I, Xinjun Yu, hereby submit this original work as part of the requirements for the degree of Doctor of Philosophy in Chemistry.

It is entitled:
Synthesis and characterization of self-assembling polymers using hydrogen bonding or hydrophobic effect

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Synthesis and characterization of self-assembling polymers using hydrogen bonding or hydrophobic effect

A dissertation submitted to the Graduate School of the University of Cincinnati in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in the Department of Chemistry of the College of Arts and Sciences by

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September 2015

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Abstract of Dissertation

This dissertation is mainly based on the works of synthesis and characterization of self-assembling polymers using hydrogen bonding or hydrophobic interactions. Firstly, \(N\)-alkyl urea peptoid oligomer was synthesized as backbone of supramolecular polymers through three step repetition cycles with high yield. One \(N\)-alkyl urea peptoid precursor was explored to simplify the synthetic process. 4 different functional groups were converted from one precursor. Then 2-ureido-4[1H]-pyrimidinone (UPy) group which is a quadruple hydrogen bonding system was incorporated to \(N\)-alkyl urea peptoid oligomers to generate supramolecules. With the experience of UPy unit, we further explored UPy containing monomer to make organogelators. Three different monomers with different \(T_g\) values were copolymerized using reversible addition-fragmentation chain-transfer (RAFT) polymerization. Organogels were afforded in both chloroform and dichlorobenzene. Critical gelation concentration and mechanic properties of organogels were examined. Cooperating another novel monomer containing pyrene unit to the above copolymers, fluorescent organogels were achieved which were suitable for potential up-conversion applications. In addition to pyrene, anthracene is another molecule which shows great up-conversion property. A series of Poly[(9-anthrylmethyl methacrylate)-co-(methyl methacrylate)] (Poly(AnMMA-co-MMA)) with different AnMMA ratios were synthesized via RAFT polymerization, resulting in tunable inter-chromophore distances. These polymers can serve as emitters, with PtOEP as sensitizer, in triplet-triplet annihilation up-conversion (TTA-UC) systems. TTA-UC intensity of the Poly(AnMMA-co-MMA)/PtOEP mixtures displays interesting dependence on the AnMMA ratio in the polymer. Interactions between chromophores on the same polymer chain play the key role in affecting the TTA-UC intensity in these
systems. It is critical to minimize intra-chain chromophore quenching in order to achieve high UC intensity. Hydrophobic effect was used to obtain a hybrid photosensitizer. By integrating amphiphilic block copolymer poly(N-isopropylacrylamide-b-styrene) (PNIPAAm-b-styrene) stabilized silver nanoparticles (Ag NPs) with hematoporphyrin (HP), HP was trapped by polystyrene block through hydrophobic effects. Hydrophilic block can increase the solubility of this photosensitizer in aqueous solution. This hybrid photosensitizer was demonstrated to enhance singlet oxygen production. Finally, a self-immolative polymer was made with a kinetically stable polymer backbone, whose chain end can respond to external stimulus by triggering a head-to-tail depolymerization. Electrospinning was used to fabricate nano-scale fibers which can be utilized in potential drug delivery system.
Acknowledgement

First of all, I would like to express my sincere gratitude to my advisor Dr. Neil Ayres for his continuous support and guidance over the past four years. I thank him for accepting me in the research group and help me growth from a fresh bachelor graduate to a polymer material scientist with his patience, motivation and immense knowledge. I also deeply thank him for giving me a lot of freedom with the direction of my project and pushed me to read more and more research papers for expanding my knowledge when I first joined the group which built me a strong polymer background. I really appreciate him for setting high standard for pursuing good science. I could not have imagined having a better advisor and mentor for my Ph. D study.

Besides my advisor, I would like to thank the rest of my thesis committee: Dr. Smithrud and Dr. Zhang, for their insightful comments, encouragement and also their challenging questions from different perspective which helps me think more during my PhD study.

Also, I would like to thank members from Ayres’ group, past and present for their contributions to this thesis and kindness to me. Sincerely many thanks to Xiaoping Chen, Leanne Taylor, Yongshun Huang, Qinyuan chai, Mary Warmin and Brett Bolton. Without them, my life in the lab would be totally different, so thank all of them for their help in and out of the lab.

Finally, and most importantly, I would like to thank my parents, Zhenchao Yu and Yuling Wang, for their faith in me and constant support to me in the past 26 years. They support every decision I made and they are my motivation to strive to do my best in the future.
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Chapter 1 General introduction

1.1 Polymer self-assembly

Self-assembly is a process of automatic arrangement of components into ordered aggregates or structures without external force.\(^1\) Self-assembling structures can be developed in synthetic polymer systems via inter- and/or intra-molecular interactions. Non-covalent interactions such as H-bonding, hydrophobic effects and π-π interactions play an important role in driving this process. In the following sections, we will discuss the non-covalent driving forces for self-assembly in detail.

1.1.1 Self-assembly from hydrogen-bonding interactions (H-bonding)

A large variety of organic molecules can self-assemble into different structures driven by complementary H-bonding. A single H-bond is rather weak and its application in well-defined assemblies is limited by low stability. There are two strategies to strengthen H-bond interactions. The first one is to make a single molecule only has one H-bond site, and then covalently connect those molecules.\(^2\) Thus the overall thermodynamic stability is improved exponentially.\(^3\) For example in Figure 1, the oligomer made of 1,1-bis(4-amino-3,5-dimethylphenyl) cyclohexane has multiple H-bond sites which can increase the stability of this structure.\(^4\)
Figure 1. The structure of 1,1-bis(4-amino-3,5-dimethylphenyl)cyclohexane zipper complex.4

The second way is to synthesize a molecule that has a rigid structure containing multiple H-bond sites. The more H-bonding sites a molecule has, the more stable the structure is. Multiple H-bond system varies from two to six H-bond sites.5-9 Figure 2 shows some examples of these multiple H-bond systems.10-13

![Figure 2](image)

Figure 2. a) 2-Acrylaminopyridine (double); b) melamine and succinimide (triple); c) 2,7-diamido-1,8-naphthyridine (Napy) and 2-ureido-4[1H]-pyrimidone (UPy) (quadruple).

Among these systems, UPy is one of the most commonly used H-bonding units. Meijer and co-workers did a lot of study on this particular unit (Figure 3).14,15 The UPy group has both H-bond donor/donor/accepter/accepter (DDAA) and donor/accepter/donor/accepter (DADA) patterns to form self-complimentary dimers. Both DDAA and DADA patterns are possible in chloroform with a dimerization constant larger than 10^6 M^{-1}. Introducing electron-withdrawing group at the 6-position can change the arrays from DDAA which is a keto to DADA which is an enol. Meijer’s group synthesized a series of UPy derivatives and UPy-polymer conjugates to further exploit this system.16-18
Figure 3. Equilibria between tautomeric forms between monomer and dimer of 2-ureido-4[1H]-pyrimidone.\textsuperscript{14}

Dankers and coworkers reported a protein delivery hydrogel containing this hydrogen bonding unit.\textsuperscript{19} UPy-end functionalized poly(ethylene glycol) (PEG) can self-assemble into linear supramolecular polymers using H-bonding which provides the material self-healing properties. Supramolecular rubbers are made with self-heal ability from fatty acid and urea.\textsuperscript{20} Compared to covalently crosslinked rubbers, supramolecular rubbers are thermoreversible due to reversibility of H-bond interactions. The afforded self-assembled supramolecular polymer possessed easy processibility and recyclablility, revealing promise applications in both industry and academia.

Inspired by the structure of DNA, self-assembly of secondary structures can be obtained via H-bond interactions. Meijer’s group reported helical self-assembled polymers from cooperative stacking of hydrogen-bonded pairs (shown in Figure 4).\textsuperscript{21} The dimerization of two self-complementary quadruple hydrogen bonding units lead to columnar
polymeric architectures and the structure and helicity of polymers can be tuned by the side group.

![Figure 4. A schematic representation of helix structures by dimerization of UPy units.](image)

In this thesis, we will report the synthesis of a quadruple H-bonding unit UPy to fulfill self-assembly architectures. In chapter 2, this H-bond unit served as a connector to link N-alkyl urea peptoid oligomers leading to self-assembly linear supramolecular polymers. And we further modified methyl methacrylate with UPy functional group to make a UPy containing monomer. By copolymerizing this monomer with several other monomers, organogelators were obtained as a consequence of self-assembled polymer chains through H-bonding interactions.

**1.1.2 Self-assembly from hydrophobic effects**

Block copolymers bear two or more chemically distinct and immiscible blocks connected through covalent bonds. In general, immiscible blocks of copolymers will microphase
separate at certain compositions into a variety of morphologies such as spheres, cylinders, lamellae, vesicles, and hierarchical assemblies (shown in Figure 5).  

![Diagram showing equilibrium morphologies of AB diblock copolymers, theoretical phase diagram of AB diblocks, and experimental phase portrait of polyisoprene-block-polystyrene copolymers.]

Figure 5. a) Equilibrium morphologies of AB diblock copolymers; b) theoretical phase diagram of AB diblocks; c) experimental phase portrait of polyisoprene-block-polystyrene copolymers.

The self-assembly process is driven by an unfavorable mixing enthalpy along with small mixing entropy. Due to the covalent bond connecting the blocks, there is no macroscopic phase separation. There are three factors affecting this process: 1) volume fraction of A and B blocks, 2) degree of polymerization and 3) the Flory–Huggins parameters, $\chi_{AB}$. The $\chi$-parameter specifies the degree of incompatibility between the A and B blocks, which drives the phase separation. The relationship between $\chi_{AB}$ and Temperature is shown in equation 1.  

\[
\chi_{AB} = \left( \frac{Z}{k_BT} \right) \left[ \varepsilon_{AB} - \frac{1}{2}(\varepsilon_{AA} + \varepsilon_{BB}) \right] \quad (1)
\]
where $z$ is the number of nearest neighbours per repeat unit in the polymer, $k_B$ the Boltzman constant, $k_B T$ is the thermal energy, and $\varepsilon_{AB}$, $\varepsilon_{AA}$, and $\varepsilon_{BB}$ are the interaction energies per repeat unit of A–B, A–A, and B–B, respectively. A lot of work has been done to investigate the process in details.\textsuperscript{22, 24-26} We will focus on applications derived from hydrophobic effects.

Diblock copolymers can be categorized as amphiphilic, double hydrophilic, and double hydrophobic according to the different solubility of each block in water.\textsuperscript{27-29} Amphiphilic block copolymers, as the most extensively studied block copolymers, attract enormous attention in various applications such as drug and gene delivery,\textsuperscript{30} biological imaging,\textsuperscript{31} semiconductor microelectronics,\textsuperscript{32} and nanoreactors.\textsuperscript{33} Various morphologies can be obtained from self-assembly of amphiphilic block copolymers in solution. Figure 6 shows the summary of different morphologies derived from poly(styrene-$b$-acryl acid) (P(Sty-$b$-AA)) block copolymers.
Figure 6. Transmission electron microscopy (TEM) micrographs and corresponding schematic diagrams of various morphologies formed from amphiphilic PS<sub>m-b</sub>-PAA<sub>n</sub> copolymers.  

Among those different morphologies, micelles have been extensively reported. A variety of species such as hydrophobic drugs, genes, proteins, and fluorescence probes can be encapsulated in the hydrophobic cores of micelles. Composition and concentration of block copolymers play important roles in determine the size and shape of micelles. We will take P(Sty-b-AA) which has been well studied as an example to understand the process of micelle formation. In normal case, P(Sty-b-AA) with a relatively long PAA
chain will form spherical micelles. The stretching of the PS chains in the core increases as the core size increases, but the stretching cannot always increase since it decreases entropy of the PS chains in the core. At some point, in order to minimize the total free energy of the system by reducing the stretching of the PS chains, the aggregates change from spheres to cylinders and lamellae/vesicles, as a consequence of decreased corona chain length. Polymer concentration also affects the formation of micelles through affecting Flory–Huggins interaction (\(\chi\)-parameter) between the hydrophobic blocks and water.\(^{41}\)

In chapter 5 of this thesis, we will report a hybrid photosensitizer made from self-assembly of amphiphilic block copolymers onto silver nanoparticles. An amphiphilic block copolymer, poly(\(N\)-isopropylacrylamide-\(b\)-styrene) (P(NIPAAm-\(b\)-styrene)), was synthesized by reversible addition–fragmentation chain transfer (RAFT) polymerization to stabilize silver nanoparticles in water. As a consequence of hydrophobic effect, lipophilic photosensitizer hematoporphyrin was trapped by polystyrene block which is directly connected to silver surface via silver-S bond. PNIPAAm block which is at outer layer of this assembly can increase the solubility of the hybrid photosensitizer in water. Thus, enhanced singlet oxygen production was observed and this hybrid assembly was demonstrated to be useful tool to inactivate bacteria.

1.1.3 Other non-covalent bond interactions

Other weak non-covalent bond interactions such as \(\pi\)-\(\pi\) stacking, host-guest interaction and chiral centers, can also contribute to the self-assembly of polymeric materials. Hayes’ group developed a supramolecular polymer which is able to self-assemble
through electronically complementary π-π stacking interactions.\textsuperscript{42} This novel perylene-based polymer demonstrates its ability to tailor π-π stacking interactions to produce healable materials.

An adamantly group end-functionalized poly(N-isopropylacrylamide) (PNIPAAm) and a β-cyclodextrin end-functionalized poly(4-vinylpyridine) (P4VP) were reported to self-assemble into two distinctly different micelles in response to pH and temperature in dilute aqueous solution through host-guest interaction (shown in Figure 7).\textsuperscript{43}

Figure 7. Schematic illustration of the micellization between two polymer chains.\textsuperscript{43}

Boden’s group reported a chiral rod-like molecule to investigate the generic self-assembling properties of β-sheet forming peptides.\textsuperscript{44} This hierarchical model also provides a guide to novel macromolecules based on a variety of self-assembling chiral units.

1.2 Polymer synthesis

1.2.1 Reversible addition–fragmentation chain transfer polymerization (RAFT)
There are many ways to facilitate the self-assembly of polymers according to what we discussed in the previous section. Next, we will focus on the synthesis of polymers. Among various strategies for polymerization, radical polymerization is one of the most widely used processes for producing high molecular weight molecules. Control over molecular weight as well as molecular weight distribution is of great importance. Three commonly used methods to control molecular weight and dispersity in radical polymerizations are nitroxide-mediated polymerization (NMP),\textsuperscript{45} atom transfer radical polymerization (ATRP),\textsuperscript{46} and reversible addition–fragmentation chain transfer polymerization (RAFT).\textsuperscript{47} Among these methods, RAFT polymerization has drawn tremendous attention in recent years due to its comparability with a wide range of reaction conditions and diversity of monomers including functional monomers.\textsuperscript{48-50} We will discuss this strategy in detail in the following part.

**Mechanism of RAFT polymerization**

Reversible addition fragmentation chain transfer (RAFT) polymerization is a controlled/"living" free radical polymerization technique. The polymerization uses reversible degenerative chain transfer reactions between thiocarbonylthio chain transfer agents (CTAs), usually referred as RAFT agents. The proposed mechanism is shown in Figure 8.\textsuperscript{49} Initiation and radical–radical termination are similar compared with conventional radical polymerization. In the pre-equilibrium step, the oligomeric radicals react with the original RAFT agent (1) to create a radical intermediate that can either fragment back to the original RAFT agent (1) or to an oligomeric RAFT agent (3). The reaction does not reach the core-equilibrium until all of the R groups have been expelled from the RAFT agent and have initiated the bulk of the polymer chains. Propagation
occurs in the core equilibrium, where the rapid interchange in the chain transfer step insures a low radical concentration, which limits the possibility of termination reactions through combination and disproportionation.

