carbon bonds connecting the salen ligand to the support would minimize decomposition of the catalyst.[44,17]

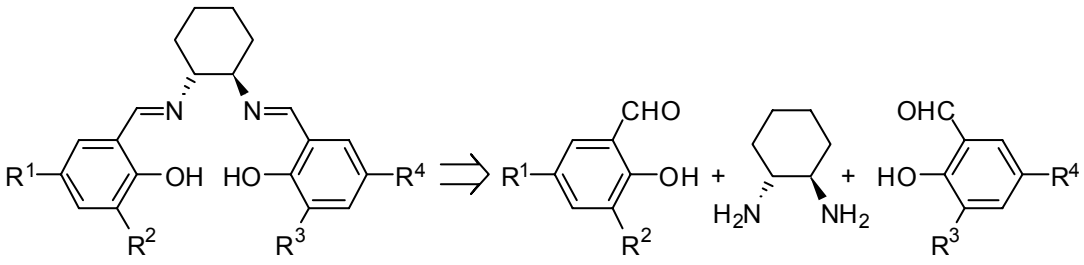
While there has been much research directed towards chiral metal-salen catalysts there has been little success developing polymer-supported catalysts. This lack of success can be attributed to not only synthetic challenges, but to the instabilities of the supported salen during various organic transformations and the lack of a modular approach that provides a simple synthetic route to the immbolization of the catalysts for a variety of different reactions.[17, 44] Almost all studies of polymeric supports report the metallation as a post-polymerization step. The problem with this method is unintentional side-effects and non-quantitative metallation. One of the goals of the Weck group, a small piece of which is presented in this appendix, was to synthesize reusable polymer supported salen catalysts that have both high activity and selectivity.

While many of the small molecule studies are based on symmetric salen ligands (i.e. those with C_2-symmetry) recent studies have demonstrated that unsymmetrical salen ligands, those with two different substituents on the two aromatic rings,[47] hold important advantages.[19, 20, 48-51] Immobilized symmetrical salen catalysts are usually prepared by attaching salicylidene moieties to supports[52] resulting in a bi-grafted, bridged geometry.[44] This rigid geometry can sterically restrict access to the catalytic center resulting in reduced activities and enantioselectivities. A more flexible immobilized

catalyst can be synthesized by employing a monofunctional attachment to the support. This can provide better access to the catalyst sites and result in better catalytic properties.[19, 20, 48, 49] Finally, it has been reported that metal complexes derived from unsymmetrical salen ligands could exhibit better enantioselectivities for several reactions in comparison with their symmetrical counterparts.[50, 51]

The condensation of a diamine and two equivalents of a salicylaldehyde has been generally practiced as the standard method for the preparation of symmetrical salen ligands in high yields.[53, 54] However, the synthesis of unsymmetrical salens has proven to be challenging (Scheme A1).[50, 55-57] Although the direct condensation of an unprotected diamine with two different salicylaldehydes subsequently has been reported to work in several cases,[58-60] a number of research groups have reported problems associated with this methodology.[50, 61, 62] Since the condensations of the two amino groups often proceed with comparable rates, the reaction produces, inevitably, a statistical mixture of an aimed unsymmetrical salen and two undesired symmetrical salens.[20, 63]

Scheme A1. Retro-synthetic analysis of unsymmetrical salen ligands



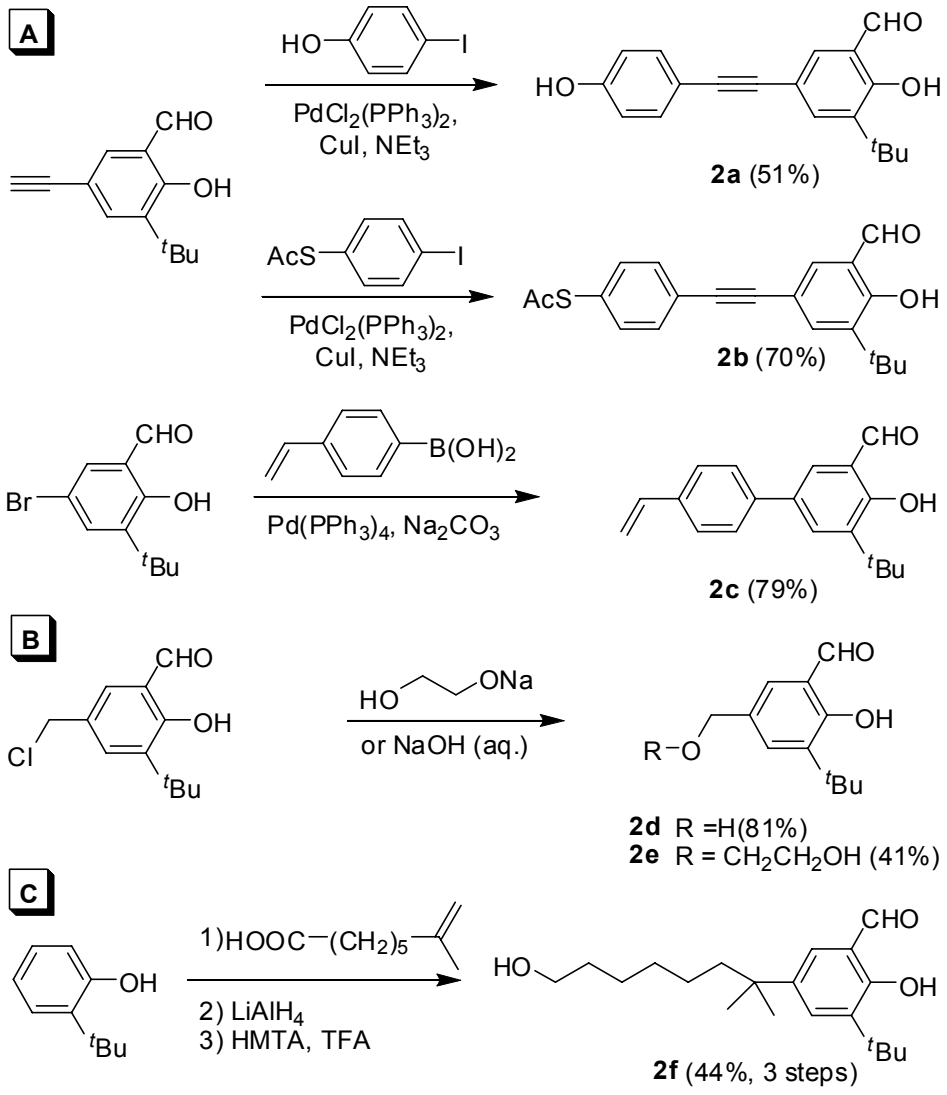
A more efficient approach is to protect one amino group of the employed diamine and to isolate the mono-imine intermediate after the first condensation step. Acids

including hydrogen chloride,[55] (+)-tartaric acid,[50] and *O*,*O*′-dibenzoyl-D-tartaric acid (DBTA)[50] have been applied to generate diamine mono-ammonium salts that can undergo stepwise condensations. Unfortunately, while this method has been reported with reasonably good yields for the synthesis of racemic unsymmetrical salens, poor yields were obtained when enantiopure diamines were used as a result of the disproportionation of the salicylidene moieties.[50] The origin for this difference between enantiopure and racemic compounds is still not understood. In this context, the development of a general and reliable preparative protocol for this important family of ligands, especially in non-racemic forms, is needed. Members of the Weck group and I have described such a protocol by introducing a straightforward one-pot synthesis of enantiopure unsymmetrical salen ligands that can be performed in high yields on the multigram scales.

A.3 Results and Discussion

These efforts were focused on the preparation of non-racemic unsymmetrical salen ligands that can be attached to a variety of supports such as organic polymers, silica, and metallic nanoparticles. For this purpose, several salicylaldehydes functionalized with an immobilizing group (–OH, –SAc, or –CH=CH_2) and either a rigid (phenylacetylene or phenylene) or a flexible spacer (alkyl or ethylene glycol) were synthesized as building blocks for the synthesis of unsymmetrical salen ligands. The synthetic pathway towards these building blocks is outlined in Scheme A2.

Scheme A2. Synthesis of the salicylaldehydes **2**



First, for the syntheses of the rigid linker-based compounds, Pd-catalyzed Sonogashira or Suzuki coupling reactions were employed to yield **2a**–**c** (Path A).[44] Both coupling reactions showed good tolerance to the presence of hydroxy, acetylsulfanyl, vinyl, and/or formyl functional groups. Second, salicylaldehydes **2d** and **2e** were produced by nucleophilic substitutions of 3-*tert*-butyl-5-chloromethylsalicylaldehyde[48, 64] with RONa (R = –H, $–CH_2CH_2OH$) (Path B).

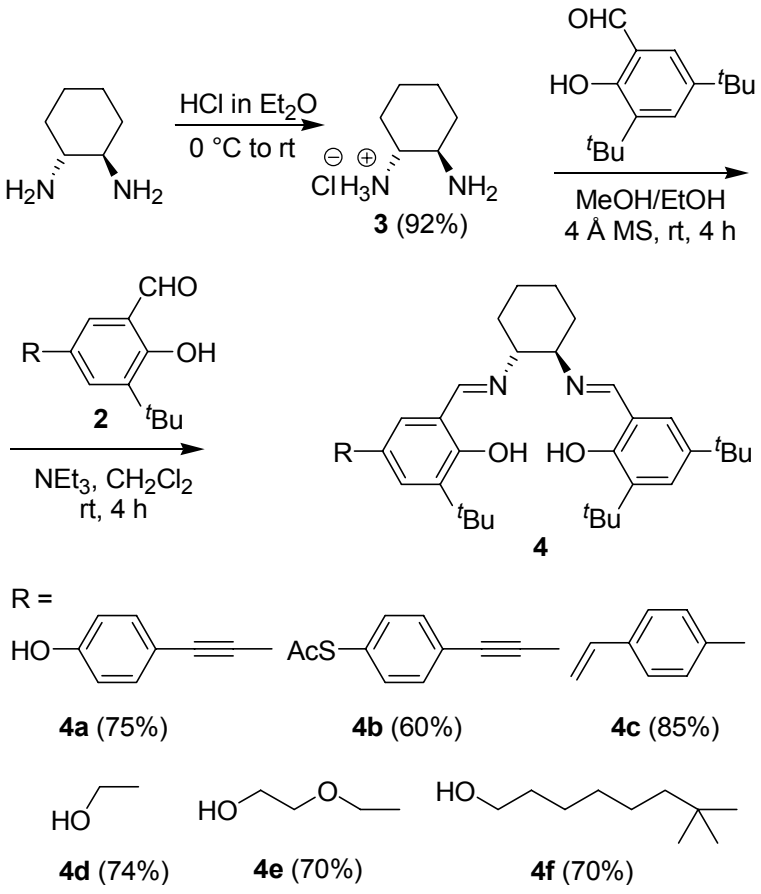
My work in this field focused on creating an unsymmetric salen that most closely mimics the Jacobsen catalyst (Path C). This ligand is thought to have many advantages i) the more stable c-c linkage attaching the ligand to the support; ii) a flexible linker allowing easy access to the metal center and iii) the same tertiary carbon electronics on the aromatic substituent that most closely mimic the Jacobsen salen. This ligand, was synthesized via the Friedel-Crafts alkylation of 2-*tert*-butylphenol with 7-methyl-7-octenoic acid, followed by the reduction of the carboxylic acid with $LiAlH_4$ and the acid-catalyzed formylation reaction produced **2f** with a long alkyl chain (Path C).

At the outset of this project it became clear that a one-pot condensation reaction would be superior to the known stepwise route[50,55] for the preparation of enantiopure unsymmetrical salen ligands (Scheme A3). A one pot approach would avoid the isolation step of the mono-imine intermediate that is prone to the undesired disproportionation reaction.

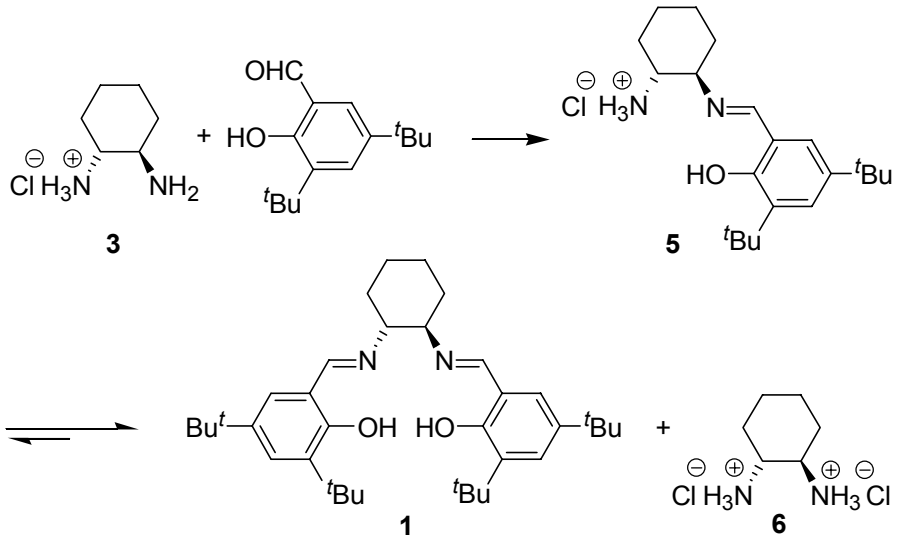
We chose hydrogen chloride as the protective acid to protect one amine group of the diamine. The mono-ammonium salt **3** was prepared in almost quantitative yield from a 1:1 molar ratio of (*R*,*R*)-diaminocyclohexane and 2.0 M hydrogen chloride in ether.[55] The first condensation between **3** and 3,5-di-*tert*-butylsalicylaldehyde was carried out in a 1:1 (v/v) mixture of anhydrous methanol and ethanol at ambient temperature. It is crucial to use activated 4 Å molecular sieves to remove the water that is formed during the reaction. This significantly reduced the reaction time to four hours and, more importantly, depressed the exchange of the salicylidene moieties. After the first condensation was complete, a solution of the functionalized salicylaldehyde **2** in dichloromethane was added to the reaction system, followed by the slow addition of an

excess of anhydrous triethylamine as a deprotective base. The TLC analysis and ^{1}H NMR spectra showed that the second condensation was completed within four hours and only traces of symmetrical salens were detected.

Scheme A3. One-pot synthesis of unsymmetrical salen ligands



Scheme A4. Disproportionation of the mono-imine intermediate



The target unsymmetrical salen ligands **4** were isolated in 60–85% yields as light yellow solids by means of column chromatography on silica gel pretreated with methanol or methanol/triethylamine. The reaction is very efficient in terms of time and reproducibility and can easily be scaled up and carried out on a multigram scale. For instance, we prepared and isolated five grams of the styryl-substituted salen **4c** within two days.

To compare our one-pot protocol to the stepwise synthesis developed by other groups[50, 55] we attempted to synthesize and separate the mono-imine intermediate **5**. Unfortunately, we were unable to obtain **5** in reasonable yields (typical yields were less than 30%). It was found that a considerable amount of symmetrical salen **1** was formed during the workup (Scheme A4). A similar phenomenon was observed by Gilheany and co-workers who employed (+)-tartaric acid instead of hydrogen chloride as the protective acid.[50] In addition, a ^{1}H NMR spectroscopic study revealed that **5** was unstable in

solution and disproportionated quantitatively into **1** and **6** in acetone-d_6 at ambient temperature within 24 hours. This observation clearly shows the advantages of the one-pot strategy over the previously employed stepwise approach for the preparation of enantiopure unsymmetrical salen ligands.