Initiation

\[
\text{Initiator} \xrightarrow{\text{M}} I^* \xrightarrow{\text{P}_1^*} 
\]

Pre-equilibrium

\[
P_m^* + S\text{-}S-R \iff P_m^*\text{-}S^*\text{-}S\text{-}R \iff P_m^*\text{-}S\text{-}S + R^*
\]

Propagation

\[
R^* \xrightarrow{\text{M}} M \xrightarrow{\text{M}} P_n^*
\]

Core-equilibrium

\[
P_n^* + S\text{-}S-P_m \iff P_n^*\text{-}S\text{-}S-P_m \iff P_n^*\text{-}S\text{-}S + P_m^*
\]

Termination

\[
P_n^* + P_m^* \iff P_{n+m}
\]

Figure 8. Mechanism of RAFT polymerization.

In RAFT polymerization, the rate of polymerization is controlled by the concentration of free-radical initiator. A higher initiator concentration leads to faster polymerization through more radicals. The concentration of the RAFT agent in the polymerization controls the molecular weight of afforded polymers since most chains are initiated by the R groups of the RAFT agent, not the free radical initiator. The thiocarbonylthio group serves as a “living end” which can further polymerize different monomers which allows a macro-RAFT agent to initiate a subsequent polymerization.
The structures of the R and Z groups (as shown in Figure 9) play critical role in desired RAFT polymerization. According to the mechanism, the R group should be a good leaving group and efficiently reinitiate monomer in pre-equilibrium step. Steric effects, radical stability, and polar effects are of great significance in determining the leaving and reinitiating ability of an R group.\textsuperscript{51, 52} The Z group should activate the C=S bond and stabilize the formed radical. Too high stability of the Z group will lead to inhibition of the polymerization or retardation since the fragmentation is not preferred.\textsuperscript{53}

When the polymerization is complete or terminated, the thiocarbonylthio end-group will be retained and the polymer isolated as stable materials. This provides the possibility for conjugating RAFT polymer with metal nanoparticles via metal-S bond and also enables RAFT polymers to conjugate with other components though thiol-ene and thiol-yne reactions.\textsuperscript{54, 55}

**Applications of RAFT polymerization**

By polymerizing functional monomers through RAFT polymerization, many applications have been explored.\textsuperscript{56-58} However functionalities in RAFT polymers are not limited to the choice of monomers. They can also be obtained from polymeric chain end groups. Due
to R group and Z group of RAFT agents, chain end functionalities can be introduced into RAFT polymers. Varieties of modifications have been reported to prepare different RAFT agent.

Since RAFT polymerization has a relatively high tolerance for functionality, the pendent group on monomers can be modified for different applications. Pyridyl disulfide ethyl methacrylate was synthesized by Davis and co-workers.\(^5^9\) Disulfide bonds were proven not to affect the polymerization. By reacting with thiol compounds, this monomer can be further modified or conjugated with other molecules. In addition, after cleavage of the disulfide bonds, free thiol was obtained which can react with DOX functionalized maleimide compounds, which can serve as anti-cancer drugs.\(^6^0\)

Monomers bearing azide or alkyne groups enable RAFT polymers to be conjugated to a variety of species, including biologics. Our group reported the synthesis and conjugation of a urea peptoid trimer to a glucose-containing polymer through a copper catalyzed alkyne/azide cycloaddition reaction (Figure 10).\(^6^1\)
Rather than adding functional molecules onto polymer backbones, functionalizing monomers themselves is an alternative way to build functional polymers. In chapter 3 of my thesis, we synthesized UPy modified methacrylate. This monomer can copolymerize with several other monomers through RAFT polymerization to generate polymeric organogelators in both dichlorobenzene and chloroform. Anthracene modified methacrylate monomer also shows unique properties when copolymerized with methacrylate. By tuning the composition between anthracene methacrylate and methyl methacrylate, distance of chromophores can be adjusted to optimize upconversion intensity.\textsuperscript{62} I will discuss this work in details in chapter 4.

In addition to functionalize monomers, RAFT agent can also be functionalized to fulfill various applications. Carboxylic acid is the most commonly used functional group for synthesizing functional polymers. These carboxyl functional groups enable the polymer to further conjugate to peptides, proteins, and carbohydrates via traditional coupling reaction. Shea and coworkers synthesized several mono- and dicarboxylic functional RAFT agents, permitting control over a wide range of monomers, such as acrylate, acrylamide, and styrene.\textsuperscript{63} RAFT agents containing hydroxyl groups have also been developed to generate poly(methyl methacrylate) and poly(n-butyl acrylate) with narrow molecular weight distribution.\textsuperscript{64} Fluorescence motifs are also compatible with RAFT agent. Anthracene and pyrene groups are used to synthesizing RAFT agent followed by polymerization of styrene with controlled molecular weight and poly dispersity.\textsuperscript{65, 66} The resulting fluorescence end group functionalized polymers were demonstrated to have enhanced fluorescence properties in both chloroform and DMF.
By reducing the thiocarbonylthio group, thiol end-functionalized RAFT polymers can be obtained. In chapter 5 of my thesis, we synthesized poly(N-isopropylacrylamide-b-styrene) (P(NIPAAm-b-Sty)) via RAFT polymerization. After reduction using sodium borohydride, this amphiphilic polymer can be conjugated onto silver nanoparticle surface through silver-S bond. The hydrophobic styrene block can trap photosensitizer while hydrophilic NIPAAm block can increase the solubility of this hybrid photosensitizer in water. The polymer was revealed to enhance inactivation of bacteria.

Guan’s group reported a block copolymer incorporating UPy as end group to generate a material which can self-healing when treated with heat (Figure 11). UPy group, as hydrogen bonding units was used to modify RAFT agent. This quadruple hydrogen bonding unit provides the RAFT polymers self-healing property in bulk condition.

![Figure 11](image1.png)

Figure 11. a) Conventional triblock copolymer elastomer. b) Supramolecular triblock copolymer elastomer.

We demonstrated that RAFT polymerization can be used to make “graft from” molecular brush by modifying urea peptoids with trithiocarbonyl group. As shown in Figure 12, step growth polymerization was used by reacting diamine with diisocynate, to build a
urea peptoid backbone from an alkyne group functionalized urea peptoid oligomer.\textsuperscript{68} Since we have already proved that CuAAC is compatible with urea peptoid, an azide modified RAFT chain transfer agent was then coupled to this polymer backbone to sequentially polymerize styrene and tert-butyl acrylate block polymer arms. After removing tert-butyl groups, this molecular brush can form micelles in aqueous solution.

![Molecular brush made from N-alkyl urea peptoid polymers.](image)

In conclusion, RAFT polymerization is an appropriate way to be considered to prepare functional polymers with good molecular weight and molecular weight distribution control.

1.3 References


60. Z. Jia, L. Wong, T. P. Davis and V. Bulmus, *Biomacromolecules*, **2008**, 9, 3106-3113.


Chapter 2. Synthesis of various $N$-alkyl-$N,N$-linked urea oligomers from a single precursor and subsequent supramolecular polymerization

2.1 Abstract

An $N$-alkyl-$N,N$-linked urea oligomer ($N$-alkyl urea peptoid) containing methoxymethyl $N$-alkyl groups has been synthesized and the ether groups converted to hydroxyl pendant groups using HCl. The afforded hydroxyl groups were used in a series of functional group interconversions to prepare oligomers containing alkyl chloride, alkyl azide and carboxylic acid moieties. Subsequently, 2-ureido-4[1H]-pyrimidinone groups were incorporated at the terminal amines of the $N$-alkyl urea peptoid oligomers leading to the formation of supramolecular polymers in CHCl$_3$ solutions. Diffusion-Ordered Spectroscopy and concentration dependent viscometry experiments were used to demonstrate the presence of polymer species.

2.2 Introduction

The potential of combining the diversity of organic chemistry with the self-assembly of biological molecules is attracting scientists with the promise of creating synthetic macromolecules that possess functions and abilities found in their natural analogues.$^{1-2}$ One way to achieve these polymers is by preparing of polypeptoid materials.$^{3-4}$ Peptoids are synthetic analogue of peptides based on an $N$-acyl glycine repeating motif.$^5$ Compared to the corresponding peptide, the pendant functionality in a peptoid is on the amide nitrogen rather than the $\alpha$-carbon, this has the consequence of losing the hydrogen bonding capability and inherent chirality of peptides. Despite this apparent drawback, polypeptoid materials have been demonstrated to possess many attractive
properties including self-assembly,\textsuperscript{6} thermoresponsiveness,\textsuperscript{7-8} gelation,\textsuperscript{9} and interfacial properties when tethered to a surface.\textsuperscript{10-12} Our lab has worked on an alternative structure to the peptoids with a a solution-based synthesis, namely \textit{N}-alkyl-\textit{N},\textit{N}-linked urea oligomers, that we have termed “\textit{N}-alkyl urea peptoids” in association to peptoids. In these molecules, urea functional groups are linked by ethylene spacers, and one of the urea N-atoms bears the pendant functional group. We have used \textit{N}-alkyl urea peptoids in polymer systems through coupling the oligomers with polymers prepared using reversible addition fragmentation chain transfer (RAFT) polymerization,\textsuperscript{13} in triblock copolymers with poly(ethylene glycol) blocks,\textsuperscript{14} as the backbone of comb-type copolymers,\textsuperscript{15} and in the synthesis of a glycosaminoglycan mimicking polymer.\textsuperscript{16} We have controlled the sequence of the \textit{N}-alkyl groups in the oligomers in our previous works by virtue of the synthesis protocols. This is an advantageous feature that could lead towards sequence controlled polymers; an area of polymer chemistry that continues to attract increasing interest.\textsuperscript{17-19} However, for many applications of polymer materials, such precise control is unnecessary. Therefore it would be beneficial synthetically to be able to prepare one “precursor” \textit{N}-alkyl urea peptoid oligomer that we could then modify with many different chemical functionalities depending upon the application envisioned. Furthermore, it would beneficial if these oligomers could be easily (co)polymerized.

Supramolecular polymers are polymeric assemblies of monomers brought together by reversible and directional secondary interactions.\textsuperscript{20} These macromolecules exhibit properties that are able to rival covalently linked polymers, but combine this ability with reversibility that permits ease in processing at elevated temperatures.\textsuperscript{21}
Supramolecular polymers are attractive counterpoints to traditional high-molecular molecules in that they are highly functional systems that provide stimuli-responsive materials able to integrate properties for a variety of functions in areas including self-healing polymers, biomedical functions, and electronic functions where π-conjugation is present.\textsuperscript{20, 22-24} For example, recent reports demonstrate supramolecular polymers being used as adhesion promoters,\textsuperscript{25} injectable and biodegradable hydrogels\textsuperscript{26} hydrogels with shape-memory properties\textsuperscript{27}, light-healable nanocomposites,\textsuperscript{28} and supramolecular polymers demonstrating solid-state emission\textsuperscript{29}. Thus, the ability to prepare diverse supramolecular polymers opens up a range of interesting possibilities.

Herein, we report the synthesis of a hydroxyl-functionalized N-alkyl urea peptoid oligomer from a methoxy methyl ether protected precursor that we are able to prepare in good yields with relatively simple procedures. We selected hydroxyl groups as they are synthetically versatile and amenable to a range of reactions, and we show that several functional groups are achievable from the starting alcohol. We subsequently modified the oligomers with the well-known four-fold hydrogen bonding 2-ureido-4[1H]-pyrimidinone (UPy) motif to form supramolecular polymers. Concentration-dependent Diffusion Ordered Spectroscopy (DOSY) NMR and concentration-dependent solution viscosity experiments were performed to demonstration the polymerization.

2.3 Experimental

Materials and Methods

All starting reagents were purchased from Aldrich at the highest available purity and used as received unless otherwise stated. \textsuperscript{1}H and \textsuperscript{13}C\{\textsuperscript{1}H\} NMR measurements were
performed in CDCl₃ with Si(CH₃)₄ standards using a 400 MHz Bruker Ultrashield (100 MHz for ¹³C); ¹H NMR and ¹³C NMR spectra were analyzed with MestReNova software. Fourier transform infrared (FTIR) spectra were collected on a Nicolet 6700 spectrometer and analyzed with OMIC 32 software. Concentration-dependent DOSY experiments on UPy end-functionalized N-alkyl urea peptoid oligomers were performed on a Bruker DMX-500 MHz NMR. Solution viscosities were measured using a Cannon semimicro Ubbelohde viscometer. Samples were filtered through 5 μm syringe filters before measurement. Experiments were performed in a constant temperature water bath at 25 °C.

**N-[2-(2-nitrophenylsulfonyl)aminoethyl]-2-nitrophenylsulfonamide** was prepared according to a published procedure.³⁰ 2-Nitrobenzenesulfonyl chloride (20.56 g, 92.80 mmol) and ethylenediamine (3.10 mL, 46.4 mmol) was dissolved in 150 mL dichloromethane and 150 mL of a saturated NaHCO₃ solution added. The reaction was allowed to proceed overnight at room temperature. The reaction mixture was filtered to afford a white powder. The product was dried in a vacuum oven overnight to yield 18.0 g of white powder. Yield: 90.2 %. ¹H NMR (d₆-DMSO): δ(ppm) 2.97-2.99 (m, 4 H, NHCH₂CH₂NH), 7.86-7.88 (m, 4H, aromatic H), 7.94-7.96 (m, 4H, aromatic H), 8.16 (m, 2H, NHCH₂CH₂NH). ¹³C NMR (DMSO): δ(ppm) 147.7, 133.9, 132.6, 132.5, 129.3, 124.3, 42.1. FT-IR (cm⁻¹): ν(NH) = 3320, ν(CH) = 2942, ν(phenyl) = 1532, ν(C=C bend) = 785. MS (TOF MS ES+): 431.0311 M+1.