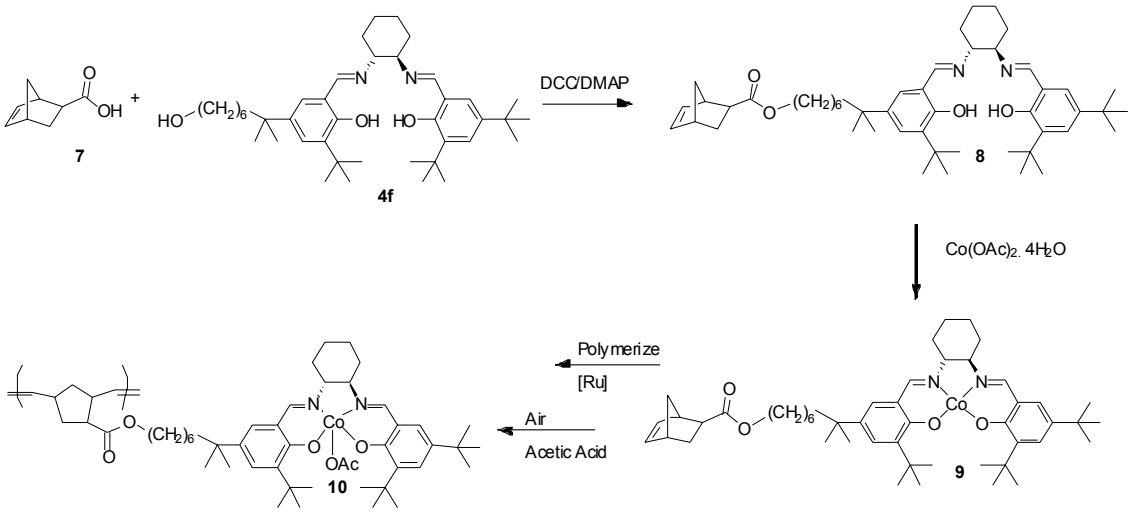
A.4 Synthesis and polymerization of unsymmetrical salen core 4f

All final asymmetric functionalized salen cores **4a-f** can be potentially immobilized in a straightforward fashion. With the mono-functionalized salen linker **4f** hand, the next step was to couple the core to the norbornene exo acid **7** via a DCC/DMAP esterification (scheme A.5). The purification of **8** proved difficult as the ligand quickly decomposed and thus resulted in very low yields. After the purification of **8**, the norbornene salen was complexed with cobalt and purified via repeated precipitations into methanol to form **9**. ROMP of monomer **9** using the 1°-generation Grubbs catalyst,[65] yielded polymer **10**. Furthermore, I prepared copolymers of **9** with an unfunctionalized norbornene octyl linker[66] to (i) site-isolate individual catalyst sites and (ii) probe the effect of catalyst loadings on the catalytic activity.

Although the complex **9** is paramagnetic, I was able to investigate the polymerization rates using ^{1}H-NMR spectroscopy by solely focusing on the signals of the olefin protons. In all cases, monomer conversions (monomer to catalyst ratios up to 50:1) were quantitative after one hour. It is well known that polyelectrolyte and metal-salt containing polymers cannot be characterized by gel-permeation chromatography (GPC), most likely due to interactions of the polymers with the packing material and the formation of aggregates during the process.[62] The same limitation holds true for my metal-containing polymer and no GPC results of any polymer could be obtained.

Therefore, no polydispersities (PDIs) or molecular weights for the high molecular weight polymers are reported.

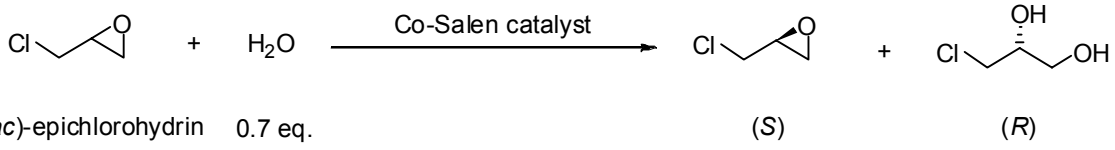
Scheme A5. Synthesis, metallation and polymerization of unsymmetrical salen complex.



A.5. Hydrolytic Kinetic Resolution (HKR)

The catalytic performance of the polymeric cobalt complex **10** was studied in the HKR of racemic epichlorohydrin (ECH) (Scheme A.6).

Scheme A.6. Hydrolytic kinetic resolution of epichlorohydrin catalyzed by cobalt-salen complexes



Since only the Co(III) complexes are catalytically active in this reaction, I oxidized the Co(II) polymer **10** by stirring a the polymer with acetic acid in methylene chloride under an atmosphere of air. After removal of the solvent and the excess AcOH *in high-vacuo*, the desired Co(III)-salen polymer **10** with acetate as a counterion was obtained.

The reaction kinetics of the HKR were studied *via* chiral GC-analysis, using either the homopolymer **10** or the monomer **9**, as the catalyst. In all experiments, the epoxide (*R*) is partially converted after five to its corresponding diol (~40% conversion), however in almost all experiments, the percent conversion of (*S*)-epicholohydrin decreased. This indicates one of two possibilities i) that the internal standard is not constant or ii) that there is a reformation of the racemic starting material or iii) the formation of a side product with similar polarity to the starting material.

To test the first hypothesis a series of internal standards were utilitized. The internal standards probed were chlorobenzene, toluene and xylene, however, regardless of the internal standard, the HKR experiments still resulted in this phenomena. As a result of these experiments, my suspicion is that there was in impurity remaining in the catalytic systems that was affecting the conversion and causing an unknown side reaction. Repeated purifications and characterizations to ensure the purity of the monomer did not have any effect on these results. Another group member, repeated the oxidation via acetic acid of the same batch of monomer **9** and was able to obtain excellent conversions and enantiomeric selectivties. This can only indicate that an impurity introduced was during the oxidation step is the cause of my poor results.

A.6. Conclusion

In conclusion, we have developed a straightforward one-pot protocol for the synthesis of mono-functionalized enantiopure unsymmetrical salen ligands, using a 1:1:1 molar ratio of a hydrogen chloride-protected chiral diamine and two different salicylaldehydes. This new synthetic method allows for the synthesis of unsymmetrical salen ligands in good to excellent yields and can be readily performed on the large scale.

While we have successfully tested this methodology in the synthesis of mono-functionalized unsymmetrical salens suitable for immobilization, this one-pot methodology can also be applied as a general and practical method for the preparation of other unsymmetrical salens.

A.7 Experimental Section

Reactions involving air- and/or moisture-sensitive compounds were carried out under an atmosphere of argon using standard Schlenk techniques. Diethylether and tetrahydrofuran (THF) were dried by refluxing over sodium/benzophenone. Dichloromethane and triethylamine were distilled over calcium hydride. 4 Å Molecular sieves were activated at 200 ^{o}C under high vacuum overnight and stored in a Schlenk tube under argon. Silica gel TLC plates (w/UV254, aluminum backed) and silica gel (technical grade, 60 Å, 200 × 400 mesh) were purchased from Sorbent Technologies. The silica gel used for the separation of salen compounds was subsequently flushed with MeOH (or MeOH with a trace of NEt_3), ethyl acetate, and hexanes to get rid of water. (*R,R*)-1,2-cyclohexanediamine mono(hydrogen chloride),[1] 5-bromo-3-*tert*-butyl-2-hydroxybenzaldehyde,[2,3] thioacetic acid *S*-(4-iodophenyl) ester,[4] 3-*tert*-butyl-5-ethynyl-2-hydroxybenzaldehyde,[5] 3-*tert*-butyl-2-hydroxy-5-(4'-vinylphenyl)benzaldehyde,[5] 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde,[6] and 3-*tert*-butyl-5-(4'-acetylsulfanylphenylethynyl)-2-hydroxybenzaldehyde[7] were synthesized following published procedures.

Chemical shifts are reported in ppm and referenced to the corresponding residual nuclei in deuterated solvents. The fine structures of the proton signals were specified with “s” (singlet), “d” (doublet), “t” (triplet), “q” (quartet), “m” (multiplet), “dd” (double-doublet),

and “br” (broad). Optical rotations were measured using a 2 mL capacity quartz cell with a10 cm path length.

2-*tert*-Butyl-4-(6'-carboxy-1',1'-dimethylhexyl)phenol

2-*tert*-Butylphenol (1.55 mL, 1.5 g, 10 mmol) and 7-methyl-7-octenoic acid (313 mg, 2.0 mmol) were charged into a 50 mL three-necked flask equipped with a magnetic stir bar, a septum, and a gas inlet. After the system was purged with argon, anhydrous CH_2Cl_2 (5 mL) was added to dissolve the substrates. The solution was cooled to –20 °C and concentrated H_2SO_4 (55 µL, 1.0 mmol) was added via a micro-syringe. The reaction mixture was allowed to warm up to rt over a period of three hours. A TLC analysis of the reaction mixture showed a complete conversion of the olefin. The slightly red reaction mixture was diluted with water (10 mL) and Et_2O (15 mL). The organic phase was separated and the aqueous phase was extracted with Et_2O (2 × 25 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$, and Brine, dried over $MgSO_4$, and concentrated under reduced pressure to give a pale red oil. Purification of the crude material by column-chromatography on silica gel (ethyl acetate/hexanes = 1:2) yielded the desired product as a pale yellow oil (424 mg, 70 %). R_F (SiO_2, ethyl acetate/hexanes = 1:5) = 0.12. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 - 1.15 (m, 2 H), 1.16 - 1.32 (m, 2 H), 1.25 (s, 6 H), 1.41 (s, 9 H), 1.49 - 1.64 (m, 4 H), 2.28 (t, *J* = 7.5 Hz, 2 H), 4.61 (br s), 6.59 (d, *J* = 8.3 Hz, 1 H), 6.99 (dd, *J* = 8.3, 2.4, 1 H), 7.21 (d, *J* = 2.4 Hz, 1 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 24.4, 24.5, 27.4, 29.6. 29.8, 32.1, 32.9, 34.0, 34.9, 37.4, 44.6, 101.9, 103.1, 116.1, 124.2, 124.6, 135.3, 141.5, 151.8, 172.3. Anal. Calcd for $C_{19}H_{30}O_3$ (306.45): C 74.47, H 9.87; found: C 74.08, H 10.14.

2-*tert*-Butyl-4-(7'-hydroxy-1',1'-dimethylheptyl)phenol

2-*tert*-Butyl-4-(6'-carboxy-1',1'-dimethylhexyl)phenol (302 mg, 1.0 mmol) was dissolved in anhydrous THF (5 mL) and slowly added to a stirred suspension of $LiAlH_4$ (1.0 M solution in THF, 5 mL) under argon at 0 °C. After stirring for 14 hours at 25 °C, the THF was removed under vacuum. The resulting white gel residue was redissolved in dichloromethane (25 mL) and cooled to 0 °C. 2 N HCl was added until the milky solution turned clear and the aqueous layer was extracted with dichloromethane (2 × 25 mL). The combined organic layers were dried with $MgSO_4$ and removal of the solvent provided the desired product (270 mg, 93%) as a pale yellow oil. R_F (SiO_2, ethyl acetate/hexanes = 1:10) = 0.2. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 - 1.15 (m, 2 H), 1.16 - 1.31 (m, 2 H), 1.26 (s, 6 H), 1.41 (s, 9 H), 1.49 - 1.59 (m, 4 H), 3.61 (t, *J* = 6.4 Hz, 2H), 4.75 (br s, 1H), 6.61 (d, *J* = 8.0 Hz, 1 H), 6.98 (dd, *J* = 1.9, 6.1, 2 H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 24.8, 25.8, 29.3, 29.8, 29.9, 30.3, 32.9, 32.5, 44.8, 63.3, 124.3, 220.2. HRMS (ESI) calcd for $C_{19}H_{32}O_2$ ($[M + 1]^+$): 306.2402; found: 306.2406. Anal. Calcd for $C_{19}H_{32}O_2$ (306.24): C 78.03, H 11.03; found: C 78.08, H 11.04.

3-*tert*-Butyl-2-hydroxy-5-(7'-hydroxy-1',1'-dimethylheptyl)benzaldehyde

A 50 mL round-bottom flask equipped with a magnetic stir bar and a reflux condenser was charged with 2-*tert*-butyl-4-(1',1'-dimethyl-7'-hydroxyheptyl)phenol (100 mg, 0.35 mmol), hexamethylene tetraamine (96 mg, 0.7 mmol) and trifluoroacetic acid (3 mL). The orange mixture was heated at 115 °C (± 5 °C) for eight hours. After the mixture was cooled to 60 °C, 33 % H_2SO_4 (5 mL) was added and the solution was heated at 130 °C for one hour. The orange-red reaction mixture was repeatedly extracted with Et_2O (3 × 25 mL). The combined organic layers were washed with water (3 × 25 mL), a

saturated aqueous $NaHCO_3$ solution, water, and brine (25 mL each) subsequently. The organic solution was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude material by column chromatography on silica gel (Et_2O/hexanes = 1:25) yielded **2f** (72 mg, 68 %) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 - 1.15 (m, 2 H), 1.16 - 1.31 (m, 2 H), 1.26 (s, 6 H), 1.41 (s, 9 H), 1.49 - 1.59 (m, 4 H), 4.30 (t, *J* = 6.4 Hz, 2H), 4.74 (br s), 7.5 (d, *J* = 2.9 Hz, 1 H), 7.3 (t, *J* = 3.4, 1 H), 9.9 (s, 1H), 11.7 (br s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 14.3, 14.4, 14.4, 22.9, 25.6, 27.1, 28.3, 29.1, 29.4, 29.5, 29.6, 31.8, 36.2, 37.4, 60.6, 68.4, 140.2, 169.3, 171.4, 197.5. Anal. Calcd for $C_{20}H_{32}O_3$ (320.47): C 74.96, H 10.06; found: C 75.02, H 10.28.

(*R,R*)-1,2-Cyclohexanediamine mono(hydrogen chloride)

(*R,R*)-1,2-Cyclohexanediamine mono(hydrogen chloride) was prepared according to a published procedure of (±)-1,2-cyclohexanediamine mono(hydrogen chloride).[1] (*R*,*R*)-1,2-diaminocyclohexane (0.951 g, 8.33 mmol) was dissolved in anhydrous ethanol (28 mL) under argon in a 100 mL three-necked flask equipped with a magnetic stir bar, an addition funnel, and a gas inlet. After the solution was cooled to 0 °C with an ice/water bath, a solution of hydrogen chloride in ether (2.0 M, 8.33 mmol) was added dropwise through the addition funnel over a period of 45 minutes. The reaction was exothermic and a white precipitate formed immediately. The reaction mixture was allowed to warm up to room temperature and stirring was continued overnight. The precipitate was collected by filtration, washed with dry Et_2O (ca. 70 mL), and dried *in vacuo* to afford **3** (1.16 g, 92 %) as a colorless powder. ^{1}H NMR (300 MHz, $CDCl_3$/MeOH): δ = 0.98 - 1.25 (m, 4 H), 1.48 - 1.69 (m, 2 H), 1.72 - 1.94 (m, 2 H), 2.43 - 2.65 (m, 2 H). The spectroscopic data were in agreement with the published data.[1]

(*R*,*R*)-*N*-(3,5-Di-*tert*-butylsalicylidene)-*N*'-[3-*tert*-butyl-5-(7'-hydroxy-1',1'dimethylheptyl)salicylidene]-1,2-cyclohexanediamine

(*R*,*R*)-1,2-Diaminocyclohexane mono(hydrogen chloride) (59 mg, 0.39 mmol), 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (92 mg, 0.39 mmol), and 4 Å molecular sieves (200mg) were charged into a 25 mL flask equipped with a magnetic stir bar and a septum. Anhydrous methanol (5 mL) was added and the bright yellow solution was stirred at room temperature for four hours. A solution of 3-*tert*-butyl-2-hydroxy-5-(7'-hydroxy-1',1'-dimethylheptyl)benzaldehyde (125 mg, 0.39 mmol) in anhydrous CH_2Cl_2 (10 mL) and anhydrous NEt_3 (0.15 mL, 0.90 mmol) were added. The red solution was stirred at room temperature for additional four hours. The reaction mixture was filtered through a short pad of dry silica gel and the silica gel was flushed with ethyl acetate. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexanes = 1:3) to afford **4f** (208 mg, 84 %) as a bright yellow powder. $[\alpha]^{20}_{D}$ – 200° (c 0.5, DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 - 1.15 (m, 2 H), 1.16 - 1.31 (m, 2 H), 1.25 (s, 6 H), 1.23 (s, 9 H), 1.28 (s, 9 H), 1.42 (s, 9 H), 1.43 – 1.59 (m, 6 H), 1.70 – 1.80 (m, 2 H), 1.88 – 1.92 (m, 2 H), 1.93 – 2.08 (m, 4 H) , 2.01 (s, 1H), 3.29 – 3.38 (m, 2 H), 3.54 (t, 2 H), 6.98 (d, *J* = 2.2 Hz, 1 H), 7.01 (d, *J* = 1.8 Hz, 1 H), 7.25 (d, *J* = 2.0 Hz, 1 H), 7.31 (d, *J* = 2.4 Hz , 1 H), 8.29 (s, 1 H), 8.31 (s, 1 H), 13.71 (s br, 2 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 24.6, 24.8, 25.7, 29.1, 29.2, 29.3, 29.6, 29.7, 30.3, 31.6, 31.7, 33.0, 33.4, 33.5, 33.6, 34.3, 35.2, 37.2, 44.6, 63.2,72.6, 76.8, 77.3, 77.7, 118.1, 126.2, 126.9, 127.0, 136.5, 136.6, 138.7, 140.1, 158.1, 158.2, 165.9, 166.0, 166.1, 220.2. MS (ESI): m/z (I_{rel}) = 635.6 (13, [M^{+}1]+). HRMS

(ESI) calcd for $C_{41}H_{64}N_2O_3$ ([M + 1]$^+$): 633.4996; found: 633.4995. Anal. Calcd for $C_{41}H_{64}N_2O_3$ (633.49): C 77.80, H 10.19, N 4.43; found: C 77.88, H 10.20, N 4.39.

7-(3-Tert-butyl-5-((E)-((1R,2R)-2-((E)-3,5-di-tert-butyl-2-hydroxybenzylideneamino)cyclohexylimino)methyl)-4-hydroxyphenyl)-7-methyloctyl bicyclo[2.2.1]hept-5-ene-2-carboxylate

Salen **4f** (58 mg, 0.09 mmol, 1 equiv.) and CH_2Cl_2 (5 mL) were added to a flame-dried round-bottomed flask (100 mL) equipped with a magnetic stir bar and a reflux condenser. To the solution, DCC (21 mg, 0.1 mmol, 1.1 equiv.), norbornene exo-acid (12.6 mg, 0.09 mmol, 1 equiv.), and DMAP (catalytic) were added. The reaction mixture was stirred at room temperature under an atmosphere of Ar, following which the reaction mixture was diluted with CH_2Cl_2 (5 mL) and filtered. The filtrate was dried over magnesium sulfate, filtered and concentrated under vacuum to afford a yellow solid. The crude mixture was subjected to flash column chromatography (20:1 hexane/EtOAc) to afford the norbornene ester as a yellow solid; yield: 37 mg (36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 13.73 (br s, 1H), 13.71 (br s, 1H), 8.32 (s, 1H), 8.3 (s, 1H), 7.3 (d, 1H, *J* = 2.5 Hz), 7.21 (d, 1H, *J* = 2.4 Hz), 6.99 (d, 1H, *J* = 2.5 Hz), 6.91(d, 1H, *J* = 2.3 Hz), 6.11 (m, 2H), 4.01 (t, 2H, *J* = 6.8 Hz), 3.33 (m, 2H), 3.2 (m, 2H), 3.0 (s, 1H), 2.9 (s, 1H), 2.2 (m, 1H), 1.83-1.94 (m, 5H), 1.72 (m, 2H), 1.4-1.6 (m, 6H); 1.39-1.4 (s (overlapping), 18H), 1.25-1.4 (m, 3H), 1.24 (s, 9 H), 1.19-1.24 (m, 2H), 1.19 (s, 3H), 1.18 (s, 3H), 1.01-1.1 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.6, 166.08, 166.01, 158.21, 158.16, 140.2, 138.7, 138.2, 136.6, 136.5, 127.4, 127.5, 127.4, 126.9, 126.3, 118.1, 118.07, 72.6 (overlapping signals), 64.8, 46.8, 46.5, 44.5, 43.4, 41.8, 37.2, 35.18, 35.16, 33.5, 33.4, 31.6, 30.5, 30.1, 29.7, 29.6

(overlapping signals), 29.22, 29.17, 28.9, 26.0, 24.7, 24.6; HRMS (ESI^+) calculated for $C_{49}H_{73}N_2O_4$ (MH^+) 753.5, found 753.5.

A.8 References

1. Canali, L.; Sherrington, D. C., Utilization Of Homogeneous And Supported Chiral Metal(Salen) Complexes In Asymmetric Catalysis *Chem. Soc. Rev.* **1999**, *28*, 85-93.

2. Katsuki, T., Chiral Metallosalen Complexes: Structures And Catalyst Tuning For Asymmetric Epoxidation And Cyclopropanation *Adv. Syn. Catal.* **2002**, *344*, 131-147.

3. Larrow, J. F.; Jacobsen, E. N., Asymmetric Processes Catalyzed By Chiral (Salen)Metal Complexes *Top. Organomet. Chem.* **2004**, *6*, 123-152.

4. Cozzi, P. G., Metal-Salen Schiff Base Complexes In Catalysis: Practical Aspects *Chem. Soc. Rev.* **2004**, *33*, 410-421.

5. Mcgarrigle, E. M.; Gilheany, D. G., Chromium- And Manganese-Salen Promoted Epoxidation Of Alkenes *Chem. Rev.* **2005**, *105*, 1563-1602.

6. Wezenberg, S. J.; Kleij, A. W., Material Applications For Salen Frameworks *Angew. Chem. Int. Ed.* **2008**, *47*, 2354-2364.

7. Fatibello-Filho, O.; Dockal, E. R.; Marcolino-Junior, L. H., Electrochemical Modified Electrodes Based On Metal-Salen Complexes *Anal. Lett.* **2007**, *40*, 1825-1852.

8. Darensbourg, D. J., Making Plastics From Carbon Dioxide: Salen Metal Complexes As Catalysts For The Production Of Polycarbonates From Epoxides And CO2 *Chem. Rev.* **2007**, *107*, 2388-2410.

9. Leung, A. C. W.; Maclachlan, M. J., Schiff Base Complexes In Macromolecules *J. Inorg. Organomet. Polym. Mater.* **2007**, *17*, 57-89.

10. Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T., Catalytic Asymmetric Epoxidation Of Unfunctionalized Olefins *Tetrahedron Lett.* **1990**, *31*, 7345-8.

11. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N., Enantioselective Epoxidation Of Unfunctionalized Olefins Catalyzed By Salen Manganese Complexes *J. Am. Chem. Soc.* **1990**, *112*, 2801-3.

12. Yoon, T. P.; Jacobsen, E. N., Privileged Chiral Catalysts *Science* **2003**, *299*, 1691-1693.

13. Jacobsen, E. N.; Kakiuchi, F.; Konsler, R. G.; Larrow, J. F.; Tokunaga, M., Enantioselective Catalytic Ring Opening Of Epoxides With Carboxylic Acids *Tetrahedron Lett.* **1997**, *38*, 773-776.

14. Wu, M. H.; Jacobsen, E. N., Asymmetric Ring Opening Of Meso Epoxides With Thiols: Enantiomeric Enrichment Using A Bifunctional Nucleophile *J. Org. Chem.* **1998**, *63*, 5252-5254.

15. Wu, M. H.; Hansen, K. B.; Jacobsen, E. N., Regio- And Enantioselective Cyclization Of Epoxy Alcohols Catalyzed By A [Coiii(Salen)] Complex *Angew. Chem., Int. Ed.* **1999**, *38*, 2012-2014.

16. Gigante, B.; Corma, A.; Garcia, H.; Sabater, M. J., Assessment Of The Negative Factors Responsible For The Decrease In The Enantioselectivity For The Ring Opening Of Epoxides Catalyzed By Chiral Supported Cr(III)-Salen Complexes *Catal. Lett.* **2000**, *68*, 113-119.

17. Angelino, M. D.; Laibinis, P. E., Polymer-Supported SALEN Complexes For Heterogeneous Asymmetric Synthesis: Stability And Selectivity *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 3888-3898.

18. Brandes, B. D.; Jacobsen, E. N., Synthesis Of Enantiopure 3-Chlorostyrene Oxide Via An Asymmetric Epoxidation-Hydrolytic Kinetic Resolution Sequence *Tetrahedron: Asymmetry* **1997**, *8*, 3927-3933.

19. Breinbauer, R.; Jacobsen, E. N., Cooperative Asymmetric Catalysis With Dendrimeric [Co(Salen)] Complexes *Angew. Chem., Int. Ed.* **2000**, *39*, 3604-3607.

20. Annis, D. A.; Jacobsen, E. N., Polymer-Supported Chiral Co(Salen) Complexes: Synthetic Applications And Mechanistic Investigations In The Hydrolytic Kinetic Resolution Of Terminal Epoxides *J. Am. Chem. Soc.* **1999**, *121*, 4147-4154.

21. Kawthekar, R. B.; Kim, G. J., Hydrolytic Kinetic Resolution Of Terminal Epoxides Catalyzed By Novel Bimetallic Chiral Co (Salen) Complexes *Synth. Commun.* **2008**, *38*, 1236-1248.

22. Madhavan, N.; Weck, M., Highly Active Polymer-Supported (Salen)Al Catalysts For The Enantioselective Addition Of Cyanide To Alpha,Beta-Unsaturated Imides *Adv. Synt. Catal.* **2008**, *350*, 419-425.

23. Lee, S. H.; Lee, E. Y.; Yoo, D. W.; Hong, S. J.; Lee, J. H.; Kwak, H.; Lee, Y. M.; Kim, J.; Cheal, K. A.; Lee, J. K., Novel Polymer-Supported Ruthenium And Iron Complexes That Catalyze The Conversion Of Epoxides Into Diols Or Diol Mono-Ethers: Clean And Recyclable Catalysts *New J. Chem.* **2007**, *31*, 1579-1582.

24. Darensbourg, D. J.; Frantz, E. B., Manganese(III) Schiff Base Complexes: Chemistry Relevant To The Copolymerization Of Epoxides And Carbon Dioxide *Inorg. Chem.* **2007**, *46*, 5967-5978.

25. Silva, M.; Freire, C.; De Castro, B.; Figueiredo, J. L., Styrene Oxidation By Manganese Schiff Base Complexes In Zeolite Structures *J. Mol. Catal.* **2006**, *258*, 327-333.

26. Sello, G.; Fumagalli, T.; Orsini, F., Recent Developments In Epoxide Preparation *Curr. Org. Syn.* **2006**, *3*, 457-476.

27. Schaus, S. E.; Brnalt, J.; Jacobsen, E. N., Asymmetric Hetero-Diels-Alder Reactions Catalyzed By Chiral (Salen)Chromium(III) Complexes *J. Org. Chem.* **1998**, *63*, 403-405.

28. Chapman, J. J.; Day, C. S.; Welker, M. E., Enantioselective Diels-Alder Reactions Of Optically Active (Buta-1,3-Dien-2-Yl)(Salen)Cobalt(III) Complexes *Eur. J. Org. Chem.* **2001**, *12*, 2273-2282.

29. Taylor, M. S.; Jacobsen, E. N., Highly Enantioselective Catalytic Acyl-Pictet-Spengler Reactions *J. Am. Chem. Soc.* **2004**, *126*, 10558-10559.

30. Sigman, M. S.; Jacobsen, E. N., Enantioselective Addition Of Hydrogen Cyanide To Imines Catalyzed By A Chiral (Salen)Al(III) Complex *J. Am. Chem. Soc.* **1998**, *120*, 5315-5316.

31. Vachal, P.; Jacobsen, E. N., Enantioselective Catalytic Addition Of HCN To Ketoimines. Catalytic Synthesis Of Quaternary Amino Acids *Org. Lett.* **2000**, *2*, 867-870.

32. Belokon, Y. N.; North, M.; Parsons, T., Vanadium-Catalyzed Asymmetric Cyanohydrin Synthesis *Org. Lett.* **2000**, *2*, 1617-1619.

33. Belokon, Y. N.; Green, B.; Ikonnikov, N. S.; North, M.; Parsons, T.; Tararov, V. I., Optimized Catalysts For The Asymmetric Addition Of Trimethylsilyl Cyanide To Aldehydes And Ketones *Tetrahedron* **2001**, *57*, 771-779.

34. Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L., Highly Enantioselective Epoxidation Catalysts Derived From 1,2-Diaminocyclohexane *J. Am. Chem. Soc.* **1991**, *113*, 7063-4.

35. Pospisil, P. J.; Carsten, D. H.; Jacobsen, E. N., X-Ray Structural Studies Of Highly Enantioselective Mn(Salen) Epoxidation Catalysts *Chem. Eur. J.* **1996**, *2*, 974-980.

36. Stinson, S. C., Chiral Drugs *Chem. Eng. News* **1992**, *70*, 46-&.

37. Xia, Q. H.; Ge, H. Q.; Ye, C. P.; Liu, Z. M.; Su, K. X., Advances In Homogeneous And Heterogeneous Catalytic Asymmetric Epoxidation *Chem. Rev.* **2005**, *105*, 1603-1662.

38. Li, C., Chiral Synthesis On Catalysts Immobilized In Microporous And Mesoporous Materials *Catal. Rev.* **2004**, *46*, 419-492.

39. Leadbeater, N. E.; Marco, M., Preparation Of Polymer-Supported Ligands And Metal Complexes For Use In Catalysis *Chem. Rev.* **2002**, *102*, 3217-3273.

40. Song, C. E.; Lee, S.-G., Supported Chiral Catalysts On Inorganic Materials *Chem. Rev.* **2002**, *102*, 3495-3524.

41. Dhal, P. K.; De, B. B.; Sivaram, S., Polymeric Metal Complex Catalyzed Enantioselective Epoxidation Of Olefins *J. Mol. Catal. A: Chem.* **2001**, *177*, 71-87.

42. Sherrington, D. C., Polymer-Supported Metal Complex Alkene Epoxidation Catalysts *Catal. Today* **2000**, *57*, 87-104.