**Compound 1.** N-[2-(2-nitrophenylsulfonyl)aminoethyl]-2-nitrophenylsulfonamide (6.00 g, 14.0 mmol) was dissolved in 30 mL of N,N-dimethylformamide (DMF) and K₂CO₃ (7.70 g, 55.8 mmol) and 1-bromo-2-(methoxymethoxy)ethane (7.10 g, 41.9 mmol) were
added. The reaction was allowed to proceed at room temperature overnight. The DMF was removed by vacuum distillation, and the residue dissolved in \(\text{CH}_2\text{Cl}_2\) and passed through Celite. The solution was concentrated and dried in vacuum to afford 8.29 g of yellow oil. Yield: 98%. \(^1\text{H} \text{NMR (d}_6\text{-DMSO): } \delta(\text{ppm}) \text{ 3.17 (s, 6 H, OCH}_3\text{), 3.48-3.53 (t, 12H, NCH}_2\text{CH}_2\text{N, NCH}_2\text{CH}_2\text{O), 4.44 (s, 4 H, OCH}_2\text{O) 7.75-8.00 (m, 8 H, aromatic H).}\)

\(^{13}\text{C} \text{NMR (DMSO): } \delta(\text{ppm}) \text{ 148.09,135.06, 132.99, 131.95, 130.15, 124.92 (aromatic C), 96.06 (2 OCH}_2\text{O), 65.21 (2 CH}_2\text{OCH}_2\text{), 55.33 (2 CH}_2\text{OCH}_3\text{), 48.73 (2 NCH}_2\text{CH}_2\text{O), 47.43(NCH}_2\text{CH}_2\text{N). FT-IR (cm}^{-1}\text{): } \nu(\text{NH}) = 3325, \nu(\text{CH}) = 2938, \nu(\text{phenyl}) = 1532, \nu(\text{C=C bend}) = 785. \text{ MS (TOF MS ES+): } 629.11953 \text{ M+Na}^+.\)

**Compound 2** Compound 1 (8.29 g, 13.7 mmol) was dissolved in 30 mL of \(\text{N}_2\text{,N}-\text{dimethylformamide (DMF) and K}_2\text{CO}_3\) (7.55 g, 54.7 mmol). The reaction flask was sealed with a rubber septum, purged with \(\text{N}_2\) for 30 min and thiophenol (5.57 mL, 54.70 mmol) added. The reaction was allowed to proceed at room temperature overnight. The DMF was removed by vacuum distillation, and the residue dissolved in \(\text{CH}_2\text{Cl}_2\) and passed through Celite. The solution was concentrated to afford the crude secondary amine which was purified using column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with \(\text{CH}_2\text{Cl}_2\text{:MeOH (10:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 3.00 g of yellow oil. Yield: 93%. \(^1\text{H} \text{NMR (CDCl}_3\text{): } \delta(\text{ppm}) \text{ 2.94-3.00 (t, 8 H, OCH}_2\text{CH}_2\text{NHCH}_2\text{H) 3.38 (s, 6 H, OCH}_3\text{), 3.70 (t, 4H, OCH}_2\text{CH}_2\text{NH), 4.44 (bs, 2 H, NH) 4.65 (s, 4 H, OCH}_2\text{O). \(^{13}\text{C} \text{NMR (CDCl}_3\text{): } \delta(\text{ppm}) \text{ 96.63 (2 OCH}_2\text{O), 65.40 (2 CH}_2\text{OCH}_2\text{), 55.46 (2 CH}_2\text{OCH}_3\text{), 48.16 (2 NCH}_2\text{CH}_2\text{O), 46.39 (NCH}_2\text{CH}_2\text{N). FT-IR (cm}^{-1}\text{): } \nu(\text{NH}) = 3325, \nu(\text{CH}) = 2930. \text{ MS (TOF MS ES+): } 237.1692 \text{ M+1.}\)**
**Compound 3.** Compound 2 (2.1 g, 8.9 mmol) was dissolved in 15 mL of pyridine and N-(2-Nitrobenzenesulfonyl-2-imidazolidone (4.82 g, 17.8 mmol), (dimethylamino)pyridine (DMAP) (1.09 g, 8.89 mmol) were added. The reaction flask was sealed with a rubber septum and purged with N₂ for 30 min. The reaction was allowed to proceed under room temperature overnight. After this time the solvent was removed using a rotary evaporator, the residue dissolved in CH₂Cl₂, and the resulting solution washed with 0.5 M aqueous HCl and dried over Na₂SO₄. The solvent was removed to afford the crude product which was purified by column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with CH₂Cl₂: MeOH (10:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 5.53 g of yellow oil. Yield: 80%. ^1^H NMR (CDCl₃): δ(ppm) 3.22 (t, J=4.0 Hz, 4 H, NCH₂CH₂N), 3.33 (s, 6 H, OCH₃), 3.39-3.45 (t, 12 H, Ns (nitrobenzenesulfonyl)NHCH₂CH₂NH, NCH₂CH₂O), 3.61 (t, J=4.0 Hz, 4 H, NCH₂CH₂O), 4.62 (s, 4 H, OCH₂O), 6.68 (bs, 2 H, NsNH), 7.70-7.76 (m, 6 H, aromatic H), 8.08 (m, 2 H, aromatic H). ^13^C NMR (CDCl₃): δ(ppm) 159.1 (NHCO), 147.91, 133.60, 133.46, 132.67, 130.99, 124.99 (aromatic C), 96.65 (2 OCH₂O), 67.35 (2 CH₂OCH₂), 55.45 (2 CH₂OCH₃), 48.99 (2 NCH₂CH₂O), 47.06 (NCH₂CH₂N), 44.23 (NsNHCH₂), 40.45 (NsNHCH₂CH₂). FT-IR (cm⁻¹): v(NH) = 3326, v(CH) = 2941, v(phenyl) = 1622, v(C=C bend) = 782. MS (TOF MS ES+): 779.2356 M⁺1.

**Compound 4.** Compound 3 (2.93 g, 3.77 mmol) was dissolved in 15 mL of N,N-dimethylformamide (DMF) and K₂CO₃ (2.08 g, 15.1 mmol) and 1-bromo-2-(methoxymethoxy)ethane (1.10 mL, 9.42 mmol) were added. The reaction was allowed to proceed at room temperature overnight. The DMF was removed by vacuum distillation, and the residue dissolved in CH₂Cl₂ and passed through Celite. The solution
was concentrated and dried in vacuum to afford 3.31 g of yellow oil. Yield: 92%. \(^1\)H NMR (CDCl\(_3\)): \(\delta (\text{ppm})\) 3.24 (s, 6 H, OCH\(_3\)), 3.32-3.64 (m, 34 H, the rest CH\(_2\) and OCH\(_3\)), 4.61 (s, 4 H, OCH\(_2\)O), 4.45 (s, 4 H, OCH\(_2\)O) 6.27 (bs, 2 H, NsNH), 7.60-7.66 (m, 6 H, aromatic H), 8.02 (m, 2 H, aromatic H). \(^1^3\)C NMR (CDCl\(_3\)): \(\delta (\text{ppm})\) 158.86 (2 NH\(_2\)CO), 148.04, 133.59, 133.29, 131.64, 130.82, 123.95 (aromatic C), 96.62, 96.33 (4 OCH\(_2\)O), 67.29, 65.31 (4 CH\(_2\)OCH\(_2\)), 55.39, 55.32 (4 CH\(_2\)OCH\(_3\)), 48.70, 48.02 (4 NCH\(_2\)CH\(_2\)O), 47.17, 46.88 (4 NsNCH\(_2\)CH\(_2\)NH), 38.65 (2 NsNCH\(_2\)CH\(_2\)NH). FT-IR (cm\(^{-1}\)): \(\nu (\text{NH}) = 3358, \nu (\text{CH}) = 2939, \nu (\text{CO}) = 1629, \nu (\text{phenyl}) = 1542, \nu (C=C\text{ bend}) = 732.\) MS (TOF MS ES\(^+\)): 955.3379 M\(^+\).

**Compound 5.** Compound 4 (9.00 g, 9.43 mmol) was dissolved in 30 mL of N,N-dimethylformamide (DMF) and K\(_2\)CO\(_3\) (5.20 g, 37.7 mmol). The reaction flask was sealed with a rubber septum, purged with N\(_2\) for 30min and thiophenol (3.84 mL, 37.7 mmol) was added. The reaction was allowed to proceed at room temperature overnight. The DMF was removed by vacuum distillation, and the residue dissolved in CH\(_2\)Cl\(_2\) and passed through Celite. The solution was concentrated to afford the crude secondary amine which was purified using column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with CH\(_2\)Cl\(_2\):MeOH (10:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 4.85 g of yellow oil. Yield: 88%. \(^1\)H NMR (CDCl\(_3\)): \(\delta (\text{ppm})\) 2.48 and 3.00-3.28 (m, 40 H, all CH\(_2\) and OCH\(_3\)), 2.69 (bs, 2 H, NHCO), 4.25 (s, 4 H, OCH\(_2\)O), 4.27 (s, 4 H, OCH\(_2\)O) 6.14 (bs, 2 H, NsNH). \(^1^3\)C NMR (CDCl\(_3\)): \(\delta (\text{ppm})\) 158.71 (2 NH\(_2\)CO), 96.16, 96.12 (4 OCH\(_2\)O), 66.88, 66.44 (4 CH\(_2\)OCH\(_2\)), 54.85, 54.70 (4 CH\(_2\)OCH\(_3\)), 48.94, 48.47 (4 NCH\(_2\)CH\(_2\)O), 48.35, 46.63 (4
NsNCH₂CH₂NH), 40.05 (2 NsNCH₂CH₂NH). FT-IR (cm⁻¹): \( \nu(NH) = 3337 \), \( \nu(CH) = 2933 \), \( \nu(CO) = 1625 \), \( \nu(\text{phenyl}) = 1537 \), \( \nu(C=\text{C bend}) = 744 \). MS (TOF MS ES⁺): 585.3862 M⁺1.

**Compound 6.** Compound 5 (1.34 g, 2.29 mmol) was dissolved in 15 mL of pyridine and \( N \)-\( (2\)-nitrobenzenesulfonyl-\( 2\)-imidazolidone (1.24 g, 4.58 mmol), (dimethylamino)pyridine (DMAP) (0.28 g, 2.3 mmol) were added. The reaction flask was sealed with a rubber septum and purged with \( N_2 \) for 30 min. The reaction was allowed to proceed under room temperature overnight. After this time the solvent was removed using a rotary evaporator, the residue dissolved in \( CH₂Cl₂ \), and the resulting solution washed with 0.5 M aqueous HCl and dried over \( Na₂SO₄ \). The solvent was removed to afford the crude product which was purified by column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with \( CH₂Cl₂: MeOH \) (10:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 2.10 g. Yield: 81%. \(^1\)H NMR (CDCl₃): δ(ppm) 2.11 (bs, 2 H, NHCO), 3.60-3.72 (m, 48 H, all CH₂ and OCH₃), 4.62 (s, 4 H, OCH₂O), 4.65 (s, 4 H, OCH₂O) 6.14 (bs, 2 H, NsNH) 7.71-7.81 (m, 6 H, aromatic H), 8.13 (m, 2 H, aromatic H). \(^{13}\)C NMR (CDCl₃): δ(ppm) 160.05, 159.94 (4 NHCO), 148.03, 133.95, 133.37, 132.57, 131.10, 124.97 (aromatic C), 96.69, 96.62 (4 OCH₂O), 67.54, 67.21 (4 CH₂OCH₂), 55.49, 55.35 (4 CH₂OCH₃), 48.62, 48.20 (4 NCH₂CH₂O), 47.74 (2 NCH₂CH₂NHCO), 46.58 (NCH₂CH₂N), 44.39 (2 NsNHCH₂CH₂NHCO), 40.46 (2 NCH₂CH₂NHCO), 40.01 (2 NsNHCH₂). FT-IR (cm⁻¹): \( \nu(NH) = 3351 \), \( \nu(CH) = 2927 \), \( \nu(CO) = 1612 \), \( \nu(\text{phenyl}) = 1543 \), \( \nu(C=\text{C bend}) = 745 \). MS (TOF MS ES⁺): 1127.4379 M⁺1.

**Compound 7.** Compound 6 (1.00 g, 0.889 mmol) was dissolved in 15 mL methanol and 30 mL 2 M HCl was added. The reaction was allowed to proceed at 40 °C for 24 h. After
that time, NaOH was added to neutralize the acid and the solvent was removed by a rotary evaporator. NaCl was removed by filtration to afford 0.78 g of yellow oil. Yield: 92.4%. $^1$H NMR (CDCl$_3$): $\delta$(ppm) 2.92-3.42 (m, 40 H, all CH$_2$ and OH), 4.87(bs, 2 H, NHCO), 6.57, 6.66 (bs, 4 H, NHCO, NsNH), 7.82 (m, 4 H, aromatic H), 7.99 (m, 2 H, aromatic H). $^{13}$C NMR (CDCl$_3$): $\delta$(ppm) 159.55, 159.50 (4 NHCO), 147.31, 133.98, 132.97, 132.69, 129.90, 124.91 (aromatic C), 59.72, 59.68 (4 CH$_2$OH), 49.67, 49.36, 47.13, 45.85, 43.13, 40.15, 38.52 (2 NHCH$_2$CH$_2$NH + 10 NCH$_2$). FT-IR (cm$^{-1}$): $\nu$(OH) = 3336, $\nu$(CH) = 2942, $\nu$(CO) = 1624, $\nu$(phenyl) = 1536, $\nu$(C=C bend) = 763. MS (TOF MS ES+): 973.3002. M+Na$^+$.

**Compound 8:** Compound 7 (1.65 g, 1.74 mmol) was dissolved in 20 mL DMSO with 1-bromo-4-chloro butane (1.80 mL, 15.6 mmol), and NaOH (0.540 g, 13.6 mmol) in 1 mL of H$_2$O were added. The reaction was allowed to proceed at 40 °C for 24 h. After the reaction was complete, the solution was washed with ethyl acetate and brine. The organic phase was collected and dried with sodium sulfate and the solvent was removed by a rotary evaporator to afford a yellow oil which was further purified by column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with CH$_2$Cl$_2$: MeOH (10:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 1.82 g of yellow oil. Yield: 70% g. $^1$H NMR (CDCl$_3$): $\delta$(ppm) 1.72-1.82 (m, 24H, CH$_2$CH$_2$CH$_2$CH$_2$), 3.28-3.58 (m, 60 H, all CH$_2$ close to N, O, and Cl), 7.60 (m, 6 H, aromatic H), 8.01 (m, 2 H, aromatic H). $^{13}$C NMR (CDCl$_3$): $\delta$(ppm) 159.49, 159.17 (4 NHCO), 147.88, 133.66, 133.12, 132.01, 130.46, 124.14 (aromatic C), 70.43, 70.35 (4 NCH$_2$CH$_2$O + 4 OCH$_2$CH$_2$CH$_2$CH$_2$Cl), 48.17, 48.11 47.29, 47.23 (2 NCH$_2$CH$_2$CH$_2$CH$_2$Cl + 2 NCH$_2$CH$_2$O + 2 NCH$_2$CH$_2$NHCO + 2 NCH$_2$CH$_2$O), 46.95 (2 NsNCH$_2$CH$_2$NHCO),...
46.89 (2 NCH₂CH₂NHCO), 46.83 (NCH₂CH₂N), 45.01 (4 OCH₂CH₂CH₂CH₂Cl), 44.40 (2 NsNCH₂CH₂), 39.01(2 NCH₂CH₂CH₂CH₂Cl) 29.62, 29.55, 29.38, 29.28, 26.96, 26.69 (2 NCH₂CH₂CH₂CH₂Cl + 4 OCH₂CH₂CH₂CH₂Cl). FT-IR (cm⁻¹): ν(NH) = 3348, ν(CH) = 2941, ν(CO) = 1630, ν(phenyl) = 1544, ν(C=C bend) = 746. MS (TOF MS ES+): 1494.4722. M+1.

**Compound 9:** Compound 8 (1.5 g, 1.00 mmol) was dissolved in 15 mL DMSO and sodium azide (0.39 g, 6.0 mmol) was added to the solution. The reaction was performed at 85 °C overnight. The mixture was washed with brine and DCM. The organic phase was dried with Na₂SO₄. The solvent was removed by a rotary evaporator to afford 1.3 g of yellow oil. Yield: 85 %. ¹H NMR (CDCl₃): δ(ppm) 1.51-1.60 (m, 24H, CH₂CH₂CH₂CH₂), 3.27-3.48 (m, 60 H, all CH₂ close to N, O, and N₃), 7.61-7.67 (m, 6 H, aromatic H), 7.97 (m, 2 H, aromatic H). ¹³C NMR (CDCl₃): δ(ppm) 159.92, 158.98 (4 NHCO), 147.78, 133.48, 133.43, 131.72, 130.64, 124.16 (aromatic C), 70.67, 70.34 (4 NCH₂CH₂O + 4 OCH₂CH₂CH₂CH₂N₃), 51.21, 51.07, 50.49 (2 NCH₂CH₂CH₂CH₂N₃ + 4 NCH₂CH₂O + 2 NCH₂CH₂NHCO), 48.17 47.20, 47.09, 39.82 (2 NsNCH₂CH₂NHCO + 2 NCH₂CH₂NHCO + NCH₂CH₂N+ 4 OCH₂CH₂CH₂CH₂N₃ + 2 NsNCH₂CH₂), 39.07 (2 NCH₂CH₂CH₂CH₂N₃), 29.71, 26.87, 26.82, 25.81, 25.73, 25.15 (2 NCH₂CH₂CH₂CH₂N₃ + 4 OCH₂CH₂CH₂CH₂N₃). FT-IR (cm⁻¹): ν(NH) = 3405, ν(CH) = 2938, ν(azide) = 2096, ν(CO) = 1631, ν(phenyl) = 1542, ν(C=C bend) = 746. MS (TOF MS ES+): 1533.7336. M+1.

**Compound 10:** Compound 7 (0.20 g, 0.21 mmol) was dissolved in 2 mL DMF, then succinic anhydride (0.09 g, 0.088 mmol) and 4-(dimethylamino)pyridine (26.8 mg, 0.210 mmol) were added. The reaction was performed at room temperature overnight. The solvent was removed by vacuum distillation to afford yellow oil which was further
purified by column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with 
CH₂Cl₂: MeOH (4:1 v/v) as the mobile phase. The solvent was removed and the product 
dried in vacuum to yield 0.15 g of yellow oil. Yield: 53%. ¹H NMR (CDCl₃): δ(ppm) 2.62-
2.64 (m, 16 H, 4 COCH₂CH₂COOH), 3.24-3.70 (m, 36 H, 14 NCH₂ + 4 OCH₂), 7.72-7.80 
(m, 6 H, aromatic H), 8.10 (m, 2 H, aromatic H). ¹³C NMR (CDCl₃): δ(ppm) 172.96, 
172.39 (4 OCO + 4 COOH), 159.21, 159.15 (4 NHCO), 147.93, 133.59, 132. 69, 132.60, 
130.96, 125.10 (aromatic C), 63.33, 63.25 (4 OCH₂), 47.69, 47.61, 46.89, 46.73, 44.13, 
40.55, 39.76 (2 NHCH₂CH₂NH + 8 NCH₂ + 2CONHCH₂), 29.69, 28.97, 28.75, 28.71 (4 
COCH₂CH₂CO). FT-IR (cm⁻¹): ν(NH) = 3306, ν(CH) = 2928, ν(COOH) = 1730, ν(phenyl) = 1538, 

2(6-isocyanatohexylaminocarbonylamino)-6-methyl-4-[1H]pyrimidinone The 
synthesis was performed according to literature.³¹ A solution of 8 mmol 2-amino-4-
hydroxy-6-methylpyrimidine in 53 mmol hexylisocyanate was heated at 100 °C for 16 
h. Hexane was added and the resulting precipitate was filtered and washed with hexane. 
The white powder was dried in vacuum oven to afford 2.0 g of product. Yield: 85%. ¹H 
NMR (CDCl₃): δ(ppm) 13.1 (s, 1H, CH₃CNH), 11.9 (s, 1H,CH₂NH(C=O)NH), 10.2 (s, 1H, 
CH₂NH(C=O)NH), 5.8 (s, 1H, CH=CH₂), 3.3 (m, 4H, NH(C=O)NHCH₂+ CH₂NCO), 2.2 
(s, 3H, CH₃C=CH), 1.6 (m, 4H, NCH₂CH₂), 1.4 (m, 2H, CH₂CH₂CH₂CH₂CH₂). ¹³C NMR 
(100 MHz, CDCl₃): 172.8 (CH₃C=CH), 156.3, 154.4 (C=CHCO + NHCONH), 148.1 
(NHC=N), 121.6 (NCO), 106.4 (C=CH), 42.6 39.5 (CH₂NCO + NHCH₂CH₂), 30.9, 29.1, 
26.0, 25.9 (NCH₂CH₂CH₂CH₂CH₂NCO), 18.7 (CH₃CNH). FT-IR (cm⁻¹): ν(CO)= 1675, 
1701, ν(NCO)= 2279, ν(OH) =3233, ν(NH) =3466. MS (TOF MS ES+): 294.3260 M+1.
Compound A: Compound 6 (1.70 g, 1.51 mmol) was dissolved in 15 mL of N,N-dimethylformamide (DMF) with K$_2$CO$_3$ (0.98 g, 7.1 mmol) added. The reaction flask was sealed with a rubber septum, purged with N$_2$ for 30 min and thiophenol (0.72 mL, 7.1 mmol) was added. The reaction was allowed to proceed at room temperature overnight. The DMF was removed by vacuum distillation, and the residue dissolved in CH$_2$Cl$_2$ and passed through Celite. The solution was concentrated to afford the crude secondary amine which was purified using column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with CH$_2$Cl$_2$:MeOH (4:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 0.8 g of yellow oil. Yield: 70%. $^1$H NMR (CDCl$_3$): δ(ppm) 2.83 (t, 4 H, NH$_2$C$_2$H$_2$CH$_2$), 3.29-3.67 (m, 42 H, CH$_2$ which close to NH and N, CH$_2$OCH$_3$), 4.63-4.64 (bs, 8 H, OCH$_2$OCH$_3$), 6.45-6.67 (bs, 4 H,CH$_2$NH$_2$). $^{13}$C NMR (CDCl$_3$): δ(ppm) 159.14 (4 NHCO), 96.55 (4 OCH$_2$O), 67.06, 67.05 (4 CH$_2$OCH$_2$), 55.34, 55.35, 55.34 (4 CH$_2$OCH$_3$), 48.52, 47.94 (4 NCH$_2$CH$_2$O), 47.15 (2 NCH$_2$CH$_2$NHCO), 46.79 (NCH$_2$CH$_2$N), 44.15 (2 NsNHCH$_2$CH$_2$NHCO), 42.14 (2 NCH$_2$CH$_2$NHCO), 40.05 (2 NsNHCH$_2$). FT-IR (cm$^{-1}$): $\nu$(NH) = 3305, $\nu$(CH) = 2929, $\nu$(CO) = 1618. MS (TOF MS ES+): 757.4868 M+1.

Compound B: Compound A (366 mg, 0.484 mmol) was dissolved in 5 mL of N,N-dimethylformamide (DMF) and 2(6-isocyanatohexylaminocarbonylamo)-6-methyl-[1H]pyrimidinone (283 mg, 0.968 mmol) was added. The reaction was performed at 50 °C overnight. The DMF was removed by vacuum distillation to afford 0.53 g of yellow powder. Yield: 81.5%. $^1$H NMR (CDCl$_3$): δ(ppm) 1.35-1.57 (NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH), 2.23 (s, 6 H, CH$_3$C(NH)=CH), 3.13-3.65 (m, 56 H, CH$_2$), 4.62 (m, 8 H, OCH$_2$O) 5.82 (s, 2 H, CH$_3$C(NH)=CH), 10.12 (s, 2 H,
\( \text{CH}_2\text{NH(C=O)NH} \), 11.74 (s, 2 H, \text{CH}_2\text{NH(C=O)NH}), 13.12 (s, 1 H, \text{CH}_3\text{CNH}). ^{13}\text{C NMR} \) (CDCl\(_3\)): \( \delta \) (ppm) 173.13 \( (2 \text{ C=CHCO} + 8 \text{ NHCONH}) \), 148.47 \( (2 \text{ NH=N}) \), 106.54 \( (2 \text{ C=CH}) \), 96.59 \( (4 \text{ OCH}_2\text{O}) \), 67.06, 66.94 \( (4 \text{ CH}_2\text{OCH}_2) \), 55.39 \( (4 \text{ CH}_2\text{OCH}_3) \), 48.42, 47.98, 47.42, 46.61, 41.50, 40.78, 40.11, 39.73, 39.33 \( (10 \text{ NHCH}_2 + 8 \text{ NCH}_2) \), 29.86, 29.36, 26.44, 26.25 \( (2 \text{ NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}) \), 18.93 \( (2 \text{ CH}_3\text{C=CH}) \). FT-IR (cm\(^{-1}\)): \( \nu(\text{NH}) = 3322, \nu(\text{CH}) = 2931, \nu(\text{CO}) = 1621, \nu(\text{C=C bend}) = 727. \) MS (TOF MS ES\(^{+}\)): 1343.7828. M\(^{+}\).

**Compound C:** Compound B (100 mg, 0.074 mmol) was dissolved in 2 mL MeOH and 4 mL 2 M HCl solution was added. The reaction was performed under 40 °C for 24 h. At that time, NaOH was added to neutralize the acid. Then solvent was removed by a rotary evaporator, NaCl was filtrated to afford yellow oil 69.5 mg. Yield: 80%. \(^{1}\text{H NMR} \) (D\(_2\)O): \( \delta \) (ppm) 1.17-1.39 \( (m, 16 \text{ H, 2 NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}) \), 2.25 \( (s, 6 \text{ H, CH}_3\text{C(NH)=CH}) \), 2.92-3.52 \( (m, 44 \text{ H, 10 NHCH}_2 + 8 \text{ NCH}_2 + 4 \text{ OCH}_2) \), 6.10 \( (s, 2 \text{ H, CH}_3\text{C(NH)=CH}) \). \(^{13}\text{C NMR} \) (D\(_2\)O): \( \delta \) (ppm) 164.54 \( (2 \text{ CH}_3\text{C}=\text{CH}) \), 160.39, 159.86, 159.71, 155.58, 153.59 \( (2 \text{ C=CHCO} + 8 \text{ NHCONH}) \), 150.97 \( (2 \text{ NHN=N}) \), 105.08 \( (2 \text{ C=CH}) \), 59.70, 59.68 \( (4 \text{ CH}_2\text{OH}) \), 49.64, 49.39, 48.87, 47.26, 45.88, 40.46, 40.17, 39.93, 38.51 \( (10 \text{ NHCH}_2 + 8 \text{ NCH}_2) \), 28.90, 28.53, 28.21, 25.56 \( (2 \text{ NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}) \), 18.55 \( (2 \text{ CH}_3\text{C}=\text{CH}) \). FT-IR (cm\(^{-1}\)): \( \nu(\text{OH}) = 3300, \nu(\text{CH}) = 2941, \nu(\text{CO}) = 1631, \nu(\text{C=C bend}) = 714. \) MS (TOF MS ES\(^{+}\)): 1167.7163. M\(^{+}\).

**Compound D:** Compound 9 (1.30 g, 0.85 mmol) was dissolved in 15 mL of N,N-dimethylformamide (DMF) with K\(_2\)CO\(_3\) (0.468 g, 3.39 mmol) added. The reaction flask was sealed with a rubber septum, purged with N\(_2\) for 30 min and thiophenol (0.35 mL, 3.39 mmol) was added. The reaction was allowed to proceed at room temperature
overnight. The DMF was removed by vacuum distillation, and the residue dissolved in CH$_2$Cl$_2$ and passed through Celite. The solution was concentrated to afford the crude secondary amine which was purified using column chromatograph on silica gel (silica gel 60 Å, 7-230 mesh) with CH$_2$Cl$_2$:MeOH (4:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 0.7 g of yellow oil. Yield: 71%. $^1$H NMR (CDCl$_3$): $\delta$(ppm) 1.55-1.70 (m, 24 H, 2 NHCH$_2$CH$_2$CH$_2$CH$_2$N$_3$ 4 OCH$_2$CH$_2$CH$_2$CH$_2$N$_3$), 3.01-3.60 (m, 60 H, 4 NHCH$_2$ + 4 CH$_2$NHCO + 8 NCH$_2$ + 8 OCH$_2$ + 6 CH$_2$N$_3$). $^{13}$C NMR (CDCl$_3$): $\delta$(ppm) 162.76, 159.49 (4 NHCO), 70.52, 69.97 (4 NCH$_2$CH$_2$O + 4 OCH$_2$CH$_2$CH$_2$CH$_2$N$_3$), 51.06, 50.89, 50.70 (2 NCH$_2$CH$_2$CH$_2$CH$_2$N$_3$ + 4 NCH$_2$CH$_2$O + 2 NCH$_2$CH$_2$NHCO), 49.45, 48.27, 47.50, 46.13, 38.79, 37.60 (2 NsNCH$_2$CH$_2$NHCO + 2 NCH$_2$CH$_2$NHCO + NCH$_2$CH$_2$N+ 4 OCH$_2$CH$_2$CH$_2$CH$_2$N$_3$ + 2 NsNCH$_2$CH$_2$ + 2 NCH$_2$CH$_2$CH$_2$CH$_2$N$_3$), 26.71, 26.23, 25.99, 25.67, 25.58, 23.27 (2 NCH$_2$CH$_2$CH$_2$CH$_2$N$_3$ + 4 OCH$_2$CH$_2$CH$_2$CH$_2$N$_3$). FT-IR (cm$^{-1}$): $\nu$(NH) = 3355, $\nu$(CH) = 2929, $\nu$(azide) =2096, $\nu$(CO) = 1618. MS (TOF MS ES+): 1163.7563 M+1.

**Compound E:** Compound D (420.2 mg, 0.0361 mmol) was dissolved in 5 mL of N,N-dimethylformamide (DMF) and 2(6-isocyanatohexylaminocarbonylamino)-6-methyl-4-[1H]pyrimidinone (212 mg, 0.0.723 mmol) and 2 drops of 1,8-diazabicyclo[5.4.0]undec-7-ene was added. The reaction was performed at 100 °C for 48 h. The DMF was removed by vacuum distillation and the residue was washed with 0.5 M HCl and DCM. The organic phase was collected and dried with sodium sulfate. DCM was removed to afford 400 mg of yellow power. Yield: 63.0 %. $^1$H NMR (CDCl$_3$): $\delta$(ppm) 1.26-1.65 (m, 40H, 2 NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH + 2 NCH$_2$CH$_2$CH$_2$CH$_2$N$_3$ + 4 OCH$_2$CH$_2$CH$_2$CH$_2$N$_3$), 2.25 (s, 6 H, CH$_3$C(NH)=CH), 3.26-3.52 (m, 68 H, 2
\[
\text{NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH} + 12 \text{NCH}_2 + 8 \text{OCH}_2 + 6 \text{CH}_2\text{N}_3 + 4 \text{CH}_2\text{NHCO}) \]

5.82 (s, 2 H, CH\text{C(NH)}=\text{CH}), 10.10 (s, 2 H, CH\text{NH(C=O)NH}), 11.86 (s, 2 H, CH\text{NH(C=O)NH}), 13.16 (s, 1H, \text{CH}_3\text{CNH}). ^{13}\text{C NMR (CDCl}_3\): \delta(\text{ppm}) 165.39(2 CH\text{C}=\text{CH}), 159.26, 159.21, 158.38, 156.22, 154.43 (2 C=\text{CHC} O + 8 \text{NHCONH}), 148.54 (2 NHC=N), 106.28 (2 C=CH), 70.69, 70.15 (4 \text{CH}_2\text{OCH}_2), 51.18, 47.96, 46.88, 46.60, 40.80, 39.84, 36.20 (8 \text{NHCH}_2 + 12 \text{NCH}_2 + 6 \text{CH}_2\text{N}_3), 30.28, 30.06, 29.66, 29.33, 26.85, 26.50, 26.09, 25.73 (2 \text{NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH} + 2 \text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}_3 + 4 \text{OCH}_2\text{CH}_2\text{CH}_2\text{N}_3), 19.03 (2 \text{CH}_3\text{C}=\text{CH}).