43. Canali, L.; Cowan, E.; Deleuze, H.; Gibson, C. L.; Sherrington, D. C., Polystyrene And Polymethacrylate Resin-Supported Jacobsen's Alkene Epoxidation Catalyst *Perkin 1* **2000**, *13*, 2055-2066.

44. Sellner, H.; Karjalainen, J. K.; Seebach, D., Preparation Of Dendritic And Non-Dendritic Styryl-Substituted Salens For Cross-Linking Suspension Copolymerization With Styrene And Multiple Use Of The Corresponding Mn And Cr Complexes In Enantioselective Epoxidations And Hetero-Diels-Alder Reactions *Chem. Eur. J.* **2001**, *7*, 2873-2887.

45. Srinivasan, K.; Perrier, S.; Kochi, J. K., Dual Pathways For Manganese Catalysis Of Olefin Oxidation With Alkyl Hydroperoxides *J. Mol. Catal.* **1986**, *36*, 297-317.

46. Srinivasan, K.; Michaud, P.; Kochi, J. K., Epoxidation Of Olefins With Cationic (Salen)Mniii Complexes. The Modulation Of Catalytic Activity By Substituents *J. Am. Chem. Soc.* **1986**, *108*, 2309-20.

47. Meier, M. A. R.; Lohmeijer, B. G. G.; Schubert, U. S., Characterization Of Defined Metal-Containing Supramolecular Block Copolymers *Macromol. Rapid Commun.* **2003**, *24*, 852-857.

48. Canali, L.; Cowan, E.; Deleuze, H.; Gibson, C. L.; Sherrington, D. C., Polystyrene And Polymethacylate Resin-Suopported Jacobsen's Alkene Epoxidation Catalst *J. Chem. Soc., Perkin Trans. 1* **2000**, 2055-2066.

49. Zheng, X.; Jones, C. W.; Weck, M., Poly(Styrene)-Substituted *Chem. Eur. J.* **2005**, In Press.

50. Renehan, M. F.; Schanz, H.-J.; Mvgarrigle, E. M.; Dalton, C. T.; Daly, A. M.; Gilheany, D. G., Unsymmetrical Chiral Salen Schiff Base Ligands. Synthesis And Use In Metal-Based Asymmetric Epoxidation Reactions *J. Mol. Catal. A: Chem.* **2005**, *231*, 205-220.

51. Kim, G.-J.; Shin, J.-H., Applicaiton Of New Unsymmetrical Chiral Mn(III), Co(II,IIII), And Ti(IV) Salen Complexes In Enantioselective Catalytic Reactions *Catal. Lett.* **1999**, *63*, 83-89.

52. Sherrington, D. C., Polymer-Supported Metal Complex Alkene Epoxidation Catalysts *Catal. Today* **2000**, *57*, 87-104.

53. Cozzi, P. G., Metal-Salen Schiff Base Complexes In Catalysis: Pratical Aspects *Chem. Soc. Rev.* **2004**, *33*, 410-421.

54. Larrow, J. F.; Jacobsen, E. N.; Cao, Y.; Hong, Y.; Nie, X.; Zepp, C. M., A Practical Method For The Large Scale Preparation Of Salen(Mn)Cl Catalyst *J. Org. Chem.* **1994**, *59*, 1939-1942.

55. Campbell, E. J.; Nguyen, S. T., Unsymmetrical Salen-Type Ligands: High Yield Synthesis Of Salen-Type Schiff Bases Containing Two Different Benzaldehyde Moieties *Tetrahedron Lett.* **2001**, *42*, 1221-1225.

56. Lopez, J.; Mintz, E. A.; Hsu, F.-L.; Bu, X. R., Novel Unsymmetric Chiral Sciff Base... *Tet. Asym.* **1998**, 3741-3744.

57. Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X., Advances In Homogeneous And Heterogeneous Catalytic Asymmetric Epoxidation *Chem. Rev.* **2005**, *105*, 1603-1662.

58. Daly, A. M.; Dalton, C. T.; Renehan, M. F.; Gilheany, D. G., Unsymmetrical Salen Ligands: Synthesis And Use In Chromium Mediated Asymmetric Epoxidation *Tetrahedron Lett.* **1999**, *40*, 3617.

59. Kureshy, R. I.; Khan, N.-U. H.; Abdi, S. H. R.; Patel, S. T.; Jasra, R. V., Enantioselective Epoxidation Of Non-Functionalized Alkenes Using A Urea-Hydrogen Peroxide Oxidant And A Dimeric Homochiral Mn(III)-Schiff Base Complex Catalyst *Tetrahedron: Asymmetry* **2001**, *12*, 433-437.

60. Kureshy, R. I.; Khan, N.-U. H.; Abdi, S. H. R.; Singh, S.; Ahmad, I.; Jasra, R. V.; Vyas, A. P., Enantioselective Epoxidation Of Nonfunctionalized Alkenes Catalyzed By Recyclable New Homochiral Dimeric Mn(III) Salen Complexes *J. Catal.* **2004**, *224*, 229-235.

61. Nielsen, M.; Gothelf, K. V., Synthesis And Catalytic Properties Of P-Acylthio(Phenylacetylene)N Substituted Chiral Manganese Salen Complexes *J. Chem. Soc., Perkin Trans. 1* **2001**, 2440-2444.

62. Kureshy, R. I.; Khan, N. H.; Abdi, S. H. R.; Patel, S. T.; Jasra, R. V., Simultaneous Production Of Chirally Enriched Epoxides And 1,2-Diols From Racemic Epoxides Via Hydrolytic Kinetic Resolution *J. Mol. Catal. A: Chem.* **2002**, *179*, 73-77.

63. Konsler, R. G.; Karl, J.; Jacobsen, E. N., Cooperative Asymmetric Catalysis With Dimeric Salen Complexes *J. Am. Chem. Soc.* **1998**, *120*, 10780-10781.

64. Minutolo, F.; Pini, D.; Salvadori, P., Polymer-Bound Chiral (Salen)Mn(III) Complex As Heterogeneous Catalyst In Rapid And Clean Enantioselective Epoxidation Of Unfunctionalized Olefins *Tetrahedron Lett.* **1996**, *37*, 3375-3378.

65. Grubbs, R. H., *Handbook Of Metathesis*. Wiley-VCH: Wilheim, 2003.

66. Pollino, J. M.; Nair, K. P.; Stubbs, L. P.; Adams, J.; Weck, M., Crosslinked And Functionalized Universal Polymer Backbones Via Simple, Rapid, And Orthogonal Multi-Site Self-Assembly *Tetrahedron* **2004**, *60*, 7205-7215.

APPENDIX B

NMR SPECTRA AND ITC DATA

B.1 NMR Spectra

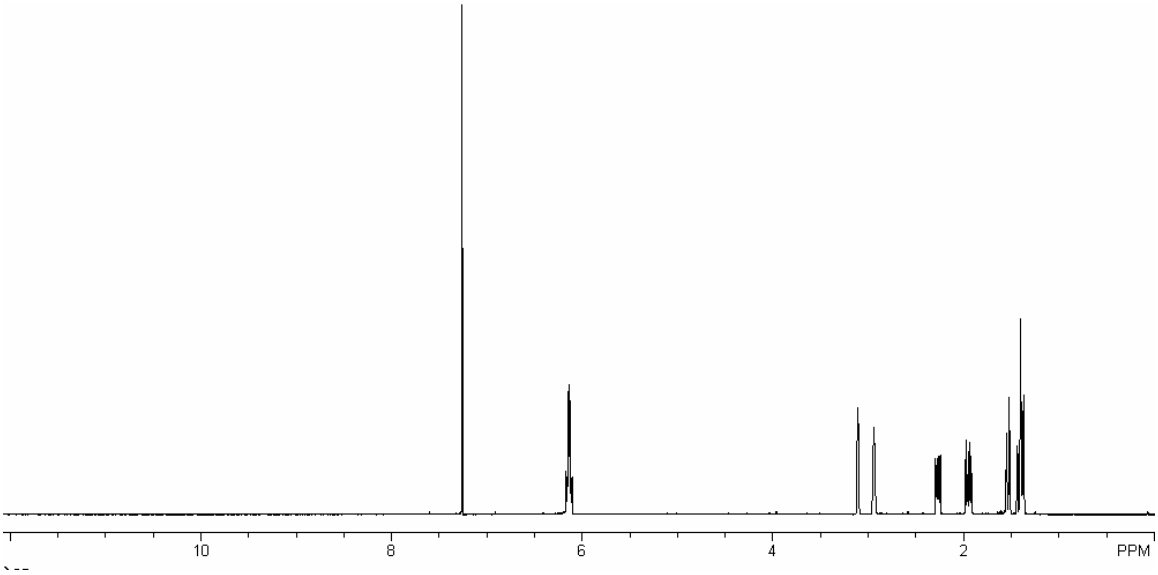


Figure B.1. ^{1}H spectra NMR of **2(3)**.

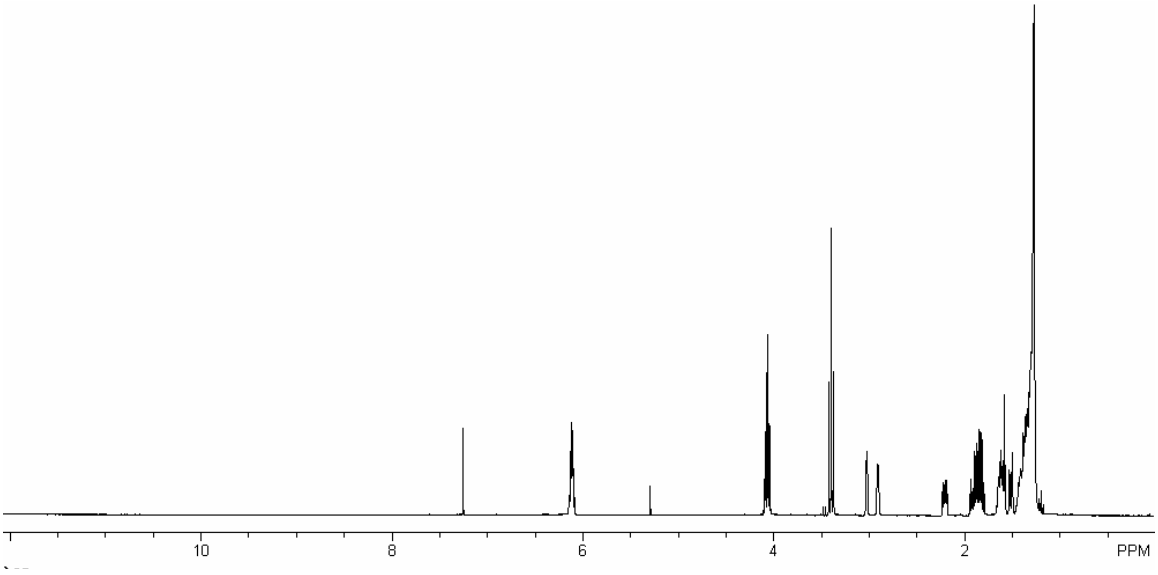


Figure B.2. ^{1}H spectra NMR of **2(4)**.

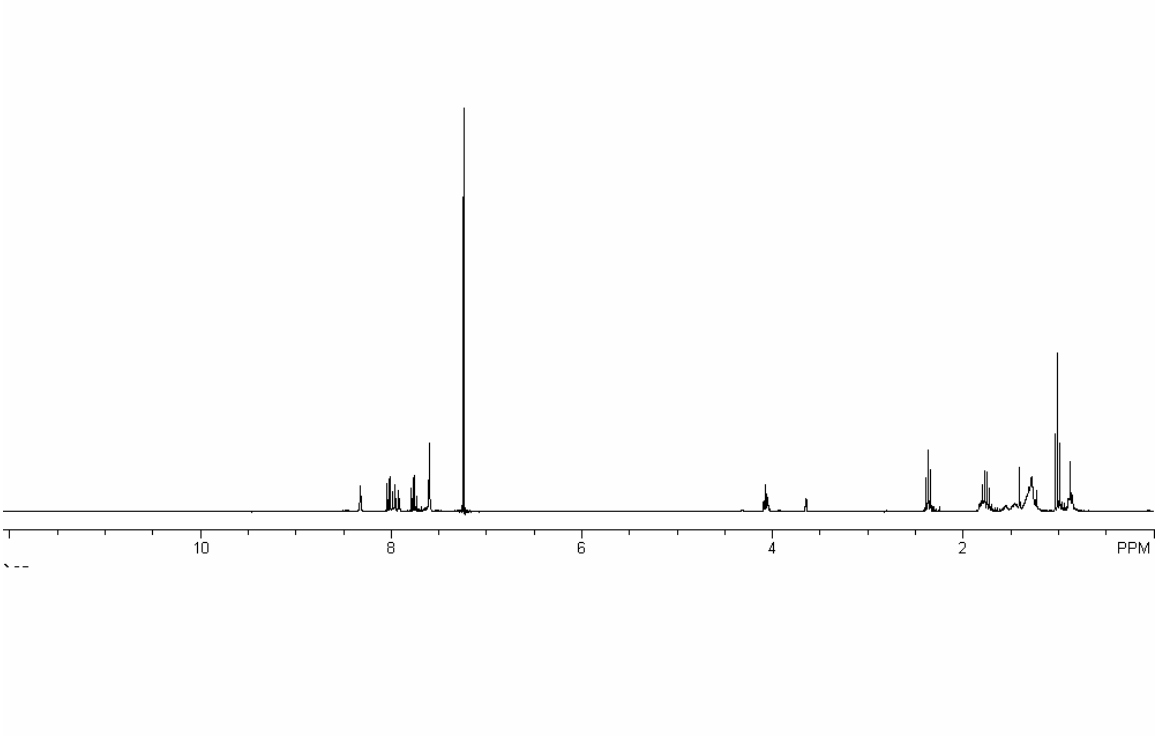


Figure B.3. ^{1}H NMR spectra of **2(6)**.

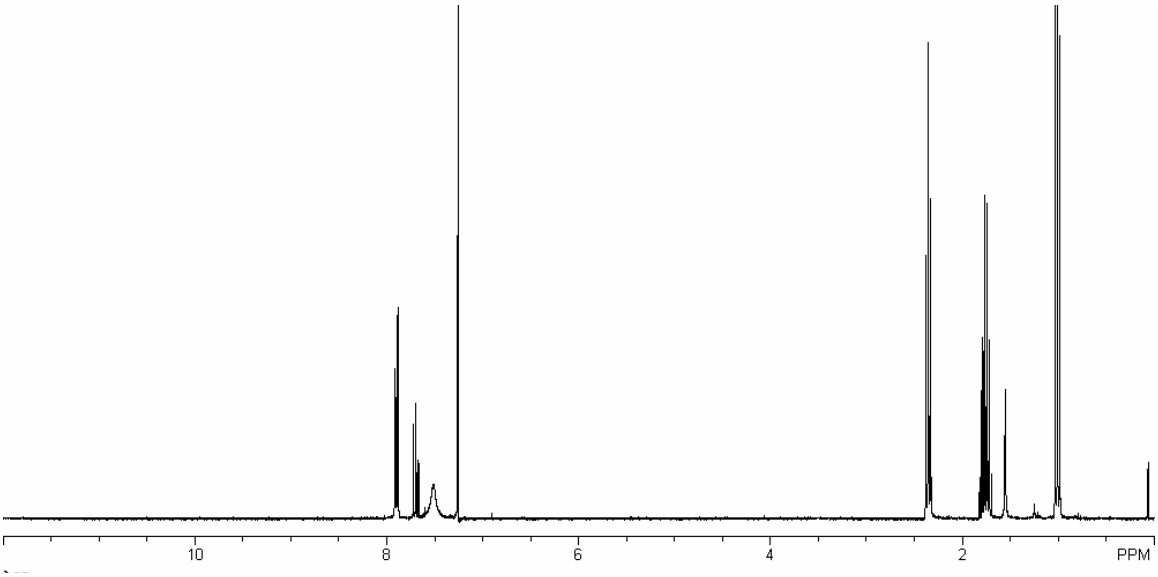


Figure B.4. ^{1}H NMR spectra of **2(5)**.