\text{FT-IR (cm}^{-1}): \nu(\text{NH}) = 3481, \nu(\text{CH}) = 2930, \nu(\text{azide}) = 2096, \nu(\text{CO}) = 1670, \nu(\text{C=C bend}) = 726. \text{MS (TOF MS ES+: 1750.0941. M+1.}

**Diffusion Ordered Spectroscopy**

Concentration-dependent DOSY experiments on UPy end-functionalized N-alkyl urea peptoid oligomers were performed on a Bruker DMX-500 MHz NMR equipped with a TXI probe with gradient capabilities (maximum gradient strength of 40 G cm\(^{-1}\)) at 25 °C. The DOSY stimulated echo sequence was used for the determination of the self-diffusion of the different components. In a typical experiment, 16 transients (with a recycle delay of 2 s per transient) for each of the 16 steps were recorded with increasing gradient strength (range from 2%-80% of the maximum gradient strength linearly). In all experiments, the 90° pulse widths were determined. The strength of the \(B_0\) field gradient was calibrated by measuring the self-diffusion coefficient of the residual HDO signal in a 1 % D\(_2\)O sample, at 25 °C (D(H\(_2\)O) = 19 \times 10^{-10} \text{ m}^2 \text{ s}^{-1})[^{32}]. The experimental diffusion constant (\(D_m\)) was obtained using the Stejskal-Tanner\(^{20}\) equation:

\[
I(G_{el}) = I(0)\exp\left(-D_m\gamma_H^2\delta^2(G_{el})^2(\Delta - \delta/3 - \tau/2)\right) \tag{1}
\]
$I(G_{zi})$ represents the experimental signal intensity at a gradient-level of $G_{zi}$(G cm$^{-1}$), $I(0)$ is the initial signal intensity, $\gamma_h$ is the magnetogyric ratio for $^1$H, $\tau$ is the time interval between the bipolar pulse pair, $\delta$ is the length of the pulsed field gradient, and $\Delta$ is the diffusion period. From this equation, $D_m$ can be determined from a plot of $\ln \frac{I(G_{zi})}{I(0)}$ versus $(G_{zi})^2$. The viscosity corrected diffusion constant ($D_c$) was calculated using the following equation:

$$D_c = D_m \times \frac{D_{sol, pure}}{D_{sol, m}}$$  (2)

$D_m$ and $D_{sol, m}$ represent the measured values for the solute and the residual solvent peak (CHCl$_3$), and $D_{sol, pure}$ is the diffusion constant measured for the residual CHCl$_3$ in pure CDCl$_3$.

2.4 Results and discussion

The synthesis of $N$-alkyl-$N,N$-linked urea oligomers is simple to perform and uses an iterative 3-step process.$^{33,13-15}$ The synthesis scheme involves extending the oligomer using the ring-opening of a cyclic imidazolidone with an amine, attachment of the pendant $N$-alkyl functionality using an alkyl halide, and then removal of a nitrobenzenesulfonyl protecting group to form a new amine that can be used in the next reaction cycle. The synthesis protocol is typically high yielding and is performed in solution, thus making it amenable to traditional laboratory techniques. We have previously shown how this synthetic strategy can be used to prepare oligomers with four different pendant groups.$^{13}$ Although each individual synthesis step is high yielding and easy to perform, this synthetic route can result in many steps when preparing longer
oligomers, and significantly, many purification and isolation steps. Often the purification and isolation of the synthetic intermediates is the most challenging component due to the similarity in polarity between the reactants and products. Therefore, for simple systems where control over the sequence of the oligomer is not required at a single residue level it would be beneficial to only need one oligomer that can be prepared in larger quantities. With this thought in mind we designed an N-alkyl-N,N-linked urea oligomer that contained a hydroxyl functionalized N-alkyl group. (Figure 1)

![Structure of N-alkyl-N,N-linked urea oligomer containing alcohol pendant groups.](image)

We chose to use a hydroxyl group as (in addition to being inherently useful) it is highly versatile and can easily be converted into, or reacted with, many other functional groups. Ultimately, large batches of this oligomer could be made and partitioned for many different uses. However, hydroxyl groups are not compatible with the oligomer synthesis route due to deleterious competing reactions in the Fukuyama reaction step. As a result we used protecting group chemistry for the hydroxyl group during the oligomer synthesis. Although other protecting groups for –OH groups exist, the methoxy methyl ether (MOM ether) group is advantageous as it is a common protecting group and therefore commercially available, and it is stable to the oligomer synthesis conditions but easy to remove from the final product. We used 1-bromo-2-
(methoxymethoxy)ethane to add a MOM ether as pendant groups in the oligomer. The synthesis of the final \(N\)-alkyl-\(N, N\)-linked urea oligomer is shown in Figure 2.

The structure of compound 6 was determined using both proton and carbon NMR spectroscopy, which showed peaks due to the methoxymethyl groups at 4.6 ppm in the proton spectrum and 96.6 ppm and 96.7 ppm in the carbon spectrum respectively. Mass spectrometry confirmed the structure and a molecular ion peak was observed at \(m/z = 1127.44\) (calculated \(m/z = 1127.44\) M+1). The MOM groups were deprotected using a 2 M HCl solution at 40 °C (Figure 3). The structure of the hydroxyl-functionalized oligomer was confirmed using NMR spectroscopy, FTIR spectroscopy, and mass spectrometry, which afforded a molecular ion peak was observed at \(m/z = 973.3002\) (calculated \(m/z = 973.3120\) for M+Na\(^+\)).
Figure 3: Deprotection of the MOM ether containing oligomer to afford the hydroxyl functionalized N-alkyl urea peptoid.

We demonstrated the synthetic versatility of the hydroxyl-functionalized oligomer by converting the –OH group to three other functional groups, namely alkyl chloride, alkyl azide and carboxylic acid, (Figure 4).
Figure 4: Functional group conversion of hydroxyl groups in the N-alkyl urea peptoid into alkyl chlorides, alkyl azides, and carboxylic acids.

The dihaloalkane 1-bromo-4-chlorobutane was reacted with the alcohol groups on the oligomer to generate alkyl halide pendant groups. Similar to hydroxyl groups, halides are versatile synthetic groups that can be used to further modify the oligomers in a variety of different ways. The product structure was confirmed using proton NMR spectroscopy where peaks at 1.7 and 1.8 ppm due to the methylene groups in the chlorobutane were observed. The alkyl chloride moieties were converted to azide functional groups through reaction with sodium azide in DMSO. The FT-IR spectra of
the final oligomer clearly showed the azide peak around 2095 cm\(^{-1}\) (Figure 5), confirming the successful reaction. The carboxylic acid groups were introduced into the oligomers using a reaction of the hydroxyl groups with succinic anhydride. Carboxylic acids are attractive groups to use as they can undergo reaction with a range of functional groups as well as be deprotonated to carboxylate anions, opening up potential stimuli responsive applications analogous to polyacrylic acid. Interestingly, repeated attempts at oxidizing the alcohol groups using chromate-based oxidizing agents were unsuccessful.

![Figure 5: FTIR spectrum of the alkyl azide containing N-alkyl urea peptoid. The azide peak at 2095 cm\(^{-1}\) is clearly visible.](image)

The ability to polymerize the oligomers into high molecular weight macromolecules is attractive in terms of accessing a variety of applications and structure-property relationships. We have previously shown that N-alkyl urea peptoid oligomers can be polymerized using a simple step-growth polymerization with a diisocyanate
comonomer.\textsuperscript{15} We continued this design by synthesizing polymers from selected oligomers prepared in the current work. This approach is similar to the “segmer assembly polymerization” (SAP) strategy developed by Meyer’s group. SAP has been used to polymerize sequence controlled polymers of polyesters from lactide-based monomers\textsuperscript{34} and the resultant polymers have shown to possess properties including defined stereochemistry,\textsuperscript{35} improved thermal properties,\textsuperscript{36} and controlled hydrolytic degradation rates.\textsuperscript{37} Similarly, the properties of long chain N-acyl glycines (“polypeptoids”) have also been shown to be tuned through sequence control. For example, controlled sequence polypeptoids and peptoid block copolymers can self-assemble into helices,\textsuperscript{38} have tunable coil-to-globule collapse,\textsuperscript{39} possess controlled persistence lengths,\textsuperscript{40} demonstrate control over crystallization and melting behavior,\textsuperscript{41} and possess tunable phase behavior\textsuperscript{42} and surface properties.\textsuperscript{43}

However, instead of using traditional step-growth approaches to the polymerization of our oligomers (as we did in our previous work),\textsuperscript{15} we chose to use supramolecular non-covalent hydrogen-bond interactions to link our N-alkyl urea peptoid oligomers. Interestingly, the reversibility arising from non-covalent interactions affords the potential for the resultant materials to be recyclable and self-healing. For example, it has been reported that terminal functionalization of poly(n-butyl acrylate)-b-polystyrene diblock copolymers with supramolecular 2-ureido-4[1H]-pyrimidinone (UPy) groups resulted in thermoplastic elastomers with dynamic self-healing properties.\textsuperscript{44} Here, we used the same four-fold hydrogen bonding UPy motif, as it can form self-complementary dimers with a relatively high dimerization constant ($K_{\text{dim}} = 6 \times 10^7 \text{ M}^{-1}$ in CHCl$_3$).\textsuperscript{45} Hydrogen bonding motifs including 2-ureido-4[1H]-pyrimidinone (UPy), diaminonaphthyridine
(Napy), and ureidoguanosine (UG) groups have all been used in supramolecular polymerization.\textsuperscript{46-49} For example, Weck\textsuperscript{50} reported the synthesis of supramolecular ABC triblock copolymers using complementary hydrogen bonding pairs on telechelic polymers using two distinct and orthogonal hydrogen-bonding receptor pairs. Similarly, Park and Zimmerman\textsuperscript{51} prepared alternating supramolecular multi-block copolymers based on the affinity of UG and Napy moieties, and Sherman and co-workers\textsuperscript{52} showed that supramolecular polymerization of AB monomers could be driven by selectivity of the hydrogen bonding pairs.

To prepare \textit{N}-alkyl urea peptoid monomers that can undergo supramolecular polymerization we attached the UPy motifs to the oligomers containing MOM side groups. We used the MOM-protected oligomers initially, rather than the subsequent functionalized oligomers, to remove potential side reactions from pendant \textit{N}-alkyl moieties with reactive chemical groups. We first deprotected the nitrobenzylsulfonyl groups at each end of the oligomer, and then reacted the afford primary amines with two equivalents of 2(6-isocyanatohexylaminocarbonylamino)-6-methyl-4-[1H]pyrimidinone in DMF at 50 °C overnight (Figure 6). This generated oligomers that possess UPy-groups at the terminal ends. The final oligomer structure was confirmed using \textit{^1}H NMR spectroscopy, where peaks at 10.12 ppm, 11.74 ppm and 13.12 ppm due to protons on the pyrimidinone ring were observed.
Figure 6: Synthetic scheme for attachment of 2(6-isocyanatohexylaminocarbonylamino)-6-methyl-4-[1H]pyrimidinone to \(\text{N-alkyl urea peptoids.}\)

When 60 mg of the UPy-end functionalized oligomer B was dissolved in 1.0 mL of CHCl\(_3\), the solution was observed to undergo a marked increase in viscosity. Indeed, after two days the vial could be inverted and the solution would not flow unless agitated. This result strongly suggested that the UPy-modified \(\text{N-alkyl urea peptoid oligomers were aggregating into higher molecular weight species.}\) Diffusion-ordered \(^1\text{H NMR spectroscopy (DOSY) is a useful technique to investigate the size of aggregates in solution.}\) Thus, to demonstrate the formation of supramolecular polymers concentration-dependent DOSY experiments were performed in CDCl\(_3\) at 25 °C. As can be observed in Figure 7, the viscosity corrected self-diffusion constant (\(D_c\)) of solutions of UPy-end functionalized oligomer containing MOM \(\text{N-alkyl groups becomes smaller with increasing concentration of oligomer in solution.}\)
Figure 7. Concentration-dependent viscosity corrected diffusion constant ($D_c$) in CDCl$_3$ at 25 °C for UPy-end functionalized oligomer containing MOM pendent $N$-alkyl groups.

The significant decrease of the diffusion coefficient with increasing concentration implies that polymeric species were formed at the higher concentrations. This result is similar to that observed by Leyong Wang and coworkers,$^{54}$ where an obvious decrease of the $D_c$ upon increasing the concentration of a solution of 2 equivalents of pillar[5]arene in a bisparaquat derivative indicated the formation of gradually larger polymeric structure from oligomers such as trimers, tetramers, to linear polymers. The $^1$H NMR spectrum in CDCl$_3$ of compound B shows two sets of signals. One set of N-H signals at 13.14, 11.84 and 10.12 ppm, which are assigned to the 4[1H]-pyrimidinone tautomer, and a second set of signals at 13.12, 11.74, and 10.04 ppm which are assigned to the pyrimidin-4-ol tautomer. This provides confirmation of the presence two self-complementary hydrogen-bonding units with both DDAA and DADA arrays.$^{55}$
The expected supramolecular polymerization was further investigated by concentration-dependent solution viscosity experiments of the UPy-end functionalized oligomers performed at 25 °C in CHCl₃. As a characteristic property of polymer molecules the relatively high solution viscosity at high concentration is a good corroboration of the presence of supramolecular polymers formed from the N-alkyl urea peptoids. A double logarithmic plot of the specific viscosity against solution concentration showed a marked change in the slope from 1.006 to 2.785 at approximately 30 mM (Figure 8).

Figure 8. Solution viscosities of Compound B (top) and Compound 6 (bottom) at varying concentrations.

The result shown in Figure 8 can be explained due to the presence of equilibrium in solution between linear supramolecular polymers and low molecular weight species.
Below the critical polymerization concentration cyclic species dominate, and above the critical polymerization concentration linear supramolecular polymers are favored. The point at which the slope of the plot in Figure 8 changes is the critical polymerization concentration. At concentrations below approximately 30 mM, the slope of almost unity demonstrates a linear relationship between the specific viscosity and solution concentration, which is characteristic for non-interacting assemblies of constant size. When the concentration increases further, a change of slope is observed indicating the formation of supramolecular polymers with increasing size. It was pleasing to note that the critical polymerization concentration found from Figure 8 agrees closely with the concentration where the viscosity corrected self-diffusion constant ($D_c$) values plateau in Figure 7.

In order to show that the UPy groups are stable to the deprotection conditions, the MOM groups were removed from Compound B using a 2 M HCl acid solution, generating UPy-end functionalized oligomers containing hydroxyl groups. (Figure 9) The structure of the hydroxyl-functionalized oligomer was confirmed using NMR spectroscopy, FTIR spectroscopy, and mass spectrometry.
Figure 9: Removal of the MOM ether protecting groups from UPy-modified N-alkyl urea peptoid oligomer B.

Having shown that UPy-end functionalized oligomers can form supramolecular polymers, and that the oligomers can undergo modifications after functionalization with UPy groups, we next demonstrated that other oligomers prepared in this work could be reacted with the UPy-isocyanate and undergo polymerization. We accomplished this by selecting the N-alkyl urea peptoid containing azide groups using a similar approach as for the MOM groups. (Figure 10) The structure of oligomer E was confirmed using NMR spectroscopy, FTIR spectroscopy, and mass spectrometry. We selected the azide modified oligomer as in addition to acting as precursors to amines, the azide group can be used in the facile and robust alkyne/azide cycloaddition reaction – known as one of the “click” chemistries” – and is therefore another avenue to a wide range of potential applications. For example, we have used the alkyne/azide cycloaddition reaction to
prepare carbohydrate functionalized $N$-alkyl urea peptoid/polymer conjugates as glycosaminoglycan mimetics.$^{16}$

Figure 10. Modification of the azide containing $N$-alkyl urea peptoid oligomer with UPy groups.

The expected supramolecular polymerization was investigated by concentration-dependent solution viscosity experiments of oligomer $E$ performed at 25 °C in CHCl$_3$. A double logarithmic plot of the specific viscosity against solution concentration showed a marked change in the slope from 1.03 to 1.29 at approximately 14 mM (Figure 11). This result is similar to that observed for the MOM-ether oligomer in Figure 8, and indicates the presence of supramolecular polymers from a concentration of 14mM in the
chloroform solution. Comparing Figure 8 with Figure 11, the increased slope changed from 2.875 to 1.29. We think it is due to the azide group. Since azide has charge on it, electrostatic repulsion will affect the H-bond interaction which will decrease the viscosity.

Figure 11. Solution viscosities of Compound E (top) and Compound 9 (bottom) at varying concentrations.

2.5 Conclusions

We have synthesized an \(N,N\)-linked-\(N\)-alkyl urea oligomer (\(N\)-alkyl urea peptoid) containing MOM-protected hydroxyl pendant \(N\)-alkyl groups as a “precursor” molecule that can be used in different ways depending upon the application. Oligomers containing alcohol functional groups were obtained by removing the MOM groups with a
2 M HCl acid solution. The hydroxyl groups were subsequently converted to carboxylic acid, alkyl chloride and azide moieties using simple organic chemistry reactions. This approach dramatically simplifies the synthesis and isolation of oligomers where all the \( N \)-alkyl pendant groups are designed to be the same. Supramolecular polymers were obtained from \( N \)-alkyl urea peptoid “monomers” by incorporating UPy motifs to the terminal ends of the MOM-protected oligomers and the azide-functionalized oligomers. Concentration dependent DOSY spectroscopy and solution viscometry experiments confirmed the presence of polymeric species in solution. We anticipate that this synthesis approach will find applications in soft materials applications analogous to segment assembly polymerizations, polypeptoids, and stimuli-responsive and self-healable supramolecular elastomers.

2.6 References


Chapter 3. Synthesis of polymer organogelators using quadruple hydrogen bonding as physical crosslinks

3.1 Abstract

The synthesis of a monomer containing four-fold hydrogen bonding groups 2-(((6-(6-methyl-4[1H]pyrimidionylureido)hexyl)carbamoyl)oxy)ethyl methacrylate (UPyEMA) and its copolymerization with monomers of different $T_g$ values using reversible addition fragmentation chain transfer (RAFT) polymerization is reported. The copolymers were synthesized with high molecular weight and narrow molecular weight distributions and formed stable organogels in both chloroform and dichlorobenzene. Critical gelation concentrations were determined and the rheology of the organogels was characterized. A novel monomer containing pyrene was copolymerized with the polymer organogelators forming fluorescent organogels. It is proposed that these gels are suitable for two photon up-conversion applications.

3.2 Introduction

Supramolecular gelators have attracted attention due to their potential in drug delivery and their light harvesting and conducting properties. Monomers in supramolecular gelators are linked using non-covalent interactions such as hydrogen bonding, host-guest interactions, π-π stacking and coordination interactions. As a consequence of these non-covalent interactions, supramolecular gelators form in a dynamic reversible manner and can be rendered stimuli-responsive using external stimuli such as temperature and pH. Rotello’s group reported forming micro-organogels using bis-thymine units to non-covalently cross-link a complementary diaminopyridine.
functionalized copolymer through hydrogen bonding. Controlling polymer stereochemistry may also enable the formation of organogels not possessing covalent crosslinks. For example, isotactic and syndiotactic polystyrene formed gels in organic solvents. Syndiotactic poly(methyl methacrylate) was also shown to be an organogelator in bromobenzene, chlorobenzene and toluene. Polypeptides or copolymers containing peptide segments have been widely used to generate organogels. The polypeptides used in organogelators are usually hydrophobic and thus different from water-soluble polypeptides that form hydrogels, however the gelation mechanism is the same with helical conformations acting as crosslinking points in three-dimensional networks. Weiss and coworkers reported that poly(allylamine) formed gels in alcohol, DMSO, and dichloromethane in the presence of CO$_2$. The side chain amine groups reacted with CO$_2$ yielding ammonium (NH$_3^+$) and carbamate (NHCO$_2^-$) moieties crosslinking polymer chains.

The key feature for a polymer organogelator is that the polymer must contain strong physical crosslink sites. Ureidopyrimidinone (UPy) is a four-fold hydrogen bonding species shown as a useful building block for various supramolecular architectures and materials due to its high dimerization constant (>10$^6$ M$^{-1}$ in CHCl$_3$) and synthetic accessibility. Although high internal phase emulsion gels (HIPE gels) and hydrogels based on polymers containing UPy moieties have been reported, UPy functionalized polymer organogelators are not as well developed.

Herein, we report the synthesis of a UPy-containing methacrylate monomer and its copolymerization with different monomers to form new polymer organogelators. The monomer is taken from the work of Berda and co-workers who used it in the preparation
of single chain nanoparticles. A novel pyrene-based methacrylate monomer was also synthesized and polymerized under RAFT control. Two organogels possessing fluorescence properties were prepared by copolymerizing the pyrene monomer with the UPy-containing methacrylate monomer and styrene.

3.3 Experimental

All starting reagents were purchased from Aldrich at the highest purity available and used as received unless stated otherwise. CDCl$_3$ and DMSO($d_6$) are from Cambridge Isotope Laboratories. $^1$H and $^{13}$C NMR measurements were recorded in CDCl$_3$ and DMSO($d_6$) with Si(CH$_3$)$_4$ as an internal standard using a Bruker Ultrashield 400 MHz (100 MHz for $^{13}$C); NMR spectra were processed using UXNMR version 2.5 and MestRe-C. Fourier transform infrared (FT-IR) spectra were collected on a Nicolet 6700 spectrometer and analyzed with OMNIC 32 software. Mass spectrometry was performed using a Micromass Q-TOF-2™ spectrometer. The critical gelation concentration values were determined in the following process: Solvents were added to the gelators and then the mixtures were heated up to make homogenous. 1.0 mL solutions in 3.0 mL vials. Gels were formed once the solutions were cooled to room temperature. The vial was inverted each time to ensure the absence of any observed flow in the solutions. This process was repeated until gels were not formed upon adding another small volume of solvents.

Rheology Measurements

All characterization was performed using a Discovery Series Hybrid Rheometer (DHR) (Model: HR-2, TA Instruments) under strain-controlled mode and fitted with a 20 mm
diameter Smart Swap flat geometry plate and insulating thermal cover. The temperature was controlled using an Advanced Peltier System. To prepare the sample, polymers were dissolved in dichlorobenzene to a concentration of 180 mg/mL, which is slightly higher than the critical gelation concentration. The solution was held at 50 °C for 5 minutes before cooling to room temperature to form a gel. All the gels were annealed at 80 °C for 10 min and held at 21 °C overnight before being measured by rheometer. To examine the rheological properties, oscillatory time sweeps (3.2 Hz, 1% strain, 25 °C), oscillatory frequency sweeps (0.1-100 Hz; 1% strain, 25 °C) and oscillatory temperature sweeps (25-80 °C, 3.2 Hz, 1% strain) were performed. For shear recovery experiments, shear thinning was performed at 250 % strain with recovery at 1 % strain at 3.2 Hz.

**Synthesis of UPyEMA**

UPyEMA was synthesized according to previous literature.\(^{26}\) 2(6-isocyanatohexylaminocarbonylamino)-6-methyl-4[1H]pyrimidinone (UPy) (500 mg, 1.71 mmol), 2-hydroxyethyl methacrylate (HEMA) (433 mg, 3.42 mmol), and 3 drops of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as catalyst in 20 mL CHCl\(_3\) was added to a round bottom flask equipped with a stir bar. The reaction was heated at 80 °C for 6 hours. Then the CHCl\(_3\) solution was washed with saturated NH\(_4\)Cl solution, NaHCO\(_3\) solution, and brine. The solvent was then removed to yield viscous oil. The oil was washed with ether 3 times to give white precipitate as pure product in 510 mg. Yield: 70%. \(^1\)H NMR (CDCl\(_3\)): δ (ppm) 1.38-1.58 (m, 8 H, 4 CH\(_2\) on hexyl link), 1.96 (s, 3 H, CH\(_3\)), 2.25 (s, 3 H, CH\(_3\)), 3.16-3.29 (m, 4 H, 2 NCH\(_2\)), 4.33 (s, 4 H, OCH\(_2\)CH\(_2\)O), 5.02 (s, 1 H, NHCO), 5.60 (s, 1 H, CH=C), 5.86 (s, 1 H, CH=C), 6.15 (s, 1 H, CH=C), 10.18 (s, 1 H, NH), 11.88 (s, 1 H, NH), 13.16 (s, 1 H, NH); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): δ (ppm) 18.33 (CH\(_3\)), 18.99
CH₃, 26.07 (CH₂), 26.24 (CH₂), 29.36 (CH₂), 29.67 (CH₂), 39.62 (NCH₂), 40.76 (NCH₂), 62.40 (OCH₂CH₂O), 65.03 (OCH₂CH₂O), 106.69 (CH=C), 126.00 (CH₂=C), 136.00 (CH=C), 148.32 (CH₂=C), 154.71 (N=C), 156.15 (C=O), 156.58 (OC=O), 167.19 (OC=O), 173.18 (OC=O); MS (TOF MS ES+): 424.20 (M + 1); FT-IR: (cm⁻¹) ν(NH) = 3428, ν(alkanes) = 2936, ν(CO) = 1699, ν(Phenyl) = 1579.

**Synthesis of poly(Styrene-s-UPyEMA)**

A 25 mL round bottom flask was charged with UPyEMA (840 mg, 1.98 mmol), styrene (1.60 mL, 14.00 mmol), cumyl dithiobenzoate (CDB) (44.8 mg, 0.16 mmol), and AIBN (8.8 mg, 0.054 mmol) in Dimethyl sulfoxide (DMSO) (3.0 mL) The reaction flask was sealed with a rubber septum and the contents purged with N₂ in an ice-bath for 30 min. The flask was placed in a pre-heated oil bath at 100 °C for 32 h. The polymerization was quenched by exposure to air (O₂) and rapid cooling. The polymer was precipitated from cold methanol and dried in vacuum to afford 1.2 g of pink powder. Isolated yield: 52%.

**Synthesis of poly(n-Butyl acrylate-s-UPyEMA)**

A 25 mL round bottom flask was charged with UPyEMA (1.03 g, 2.43 mmol), n-butyl acrylate (nBuA) (2.0 mL, 13.76 mmol), CDB (43.6 mg, 0.16 mmol), and AIBN (8.8 mg, 0.054 mmol) in N,N-dimethylformamide (DMF) (6.0 mL) The reaction flask was sealed with a rubber septum and the contents purged with N₂ in an ice-bath for 30 min before the flask was put in a pre-heated oil bath at 80 °C for 6 h. The polymerization was quenched by exposure to air (O₂) and rapid cooling. The polymer was precipitated from cold methanol and dried in vacuum to afford 1.3 g of pink powder. Isolated yield: 46%.
Synthesis of poly(tert-Butyl acrylate-s-UPyEMA)

A 25 mL round bottom flask was charged with UPyEMA (1.03 g, 2.43 mmol), tert-butyl acrylate (tBuA) (2.0 mL, 13.76 mmol), CDB (43.6 mg, 0.16 mmol), and AIBN (8.8 mg, 0.054 mmol) in DMF (6.0 mL) The reaction flask was sealed with a rubber septum and the contents purged with N₂ in an ice-bath for 30 min before the flask was placed into a pre-heated oil bath set at 80 °C for 8 h. The polymerization was quenched by exposure to air (O₂) and rapid cooling. The polymer was precipitated from cold methanol and dried in vacuum to afford 1.2 g of pink powder. Isolated yield: 42%.

Synthesis of pyrene-containing monomer (PyEMA)

A solution of triphosgene (163 mg, 0.55 x 10⁻³ moles) in 6 mL of dichloromethane (DCM) was added to a Schlenk tube and stirred at 0 °C while 1-amino pyrene (0.30 g, 1.38 x 10⁻³ moles) and Et₃N (279 mg, 2.76 x 10⁻³ moles) in 6.0 mL of DCM were added dropwise using a syringe. The ice bath was removed after 15 min and the reaction was allowed to proceed at room temperature for 30 min before HEMA (215.6 mg, 1.66 x 10⁻³ moles) was added and the reaction stirred at room temperature overnight. The solution was washed with saturated NH₄Cl solution, NaHCO₃ solution, and brine. A viscous oil was obtained after drying and concentrating the organic layer, and this was purified using column chromatography on silica gel with CH₂Cl₂ as the mobile phase. The solvent was removed and the product dried in vacuum to give 352 mg product. Yield: 68%. 

¹H NMR (CDCl₃): δ (ppm) 2.00 (s, 3 H, CH₃), 4.50-4.56 (m, 4 H, OCH₂CH₂O), 5.64 (bs, 1 H, CH=C), 6.21 (bs, 1 H, CH=C), 8.01-8.22 (m, 9 H, proton on pyrenyl), 8.40 (s, 1 H, NH); ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 18.37 (CH₃), 62.92 (OCH₂CH₂O), 63.30
Kinetic study of pyrene base monomer (PyEMA)

A 25 mL round bottom flask was charged with PyEMA (600 mg, 1.61 mmol), cumyl dithiobenzoate (CDB) (8.8 mg, 0.032 mmol), and azobisisobutyronitrile (AIBN) (0.52 mg, 0.003 mmol) in Anisole (4.0 mL) The reaction flask was sealed with a rubber septum and the contents purged with N\textsubscript{2} in an ice-bath for 30 min before the flask was heated to 85 °C. The polymerization was sampled every 40 min before being quenched by exposure to air (O\textsubscript{2}) and rapid cooling. The polymer was precipitated from ether and dried in vacuum to afford 310 mg of pink powder. Isolated yield: 51%.