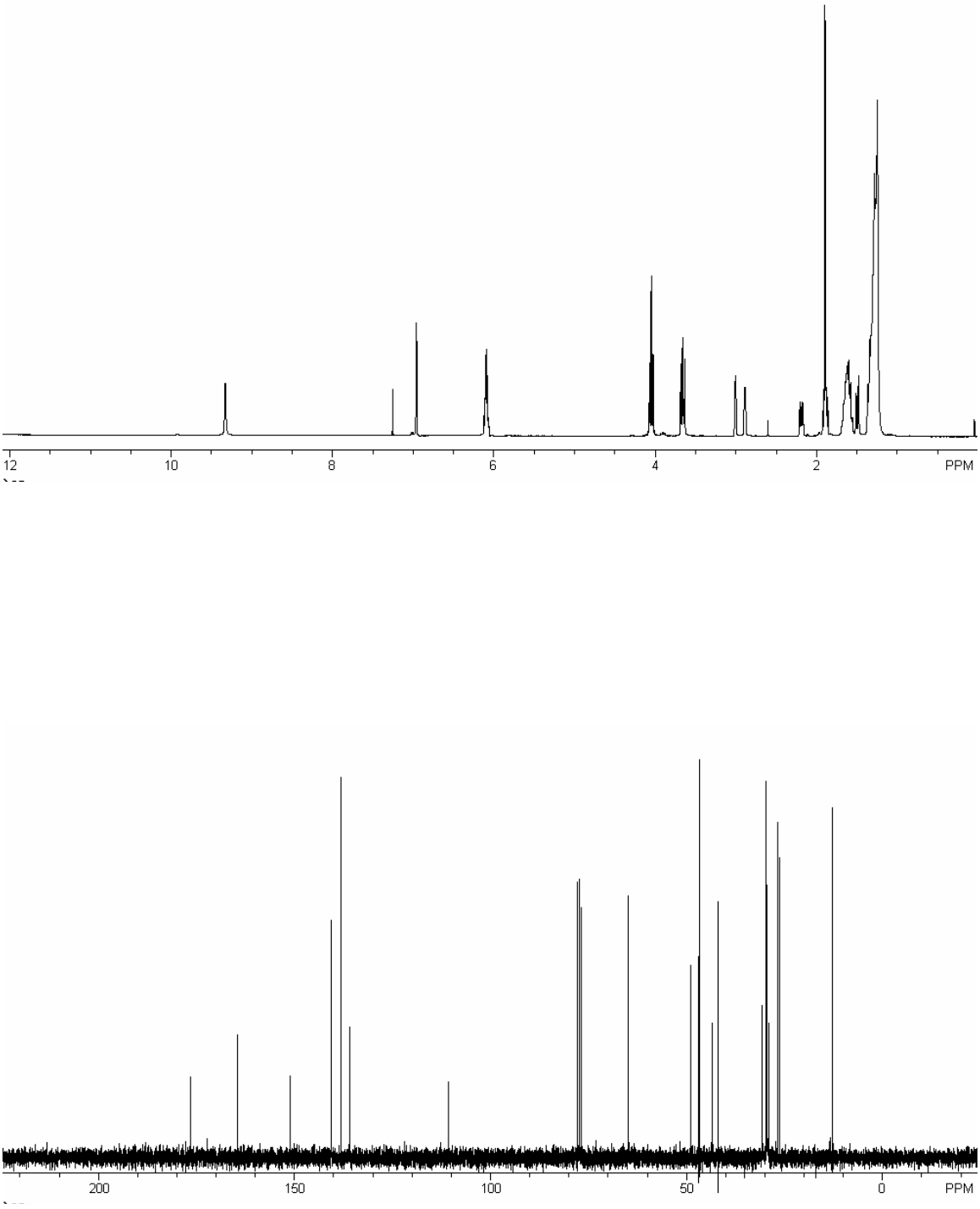


Figure B.5. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **2(1)**.

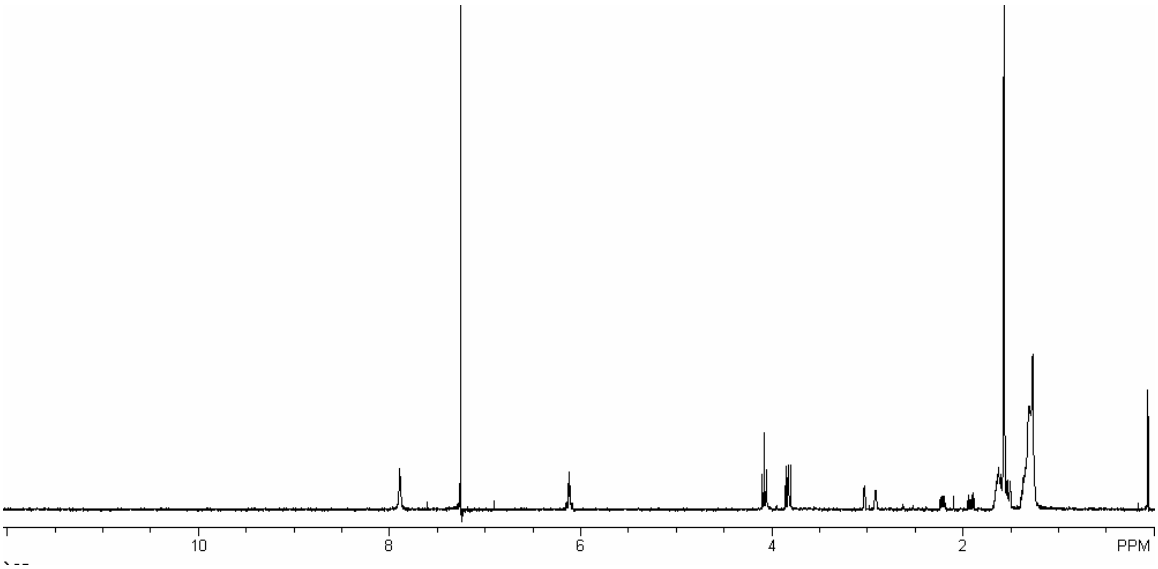


Figure B.6. ^{1}H NMR spectra of **2(2)**.

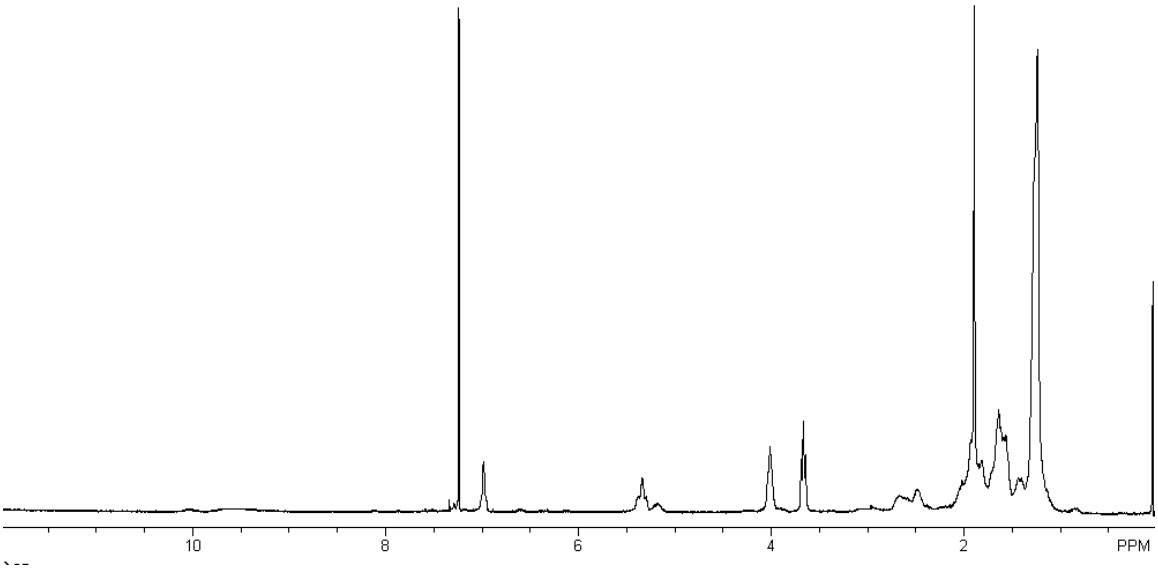


Figure B.7. ^{1}H NMR spectra of **2(poly-1)**.

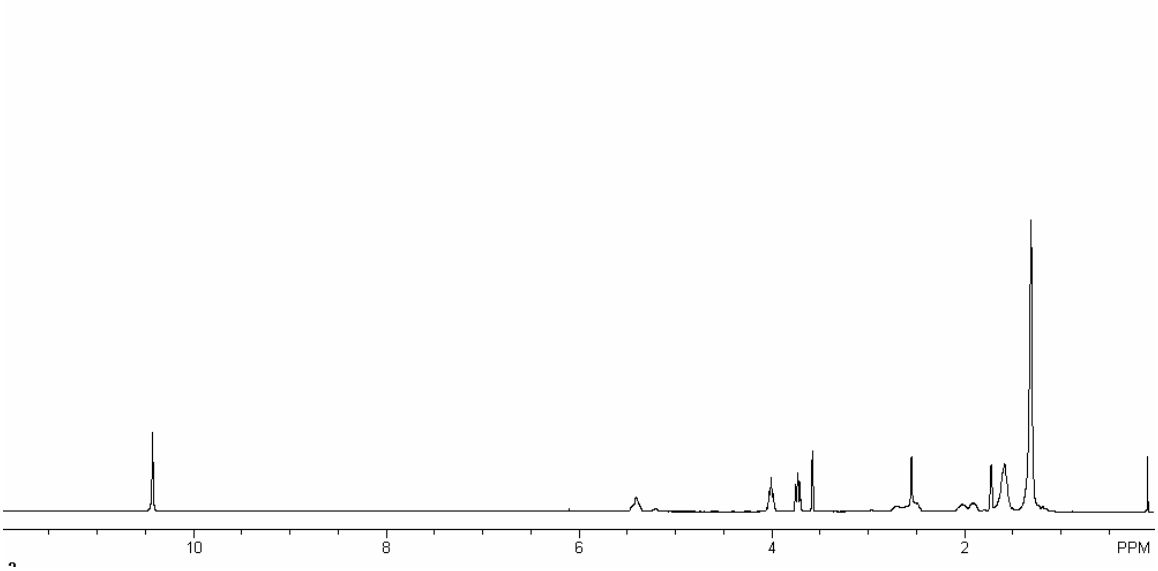


Figure B.8. ^{1}H NMR spectra of **2(poly-2)**.

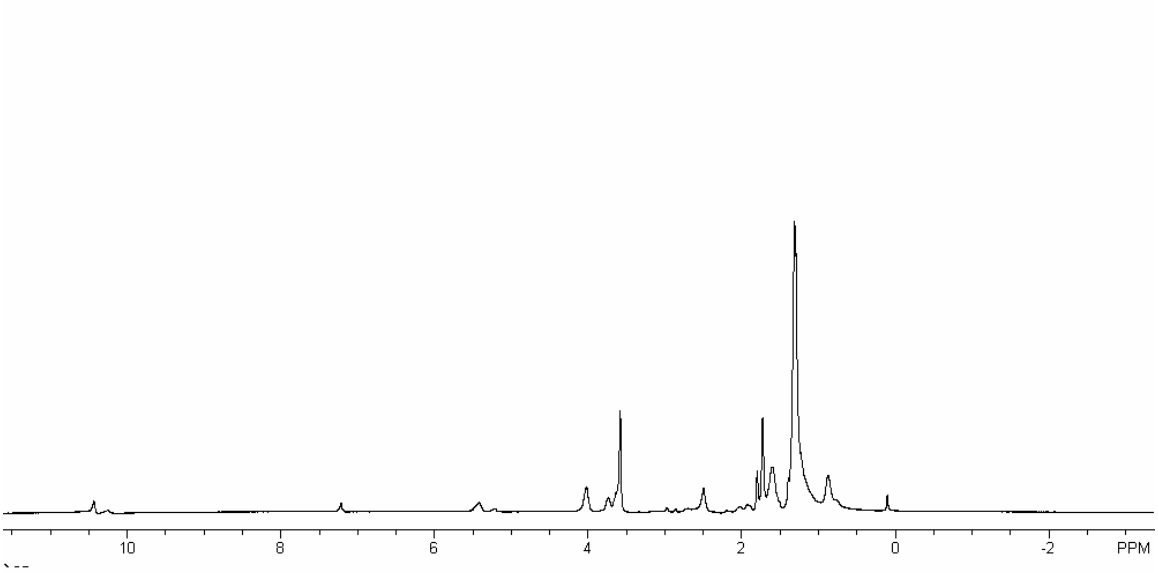


Figure B.9. ^{1}H NMR spectra of **2(block co-poly-1:2)**.

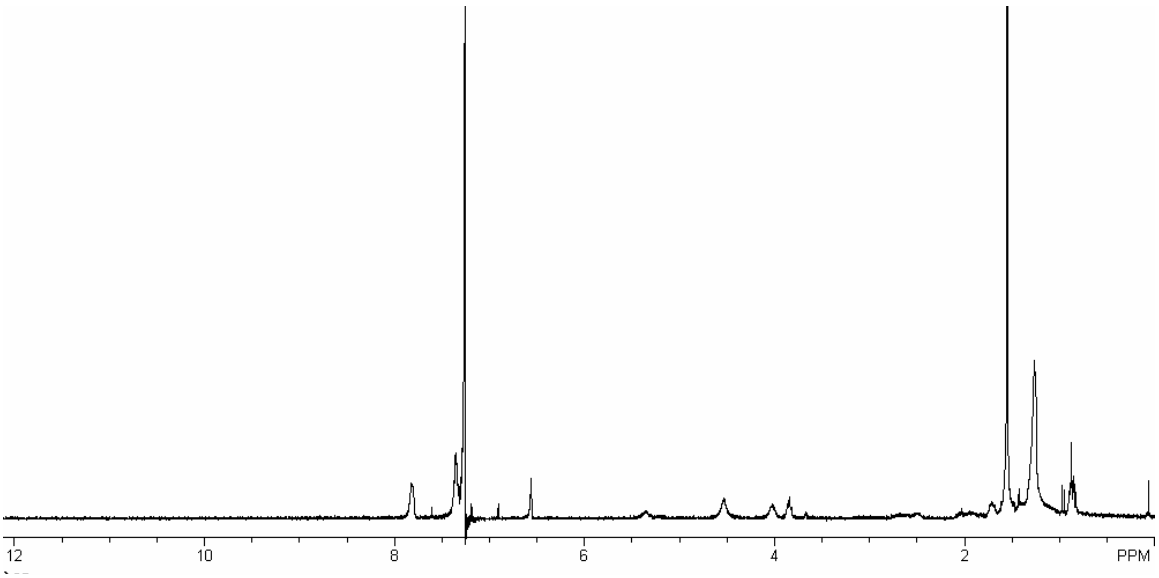


Figure B.10. ^{1}H NMR spectra of **3(1)**

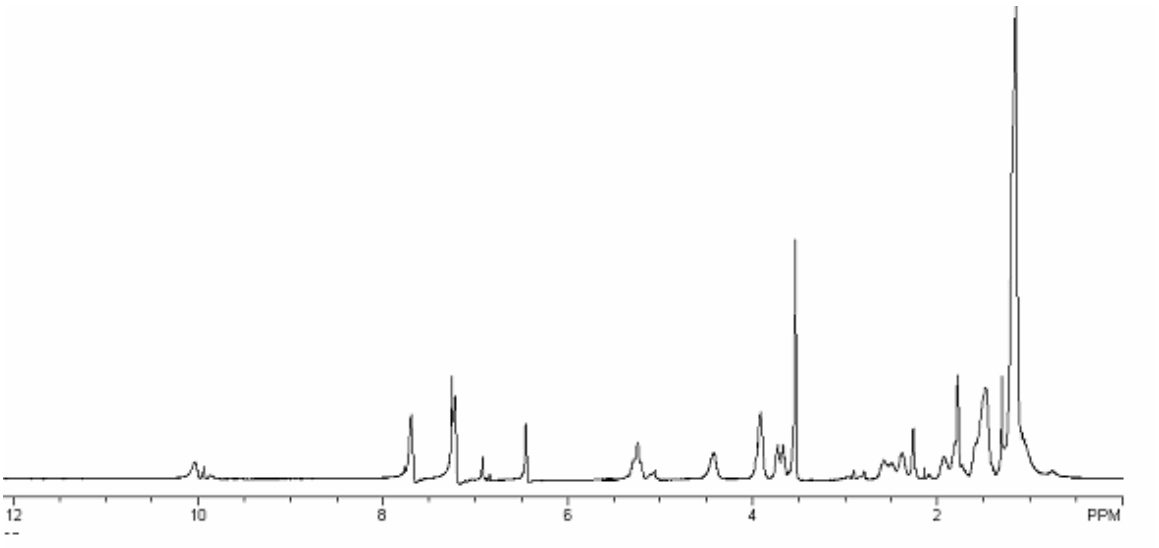


Figure B.11. ^{1}H NMR spectra of **3(1:2:3 triblock copolymer)**

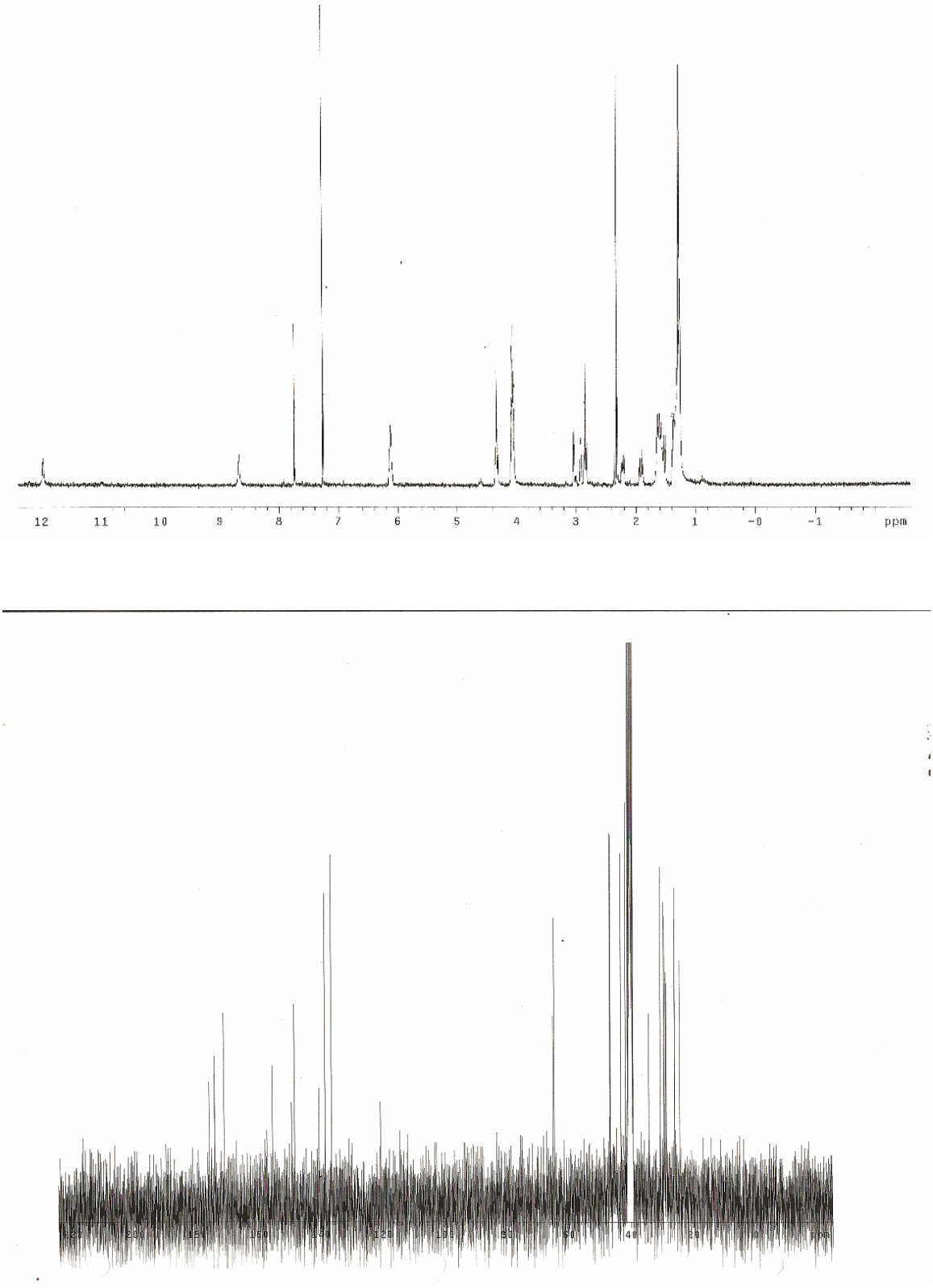


Figure B.12. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **4(2)**

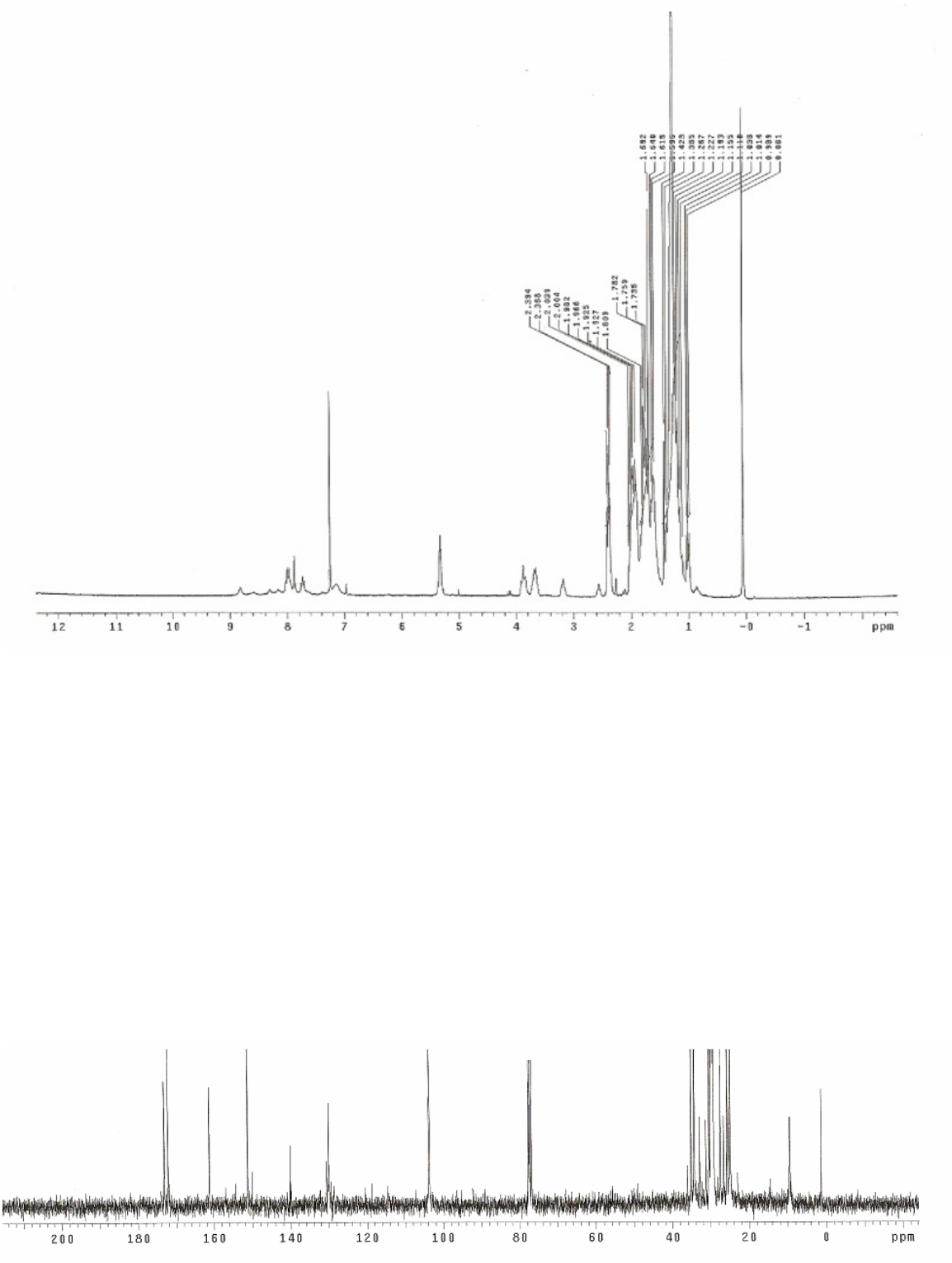


Figure B.13. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **4(9)**.

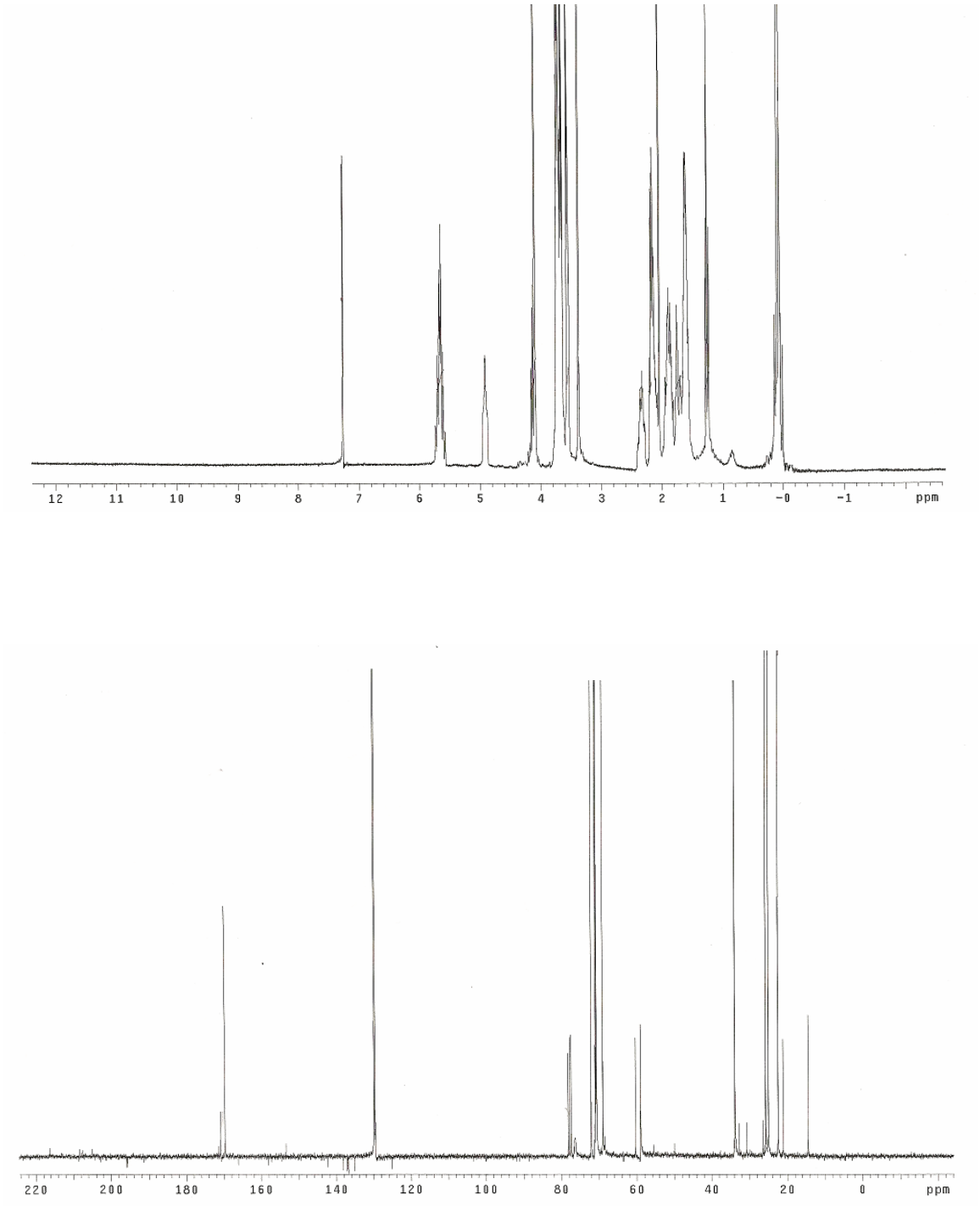


Figure B.14. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **4(4)**.

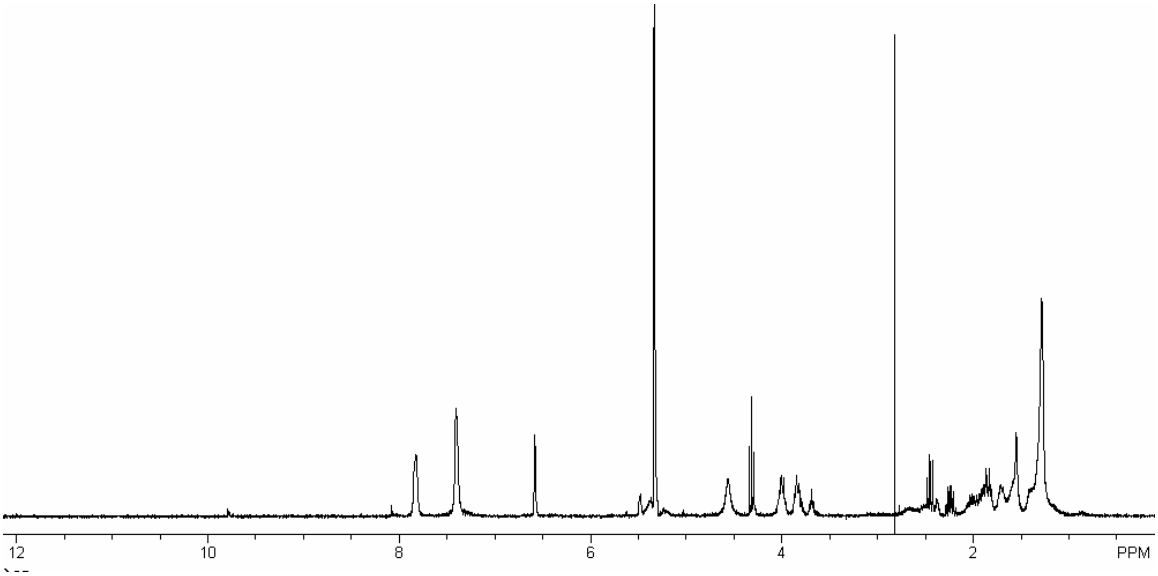


Figure B.15. ^{1}H NMR spectra of **4(poly-A)**.