Synthesis of poly(sty-s-UPyEMA-s-PyEMA\textsubscript{1%})

A 25 mL round bottom flask was charged with UPyEMA (840 mg, 1.98 mmol), Styrene (1.6 mL, 14 mmol), PyEMA (66 mg, 0.17 mmol), CDB (45.1 mg, 0.165 mmol), and AIBN (9.1 mg, 0.055 mmol) in DMSO (3.0 mL) The reaction flask was sealed with a rubber septum, the contents purged with N\textsubscript{2} in an ice-bath for 30 min, and then the flask placed in a pre-heated oil bath at 100 °C for 32 h. The polymerization was quenched by exposure to air (O\textsubscript{2}) and rapid cooling. The polymer was precipitated from cold methanol and dried in vacuum to afford 1.87 g of pink powder. Isolated yield: 63%.

Synthesis of poly(sty-s-UPyEMA-s-PyMA\textsubscript{10%})
A 25 mL round bottom flask was charged with UPyEMA (840 mg, 1.98 mmol), Styrene (1.4 mL, 12.32 mmol), PyMA (612.8 mg, 1.64 mmol), CDB (44.6 mg, 0.16 mmol), and AIBN (9.0 mg, 0.055 mmol) in DMSO (3.0 mL) The reaction flask was sealed with a rubber septum and the contents purged with N₂ in an ice-bath for 30 min. The flask was then put in a pre-heated oil bath at 100 °C for 32 h. The polymerization was quenched by exposure to air (O₂) and rapid cooling. The polymer was precipitated from cold methanol and dried in vacuum to afford 1.2 g of pink powder. Isolated yield: 44%.

3.4 Results and Discussion

The UPy-containing methacrylate monomer UPyEMA was synthesized using 2-hydroxylethyl methacrylate and a UPy-functionalized isocyanate in 70% yield (Scheme 1a). The product structure was confirmed using ¹H nuclear magnetic resonance (NMR) spectroscopy. UPyEMA shows two single peaks in the NMR spectrum at 1.96 and 2.25 ppm arising from the methacrylate methyl group and pyrimidone methyl group respectively, and three singlet peaks from UPy above 10.0 ppm. Mass spectrometry further confirmed the structure, and a molecular ion peak was observed at m/z = 424.20 (calculated m/z = 424.22) for UPyEMA. Meijer’s group previously used this monomer for producing single chain nanoparticles, where the UPy groups induced the intramolecular collapse. A similar UPy-containing monomer UPyMA was previously synthesized by Long’s group via the reaction of 2-amino-4-hydroxy-6-methylpyrimidine and 2-isocyanatoethyl methacrylate. The UPyEMA synthesized by our method contains an extra six-carbon chain and a carbamate functional group compared to Long’s UPyMA. We hoped the additional alkyl and carbamate groups would increase the solubility of our monomer allowing for higher mole ratios of UPyEMA in copolymers.
Scheme 1. (a) Synthesis of the UPyEMA monomer. (b) Synthesis of gelators 1-3.

We prepared three polymeric gelators using UPyEMA as a comonomer (Scheme 1b). We chose tert-butyl acrylate (t-BA), n-butyl acrylate (n-BA) and styrene (Sty) respectively for the major component of each gelator. These monomers were selected as their homopolymers give a range of $T_g$ values. We copolymerized t-BA and UPyEMA under reversible addition-fragmentation chain-transfer (RAFT) polymerization control using cumyl dithiobenzoate (CDB) to obtain gelator 1, poly(tBuA-s-UPyEMA). We determined that UPyEMA was incorporated in a 16% molar ratio in the copolymer using $^1$H NMR spectroscopy comparing the peak from the CH proton on UPy against the tert-butyl methyl groups. The polymer formed a stable gel (Figure 1, left vial) in chloroform, and the critical gelation concentration (CGC) was determined as 5.1% weight percent. The other gelators shown in Scheme 1 were synthesized and
characterized in the same manner as poly(tBuA-s-UPyEMA). Although the gelators exhibited different physical states (sticky solid→wax like solid→powder for polymers from low \( T_g \) to high \( T_g \)) at room temperature, solutions of all three gelators formed gels that were stable to inversion after heating and cooling cycles (Figure 1). The CGC in chloroform was 8.0 wt % for Poly(nBA-s-UPyEMA) and 6.3 wt % for Poly(Sty-s-UPyEMA).

![Image of inverted vials showing gels formed from chloroform solutions of gelators 1-3.](image)

**Figure 1.** Inverted vials showing gels formed from chloroform solutions of gelators 1-3 (from left to right) at their critical gelation concentration.

As we described, we initially prepared the gels in chloroform. This was due to the fact that the UPy dimerization is well-known to occur in non-polar solvents such as chloroform, and it enabled comparison of the polymers with low molecular weight organogelators we have previously reported. However, although the polymers formed stable gels in chloroform we chose to further examine the polymer gels in 1,2-dichlorobenzene as it is a higher boiling solvent, allowing us to probe the rheology of the
gels, and could also afford a greater range of applications. The polymers prepared for study in 1,2-dichlorobenzene are described in Table 1. The CGCs are slightly higher in dichlorobenzene compared to chloroform, as expected due to the less favorable conditions for UPy dimerization.

Table 1. CGC trends for different UPy polymers.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>CGC (dichlorobenzene)</th>
<th>Monomer Ratio$^b$</th>
<th>$M_n$ (g/mol)$^c$</th>
<th>$\mathcal{D}$$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly(tBA-s-UPyEMA)</td>
<td>7.8 wt%</td>
<td>84:16</td>
<td>11 900</td>
<td>1.45</td>
</tr>
<tr>
<td>Poly(nBA-s-UPyEMA)</td>
<td>8.2 wt%</td>
<td>88:12</td>
<td>12 900</td>
<td>1.55</td>
</tr>
<tr>
<td>Poly(Sty-s-UPyEMA)</td>
<td>6.9 wt%</td>
<td>86:14</td>
<td>12 000</td>
<td>1.38</td>
</tr>
</tbody>
</table>

$^a$Critical Gel Concentration (CGC)
$^b$Monomer ratio is expressed as a percentage
$^c$$M_n$ = number average molecular weight
$^d$Dispersity = weight average molecular weight/number average molecular weight

After annealing the gels at 80 °C the storage modulus $G'$ and loss modulus $G''$ in 1,2-dichlorobenzene were plotted against time at room temperature (Figure 2).
Figure 2. Representative oscillatory time sweeps showing storage modulus ($G'$, filled symbols) and loss modulus ($G''$, open symbols) of gels composed of (A) poly(tert-butylacrylate-s-UPyEMA), (B) poly($n$-butylacrylate-s-UPyEMA) and (C) poly(styrene-s-UPyEMA).

For all three gels, $G'$ and $G''$ remained at equilibrium values with $G'$ higher than $G''$. While this observation has been used to show the formation of a stable gel 29, compared with most organogels 30, 31 our polymers in dichlorobenzene form weak gels with the difference between $G'$ and $G''$ less than one order of magnitude. Furthermore, the gels in dichlorobenzene appear to be weaker than those formed chloroform. Gels prepared in chloroform were more transparent and stiffer than their counterparts in dichlorobenzene. Despite the fact we formed weaker gels in dichlorobenzene than in chloroform, we continued to examine the rheology of dichlorobenzene gels as interesting behavior was revealed. Figure 3 shows the effect of temperature on $G'$ and $G''$. Both $G'$ and $G''$ decrease gradually with the increasing temperature, with $G'$ decreasing at a faster rate.
Figure 3. Representative oscillatory temperature sweeps showing storage modulus ($G'$, filled symbols) and loss modulus ($G''$, open symbols) of gels composed of (A) poly(tert-butylacrylate-s-UPyEMA), (B) poly(n-butylacrylate-s-UPyEMA) and (C) poly(styrene-s-UPyEMA).

The temperature at which $G'$ and $G''$ intersect is the gel transition temperature ($T_{gel}$)\textsuperscript{32}, below this temperature the polymer chain interactions are strong enough to give the material elastic behavior. These interactions are lost with increasing temperature, which results in a gel-to-sol transition as the network breaks. All the three gels show a similar $T_{gel}$ temperature around 30 °C. Both $G'$ and $G''$ decrease with increasing temperature due to loss of interactions between polymer chains. The dimerization constant of UPy is known to be highly temperature and solvent dependent. We speculate that the lifetime of individual hydrogen bonds is decreased under these conditions, leading to the flow observed in the Figure 3. Since the lifetime of hydrogen bonding shortens considerably with increased temperature\textsuperscript{33}, we believe that above 30 °C the relaxation rate of the polymer chains is faster than the shear rate applied.
Oscillatory frequency sweeps at room temperature were carried on all the gels to further study their rheological properties (Figure 4).

![Graphs showing storage modulus (G’, filled symbols) and loss modulus (G”, open symbols) of gels composed of (A) poly(tert-butylacrylate-s-UPyEMA), (B) poly(n-butylacrylate-s-UPyEMA) and (C) poly(styrene-s-UPyEMA).]

**Figure 4.** Representative oscillatory frequency sweeps showing storage modulus (G’, filled symbols) and loss modulus (G”, open symbols) of gels composed of (A) poly(tert-butylacrylate-s-UPyEMA), (B) poly(n-butylacrylate-s-UPyEMA) and (C) poly(styrene-s-UPyEMA).

For all three gels, the loss modulus is larger than the storage modulus at low frequencies until a crossover point is reached, and the storage modulus becomes larger than the loss modulus. The similar G’ and G” crossover frequency value implies all three gels have the same polymer chain relaxation behavior, which suggests that the gelation is driven by the four-fold hydrogen bonding in UPy. The G’ of the tested gels was observed as high as $10^4$ Pa, which is comparable with permanently crosslinked gels. Furthermore, the rheology behavior shown in Figure 4 is qualitatively different than that observed for our UPy-functionalized low molecular weight organogelators.
This is explained by the different gelation mechanisms for the polymer gelators (H-bonding) and low molecular weight gelators (phase separation).

Interestingly, self-healing behavior is typically seen in polymers with rheology similar to that observed in Figure 4\textsuperscript{35}. Considering the reversible nature of hydrogen bonding, the poly(Sty-s-UPyEMA) gel was subjected to cycles of large amplitude oscillatory strain followed by low amplitude oscillatory strain to examine the time scale of material recovery. Under cyclic deformation at room temperature, the materials shows a clear drop in both $G'$ and $G''$ values and a gel-sol transition at the onset of high strain (Figure 5). In the transition from high strain to low strain conditions, more than 90 \% of the initial mechanical behavior can be recovered in less than 100 s. In other words, our gels are capable of near-immediate recovery following shear thinning\textsuperscript{36}.

**Figure 5.** Cyclic deformation of 1 \% (low, unshaded areas) and 200 \% (high, shaded, areas) strain at 20 rad/s on poly(Sty-s-UPyEMA) gel showing storage modulus ($G'$, filled symbols) and loss modulus ($G''$, open symbols).

Our group has a growing interest in photon upconversion and we recently reported a polymer supported photon upconversion system demonstrating the interplay between
emitters on different polymer chains \(^\text{37}\). Furthermore, we previously showed that pyrene, itself a potential emitter molecule for photon upconversion, could be used in a low molecular weight organogelator \(^\text{29}\). Therefore, a natural extension of this work was to prepare a pyrene containing polymer organogelator \(^\text{38-42}\). Compared to small molecule pairs, polymeric upconversion systems can be used under ambient conditions resulting in decreased oxygen quenching effects \(^\text{43}\). However, phase separation of the polymer and chromophore leads to limited practical applications of many polymer systems to date. It has been proposed to circumvent this constraint by conjugating chromophores into polymer chains \(^\text{37}\). Pyrene and tris(2-phenylpyridine) iridium (III) are commonly used triplet triplet annihilation pairs for upconversion applications \(^\text{44}\). We modified pyrene to afford a monomer that could be copolymerized with styrene and UPyEMA for use in polymer organogels. A pyrene isocyanate was generated \textit{in situ} by treating 1-amino pyrene with triphosgene, followed by addition of HEMA to produce the monomer 2-((pyrenylcarbamoyl)oxy)ethyl methacrylate (PyEMA) in 50 \% yield (Scheme 2). The structure of the monomer was confirmed using NMR spectroscopy and mass spectrometry in the same manner as UPyEMA. The \(^1\text{H}\) NMR spectrum of PyEMA showed a peak at 2.00 ppm due to the methyl groups of the methacrylate, and the pyrene protons were present at 8.01-8.22 ppm. Mass spectrometry gave the molecular ion peaks at \(\text{m/z} = 396.12\) (calculated \(\text{m/z} = 396.12\ M+\text{Na}\)).
Scheme 2. Synthesis of the pyrene based monomer PyEMA and its subsequent polymerization with CDB.

We demonstrated that PyEMA could be polymerized in a controlled/“living” manner by determining the kinetics of PyEMA polymerization using a pseudo-first order kinetic plot (Figure 6a). We chose cumyl dithiobenzoate as the chain transfer agent to control the RAFT polymerization of PyEMA. Figure 6 also shows the plots of number-average molecular weight ($M_n$) and dispersity of the obtained polymers against monomer conversion. The $M_n$ increased linearly with monomer conversion and the polymer dispersity remained narrow ($M_w/M_n < 1.2$) throughout the polymerization with unimodal peaks in the GPC spectra (Figure 6d). These results indicated the RAFT polymerization of PyEMA mediated with CDB proceeded in a controlled manner. The observed $M_n$ is higher than theoretically predicted, probably due to consumption of the CDB RAFT agent through some irreversible termination events.
Figure 6. Characterization of the RAFT polymerization of PyEMA with AIBN as an initiator and CDB as a RAFT agent at 80 °C in anisole using the (a) pseudo-first order kinetic plot; (b) $M_n$ vs. conversion plot; (c) dispersity vs. conversion plot; (d) GPC traces of poly(PyEMA) during polymerization sampled at 40, 80, 120, 160, 200 minutes.

We prepared two statistical copolymers containing the PyEMA monomer to form fluorescent polymer organogelators. The PyEMA feed ratio of the two polymerizations was set at 1% (gelator 4) and 10% (gelator 5) with the remaining monomer being 20 % UPyEMA and the rest styrene. We chose styrene as the comonomer for proof-of-principle purposes. The polymerizations were performed in DMSO at 100 °C for 32 h and the polymers precipitated into methanol, as the unreacted UPyEMA and PyEMA monomer is soluble in methanol. GPC analysis showed gelators 4 and 5 possessed $M_n$
values of 17 900 g/mol and 19 600 g/mol respectively with dispersity of 1.52 and 1.58 respectively.

We determined the composition of gelator 4 as poly(styrene$_{100}$-s-UPyEMA$_{17}$-s-PyEMA$_2$) and gelator 5 as poly(styrene$_{90}$-s-UPyEMA$_{13}$-s-PyEMA$_{13}$) using $^1$H NMR spectroscopy in dueterated DMSO. We did not use higher molar ratios of PyEMA due to concerns of fluorescence self-quenching at higher dye concentrations $^{37}$. The CGC of gelator 4 was determined as 6.3 % weight percent in chloroform and the CGC of gelator 5 was 9.2 % weight percent in chloroform. We returned to using chloroform for these measurements, as we knew they would result in more stable gels. We measured the UV absorption and fluorescence emission of dilute solutions of gelator 4 and 5. We measured the solution of 5 at a 1/10 concentration of the solution of 4, as the incorporation of pyrene in gelator 5 was much higher than in gelator 4. Both 4 and 5 showed characteristic pyrene absorption around 350 nm (Figure 7b) and fluorescence emission between 380-450 nm (Figure 7c).

a. 

b. 

\[
\text{Absorbance}
\]

\[
\text{Wavelength (nm)}
\]
c.