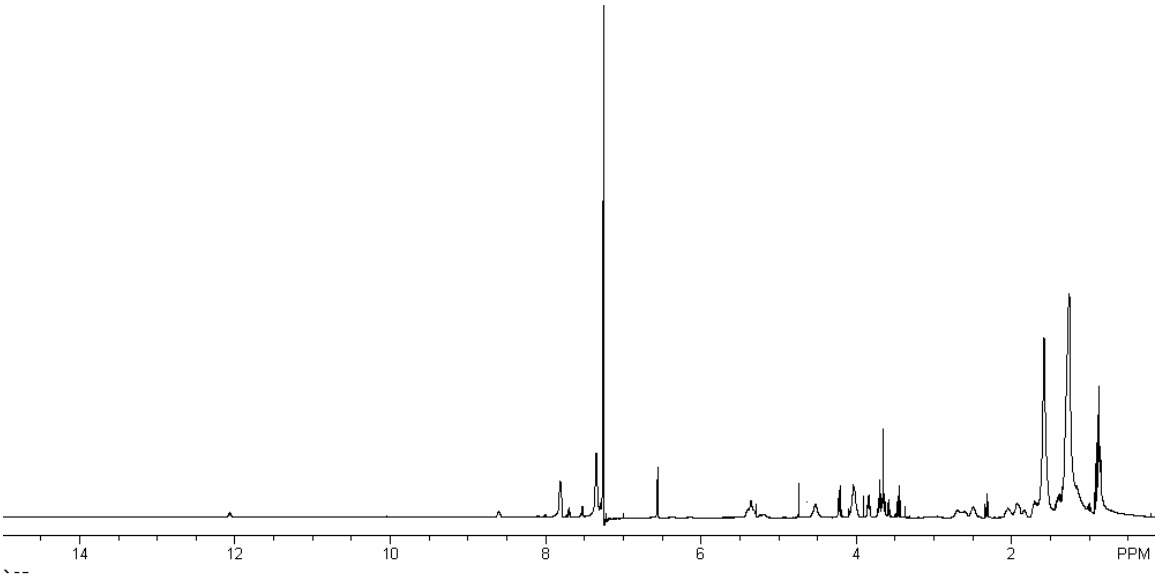


Figure B.16. ^{1}H NMR spectra of **4(poly-B)**.

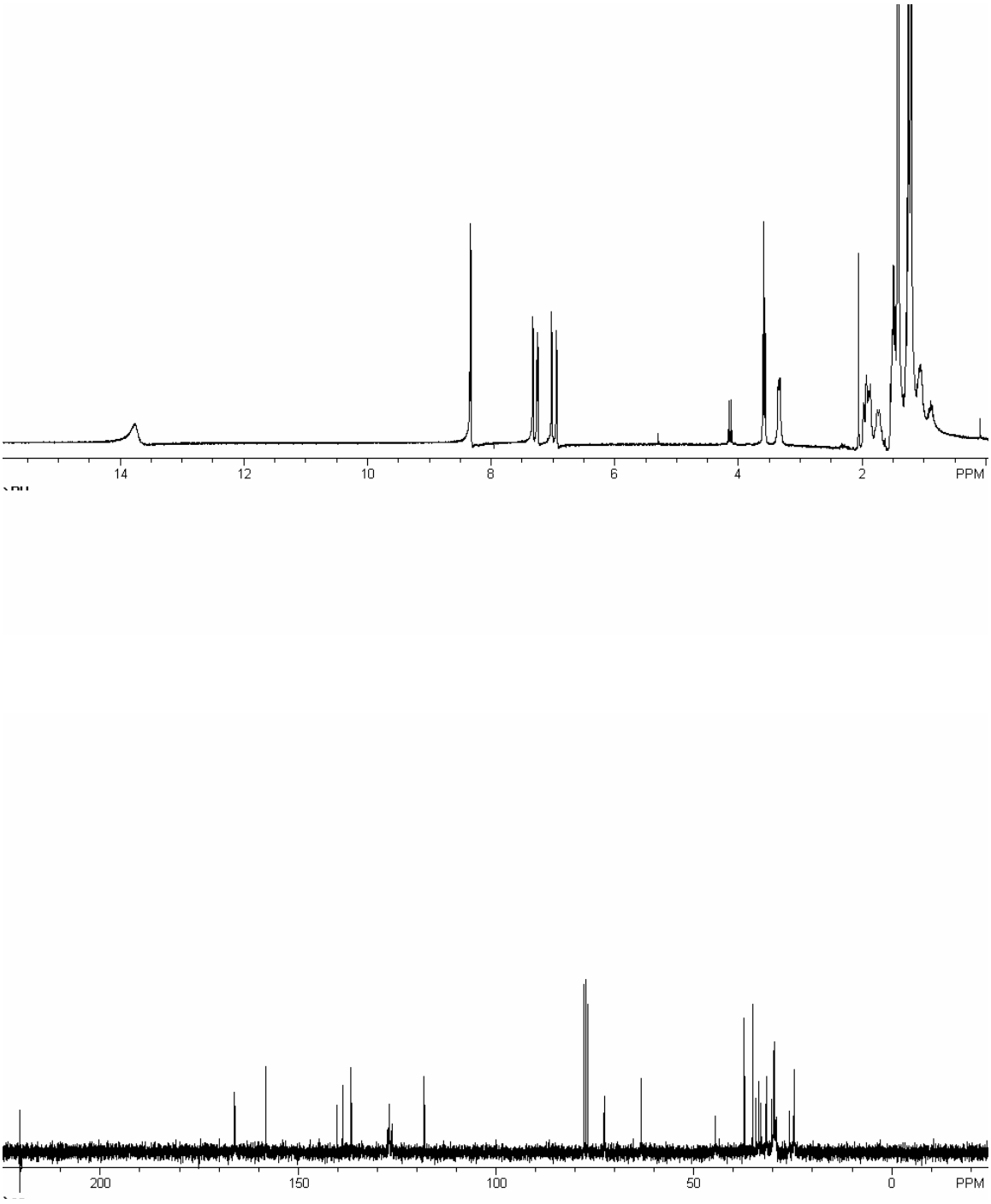


Figure B.17. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **A(4f)**.

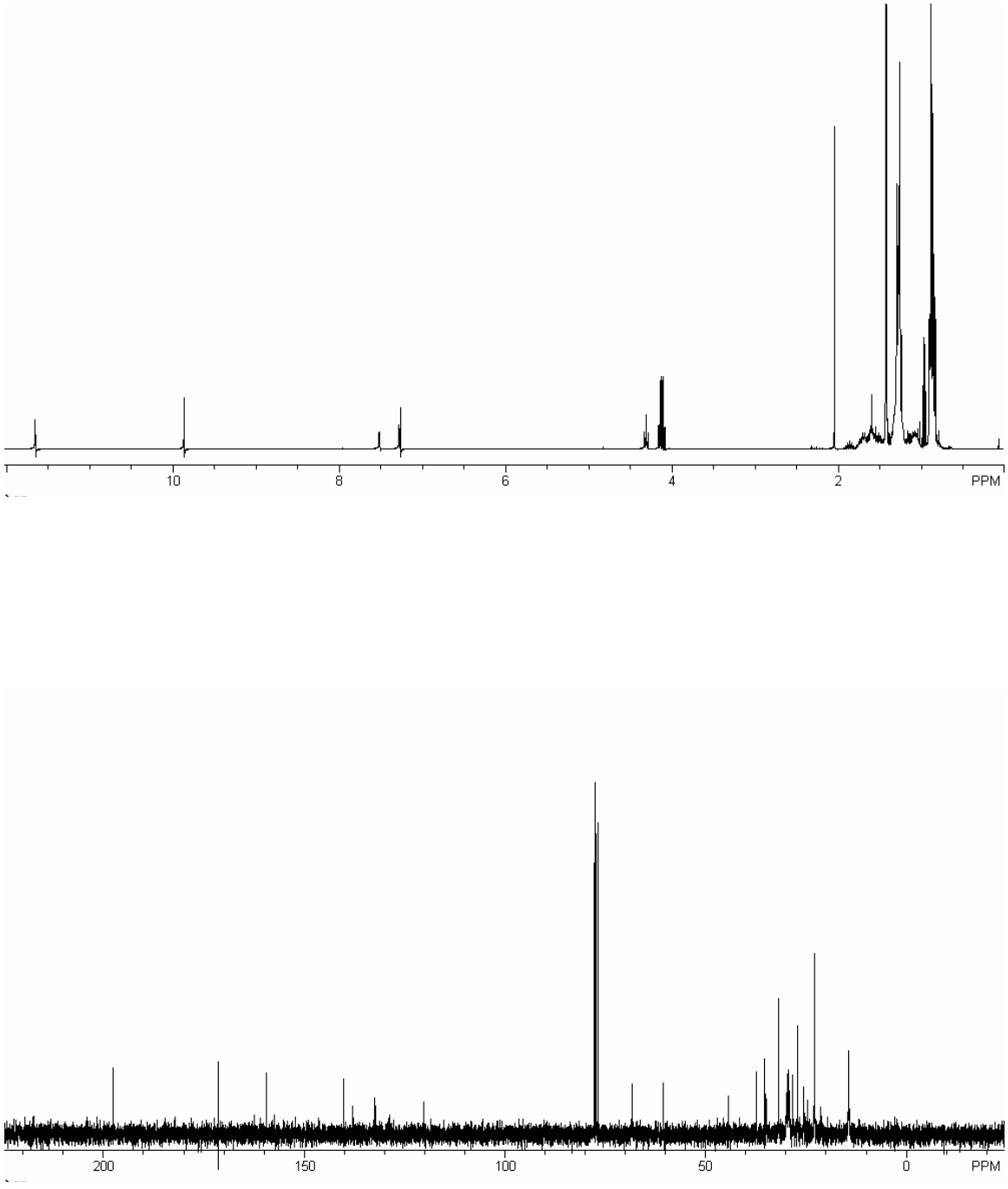


Figure B.18. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **A(2f)**.

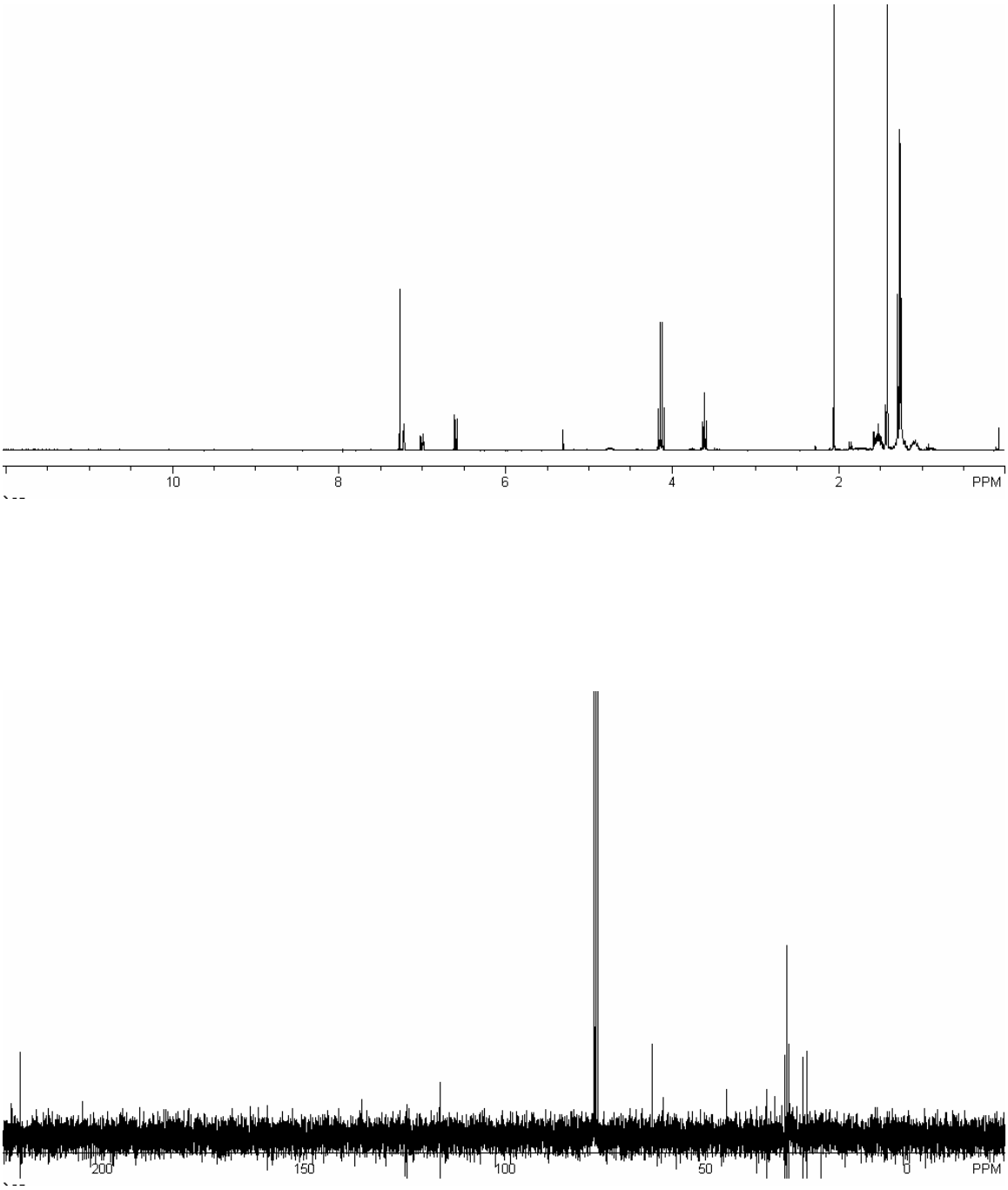


Figure B.19. ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **A(2-*tert*-Butyl-4-(6'-carboxy-1',1"-dimethylhexyl)phenol)**

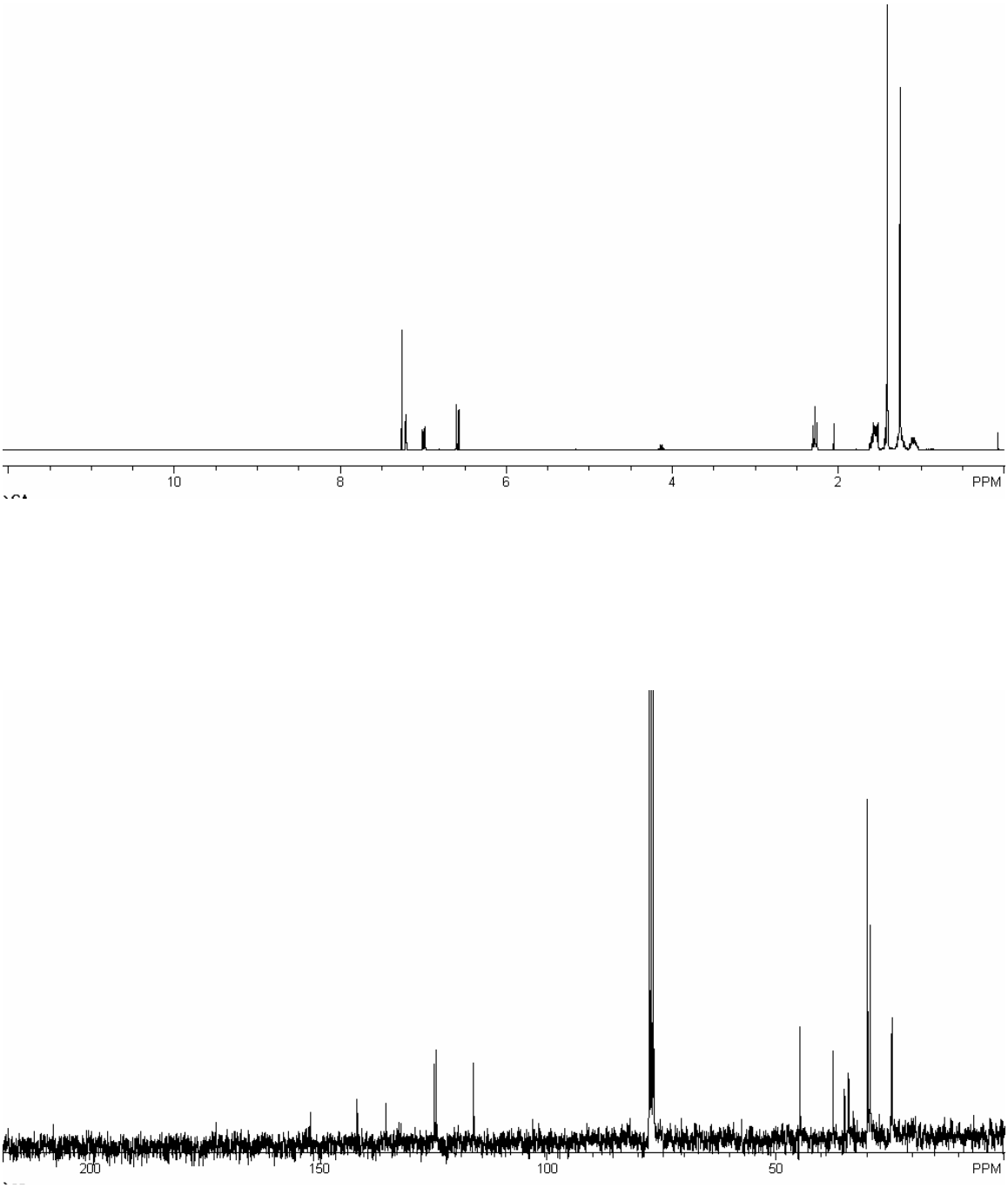


Figure B.20 ^{1}H NMR (top) and ^{13}C NMR spectra (bottom) of **A(2-*tert*-Butyl-4,6'-carboxy-1',1'-dimethylhexylphenol)**

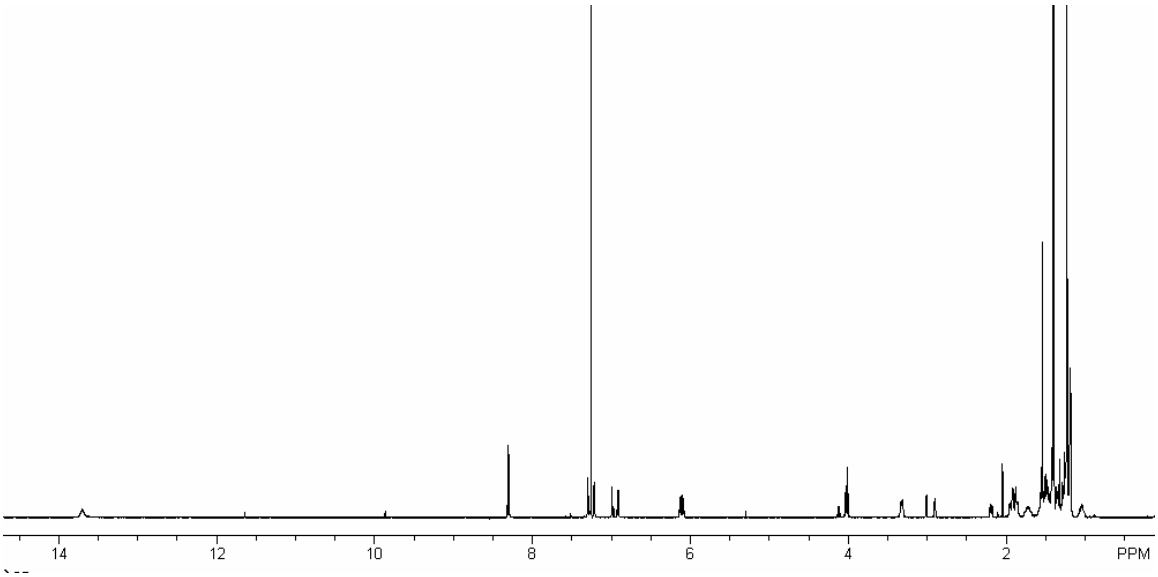


Figure B.21. ^{1}H NMR spectra of **A(8)**.

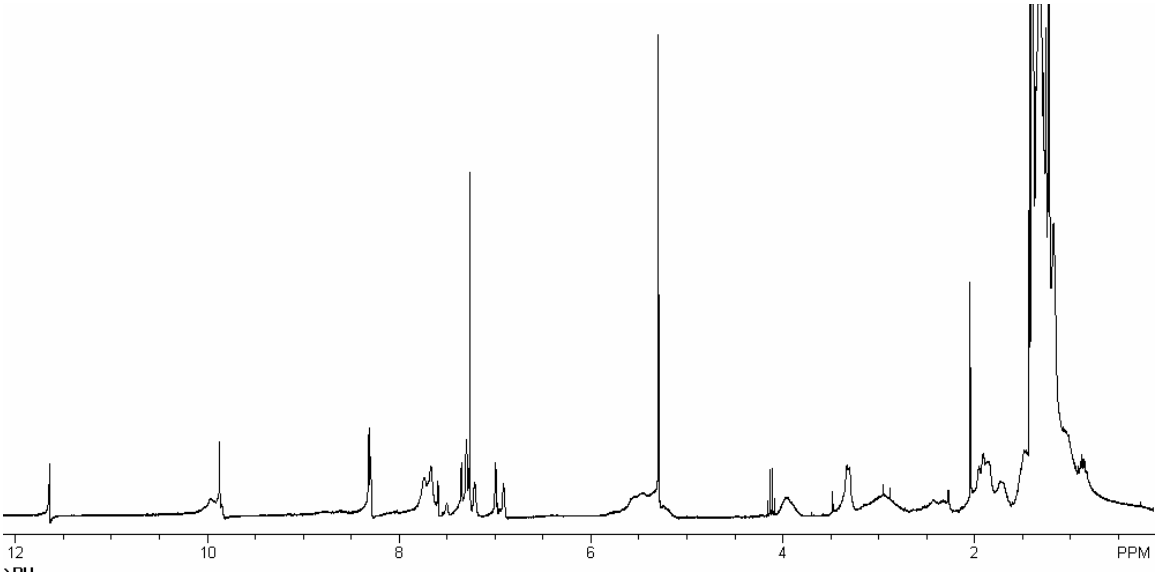


Figure B.22. ^{1}H NMR spectra of **A(poly-8)**.

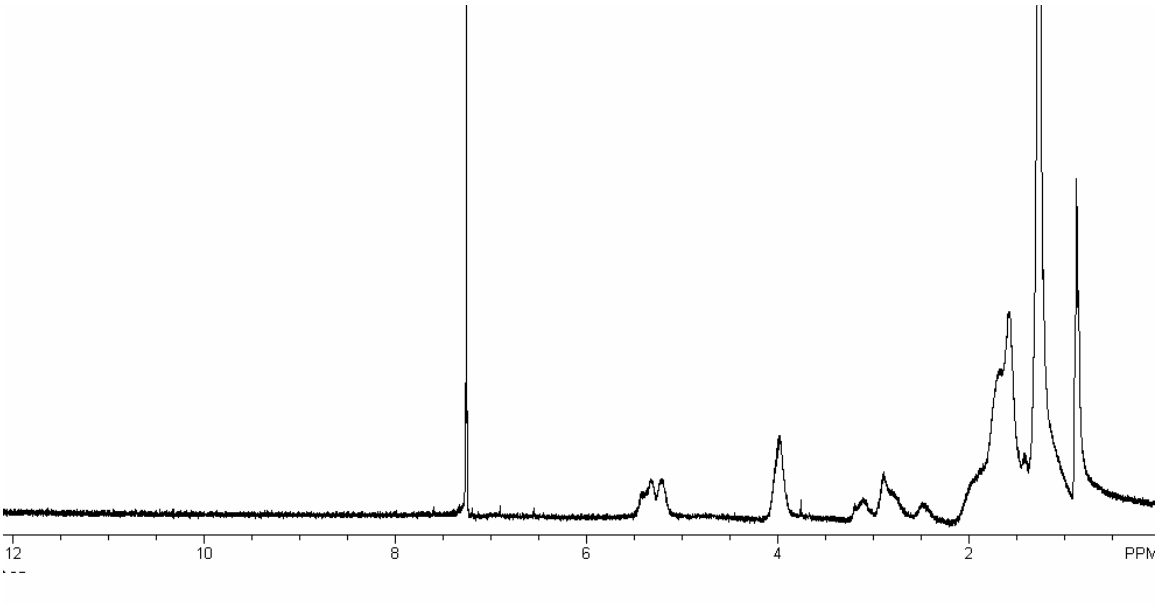


Figure B.23. ^{1}H NMR spectra of **A(10)**.

B.2 Representative ITC Binding Isotherms

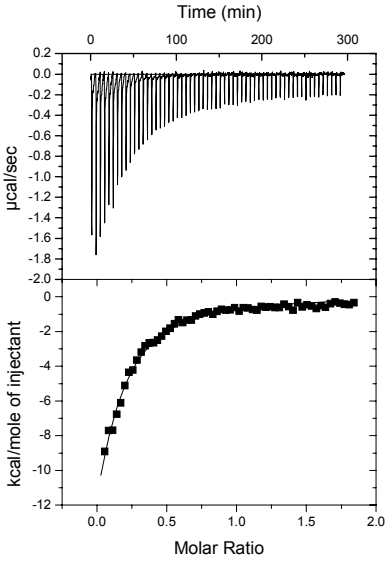


Figure B.24. ITC Binding Isotherm of 4(**Poly-A: poly-B'**)

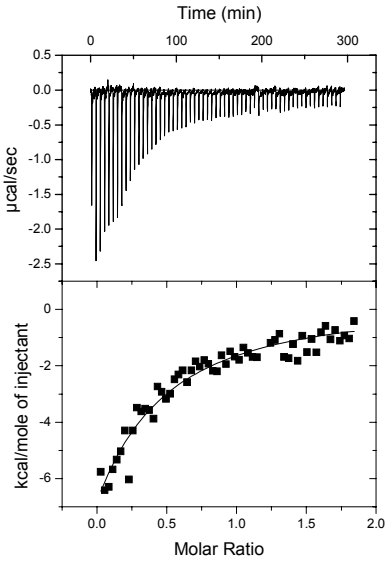


Figure B.25. ITC Binding Isotherm of 4**(Poly-A: 5):(poly-B': 6)**

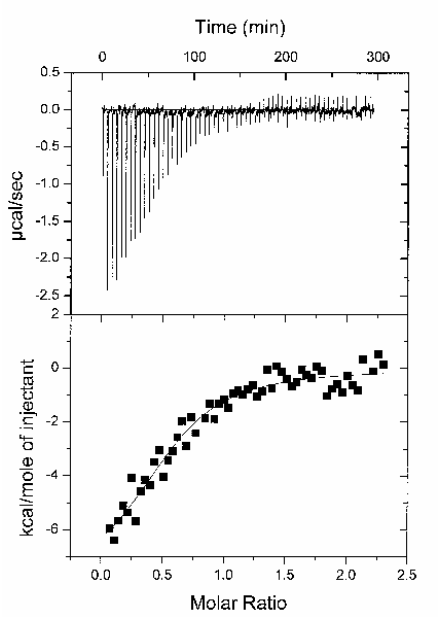


Figure B.26. ITC Binding Isotherm of 4**(Poly-A):(poly-B)**

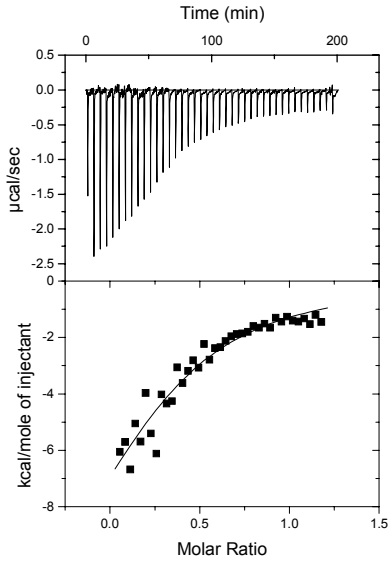


Figure B.27. ITC Binding Isotherm of 4**(Poly-A:5):(poly-B:6)**

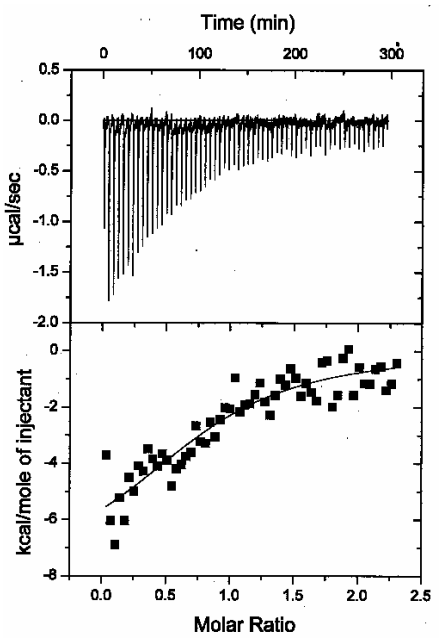


Figure B.28. ITC Binding Isotherm of 4**(Poly-A:5):(poly-B)**

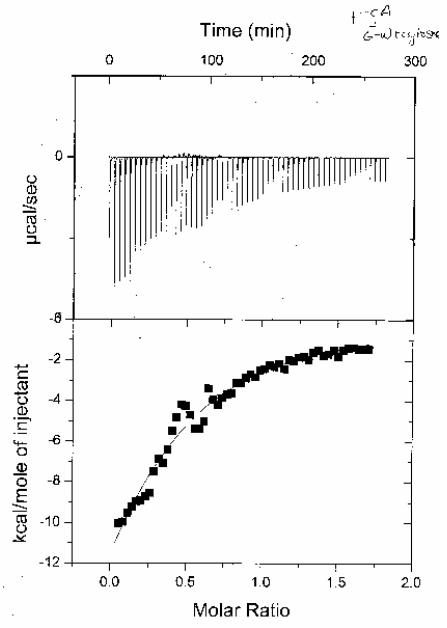


Figure B.29. ITC Binding Isotherm of 4**(Poly-A):(poly-B:6)**