**Figure 7.** (a) Inverted vials showing gels formed from chloroform solutions of gelators 4 and 5 at their critical gelation concentration; (b) UV-Vis spectra of gleator 4 (0.2 mg/mL) and gelator 5 (0.02 mg/mL); (c) fluorescence spectra of gleator 4 (0.2 mg/mL) and gelator 5 (0.02 mg/mL).

The gels were highly colored due to the dithiobenzoate RAFT chain transfer agent used in the polymerization. However, reducing the thiocarbonyl-thio group or removing the terminal dithiobenzoate group using an excess of low molecular weight radical species can easily remove the color. Indeed, we have used this strategy with AIBN to remove the thiol end-groups in these polymers. We are currently exploring the use of these gels in photon up-conversion applications and we will report the results in future communications.

**3.5 Conclusion**

We have prepared a set of copolymers using RAFT polymerization that form organogels through UPy-mediated hydrogen bonding and two organogels possessing fluorescence
properties were prepared by copolymerizing a pyrene-containing monomer. Despite the
dry polymers having different physical appearances the gels possessed similar $T_{gel}$
vvalues and rheology behavior, and the CGCs trended with the amount of UPy moieties
in the polymers. These observations imply that gelation is driven by the UPy groups and
is not influenced by the comonomer. All of the copolymers appear to form gels through
hydrogen bonding rather than phase separation, which was the mechanism we
postulated for similar UPy-containing low molecular weight organogels. The polymers
formed stable gels in chloroform as observed using inversion tests, however, gels
formed in 1,2-dichlorobenzene (a higher boiling solvent and suitable for rheology) were
quite weak with storage moduli less than one order of magnitude higher than loss
moduli. However, the gels in dichlorobenzene demonstrated interesting rheology
properties, including shear recovery properties. We anticipate that the pyrene-
containing gels will find applications in two-photon upconversion studies where the
ability to use various comonomers and form stable gels may prove advantageous.

3.6 References

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Chapter 4. Synthesis of rationally designed polymeric emitters with tunable interchromophore distances

4.1 Abstract

A series of Poly[(9-anthrylmethyl methacrylate)-co-(methyl methacrylate)] (Poly(AnMMA-co-MMA)) with different percentages of AnMMA were synthesized using reversible addition-fragmentation chain-transfer (RAFT) polymerization. Those random copolymers were used as polymeric emitters working with platinum octaethylporphyrin as sensitizer to form triplet-triplet annihilation upconversion (TTA-UC) system. Effect of inter-chromophore distances on TTA-UC intensity was investigated. With increasing AnMMA ratio, TTA-UC intensity first increases, and then decreases when the ratio gets to a optimal value which illustrated the key factors affecting polymeric TTA-UC system.

4.2 Introduction

Photon upconversion is a process in which two lower energy photons combine to emit a single higher energy photon. Triplet-triplet annihilation upconversion (TTA-UC) as one of upconversion methods, since first reported by Parker and Hatchard fifty years ago,\(^1\) has proposed in applications such as solar cells, semiconductors, and controlled drug release.\(^2^4\) TTA-UC is particularly interesting because of its specific advantages like high quantum yield with relatively low excitation intensity and using non-coherent light so that sunlight can be used as the energy source.\(^5\) The TTA-UC mechanism involves energy transfer from a sensitizer to an emitter. By absorbing incident light, the sensitizer singlet excited state (\(^1\)S*) is converted to a sensitizer triplet state (\(^3\)S*) upon intersystem crossing (ISC), then triplet-triplet energy transfer (TTET) to an emitter triplet (\(^3\)E*)
following by triplet-triplet annihilation (TTA) of two emitter triplets to populate the excited singlet emitters ($^1E^*$). Since the emission from the excited singlet emitters has a higher energy than the initial excitation of the sensitizer, upconversion is achieved. Systems using TTA-UC were limited to small molecular pairs for a long time, recently however; TTA-UC has been used in polymeric system such as solid polymer matrix, melt-processed polymer glasses, oligofluorene emitters and organic nanofibers. Compared to small molecule pairs, polymeric upconversion system can be used under ambient conditions resulting in decreased effects of oxygen quenching. However, phase separation of polymeric matrix and chromophores in these systems will limit practical applications of polymer systems to date. We speculated that conjugating chromophores into polymer chain would overcome these limits.

Herein, we report an investigation of a polymeric upconversion system, whose emitters were covalently linked to a polymer backbone. The monomers 9-anthrylmethyl methacrylate (AnMMA) and methyl methacrylate (MMA) were chosen and polymerized using reversible addition-fragmentation chain transfer (RAFT) polymerization conditions. Platinum (II) octaethylporphyrin (PtOEP) was used as the sensitizer. The Pt present in this molecule is in favor of the spin-orbit coupling, and consequently the singlet-triplet intersystem crossing efficiency is near unity making PtOEP a very good sensitizer.

4.3 Experimental

Materials

All chemicals were purchased from Sigma-Aldrich at the highest available purity and used as received unless otherwise stated. $^1H$ and $^{13}C$ NMR measurements were
performed in CDCl₃, with Si(CH₃)₄ standard, using a 400 MHz Bruker Ultrashield (100 MHz for ¹³C). ¹H NMR and ¹³C NMR spectra were analyzed with MestReNova software. Fourier transform infrared (FTIR) spectra were collected on a Nicolet 6700 spectrometer and analyzed with OMIC 32 software. Mass spectrometry was performed using a Micromass Q-TOF-2™ spectrometer.

**Synthesis of 9-anthrylmethyl methacrylate (AnMMA)**

9-Anthracenemethanol (4.00 g, 19.2 mmol), triethylamine (5.80 g, 57.4 mmol) were added to 100 mL THF in a round-bottom flask equipped with septum and stir bar. The mixture was cooled in ice bath for 30 min. Methacryloyl chloride (6.00 g, 57.4 mmol) was added to the flask through a syringe dropwise at 0 °C. The reaction was allowed to proceed under room temperature overnight. THF was removed by vacuum distillation, and the residue dissolved in CH₂Cl₂ and washed with 1 M HCl solution, NaHCO₃ solution and brine. The solution was dried over Na₂SO₄ and then concentrated to afford the crude product which was purified using column chromatograph on silica gel (silica gel 60 Å, 70–230 mesh) with DCM:Hexane (3:1 v/v) as the mobile phase. The solvent was removed and the product dried in vacuum to yield 4.0 g of yellow powder. Yield: 70%. ¹H NMR (CDCl₃): δ (ppm) 1.92 (s, 3 H, OCH₃), 5.51 (s, 1 H, C=CH₂), 6.05 (s, 1 H, C=CH₂), 6.22 (s, 2 H, CH₂O), 7.48–7.51 (t, 2 H, J = 8.0 Hz, aromatic H), 7.56–7.59 (t, 2 H, J = 8.0 Hz, aromatic H), 8.03–8.05 (t, 2 H, J = 8.0 Hz, aromatic H), 8.37–8.39 (t, 2 H, J = 8.0 Hz, aromatic H), 8.52 (s, 1 H, aromatic H). ¹³C NMR (CDCl₃): δ (ppm) 167.64 (C=O), 136.25, 131.51, 131.23, 129.26, 126.72, 126.52, 126.17, 125.22, 124.17 (sp²–C), 59.28 (CH₂O), 18.50 (C=CH₂CH₃). FT-IR (cm⁻¹): ν(NH) = 3325, ν(CH) = 2930. MS (TOF MS ES+): 299.1057 M+Na⁺ (Calculated: 299.1048).
**Figure 1.** 1H NMR spectrum of 9-anthrylmethyl methacrylate.

**Synthesis of poly[(9-anthrylmethyl methacrylate)-co-(methyl methacrylate)] (Poly(AnMMA-co-MMA))**

**General procedure for polymerization:**

For the polymerization of Poly(AnMMA-co-MMA) with a 15/85 mol ratio of AnMMA and MMA in the feed, the procedure is as follows: 9-anthrylmethyl methacrylate (1.0 g, 3.6 mmol), methyl methacrylate (2.20 mL, 20.5 mmol), cumyl dithiobenzoate (65.6 mg, 0.240 mmol), azobisisobutyronitrile (AIBN, 13 mg, 0.08 mmol) and 8 mL anhydrous THF were added to a round bottom flask. The reaction flask was sealed with a rubber septum and purged with N₂ for 30 min. The reaction was allowed to proceed at 80 °C for 21 h and stopped by exposure the reaction to air. The residue was then precipitated in cold methanol twice to afford pink solids. AIBN was used to remove thiocarbonylthio
groups from the prepared polymers. Equal mass AIBN and polymer were dissolved in anisole and purged with N₂ for 30 min. The reaction was allowed to proceed at 80 °C for 2 h. The residue was then precipitated in cold methanol twice to afford the final polymer as white powder. The polymerization of the other copolymers was performed under identical conditions with the appropriate amounts of AnMMA and MMA.

4.4 Results and Discussion

A series of Poly(AnMMA-co-MMA)s with different AnMMA to MMA ratios were synthesized through RAFT polymerization. AnMMA, was synthesized by reacting 9-anthracenemethanol with methacryloyl chloride (Scheme 1a). AnMMA was polymerized with methyl methacrylate (MMA) in a statistical copolymerization with azobisisobutyronitrile (AIBN) as initiator and cumyl dithiobenzoate (CDB) as RAFT chain transfer agent (CTA) (Scheme 1b).

**Scheme 1.** a) Synthesis of AnMMA; and b) synthesis of Poly(AnMMA-co-MMA).
The distance between individual chromophores can be tuned by the use of a copolymer as the polymeric emitter. MMA is chosen as the co-monomer since it can generate a tertiary carbon propagating radical, which can match the reactivity of the AnMMA propagating radical. By varying the molar ratio of AnMMA/MMA in the feed, a series of copolymers were synthesized (shown in Table 1).

Table 1. Characteristics of Poly(AnMMA-co-MMA) copolymers.

<table>
<thead>
<tr>
<th>Mole feed ratio</th>
<th>3/97</th>
<th>4/96</th>
<th>6/94</th>
<th>10/90</th>
<th>10/90</th>
<th>20/80</th>
<th>25/75</th>
<th>60/40</th>
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<td>$M_n (x10^4)$</td>
<td>1.53</td>
<td>1.46</td>
<td>1.59</td>
<td>1.43</td>
<td>1.82</td>
<td>1.86</td>
<td>1.85</td>
<td>1.98</td>
</tr>
<tr>
<td>PDI</td>
<td>1.02</td>
<td>1.10</td>
<td>1.03</td>
<td>1.07</td>
<td>1.03</td>
<td>1.06</td>
<td>1.10</td>
<td>1.05</td>
</tr>
<tr>
<td>Actual ratio</td>
<td>2/98</td>
<td>4/96</td>
<td>8.8/91.2</td>
<td>12/88</td>
<td>17.5/82.5</td>
<td>28.4/71.6</td>
<td>40/60</td>
<td>66/34</td>
</tr>
</tbody>
</table>

Poly(AnMMA-co-MMA) and PtOEP were dissolved separately in N,N-dimethylformamide (DMF) before being mixed together. All mixtures were thoroughly deoxygenated by the freeze-pump-thaw method before spectroscopic measurements, which were excited by a 532 nm laser.

Two series of upconversion measurements were carried out. In the first series, the mixtures contained the same concentrations of PtOEP and Poly(AnMMA-co-MMA) with different AnMMA ratios. Results are shown in Figures 2. With the increase of the AnMMA ratio in the Poly(AnMMA-co-MMA) polymers, more emitting chromophores (AnMMA) are present in the mixture, and the average distance between the chromophores in the same polymer chain decreases. The probability of collision between chromophore triplets increases, which would be favorable to higher TTA-UC
intensity. However, the TTA-UC intensity in this series of mixtures does not increase monotonically with the increase of the AnMMA ratio. It first increases when the AnMMA ratio increases up to ~8.8%, then decreases when the AnMMA ratio increases further, down to almost zero at the AnMMA ratio of 40%. Note that it is unlikely that the chromophores (AnMMA) in these polymers aggregate or have phase separation when the AnMMA ratio increases, as they are covalently attached to the polymer chains and all Poly(AnMMA-co-MMA) polymers disperse well in the solvent. Therefore, simply increasing the number of chromophores in the polymer chain does not always improve the TTA-UC efficiency.

![TTA-UC spectra of mixtures containing Poly(AnMMA-co-MMA)](image)

**Figure 2.** (a) TTA-UC spectra of mixtures containing Poly(AnMMA-co-MMA) (0.25 mM polymer) with different AnMMA ratios and PtOEP (10 μM) in deoxygenated DMF solutions under 532 nm excitation (32 mW/cm²). (b) Relationship of integrated TTA-UC intensity of the mixtures vs. AnMMA ratio.

In the second series, the mixtures contained the same concentrations of PtOEP, while the concentrations of poly(AnMMA-co-MMA) with different AnMMA ratios were adjusted so that all mixtures had the same concentration of the AnMMA unit. Results are shown
in Figure 3. Again, the TTA-UC intensity in this series of mixtures first increases when the AnMMA ratio increases up to 4%, then decreases when the AnMMA ratio increases further.

**Figure 3.** (a) TTA-UC spectra of mixtures containing Poly(AnMMA-co-MMA) (1.5 mM AnMMA unit) with different AnMMA ratios and PtOEP (10 μM) in deoxygenated DMF solutions under 532 nm excitation (32 mW/cm²). (b) Relationship of integrated TTA-UC intensity of the mixtures vs. AnMMA ratio.

Both results indicate that there is an optimal range of the AnMMA ratio in Poly(AnMMA-co-MMA), where the TTA-UC is most efficient. Considering all triplet chromophores (AnMMA) in the mixtures, there are three types of possible collisions among them that could lead to annihilation, as illustrated in the diagram shown in Figure 4: (1) two chromophores attached to two different polymer chains, noted as TTA I, (2) two adjacent chromophores attached to the same polymer chain, noted as TTA II, and (3) two non-adjacent chromophores attached to the same polymer chain, noted as TTA III. TTA I is inter-chain type, while TTA II and TTA III are intra-chain type. Under the conditions (excitation power and concentrations of PtOEP and polymer) used in these
experiments, it is unlikely that a second triplet sensitization process takes place within the lifetime of the triplet state of AnMMA in the same polymer chain, and the inter-chain TTA can be the only significant UC process occurring. Yet simply increasing the number of the polymer chains in the mixture does not always increase the observed TTA-UC intensity, as shown in Figure 3.

Figure 4. Schematic illustration of collisions among sensitizer and emitters leading to TTA-UC in Poly(AnMMA-co-MMA)/PtOEP mixtures. “M” represents methyl methacrylate. These results combine to suggest that the observed UC intensity is directly related to the net abundance of the excited singlet of the chromophores. The generation of the excited singlet of the chromophores is attribute to the inter-chain TTA, while its quenching is due to the intra-chain interaction. In other words, TTA I processes promote UC while interaction among excited singlets in the same polymer suppress UC, and the amount of AnMMA in the polymer (and hence overall in the mixture) controls the observed UC intensity. At low AnMMA ratios, the intra-chain quenching is negligible, so with increasing AnMMA ratio, the observed UC intensity is increasing. At high AnMMA
ratios, the intra-chain quenching of the excited singlet of the chromophores becomes predominant, lead to very low UC intensity eventhough the total polymer concentration is increasing. Therefore, an optimal range for AnMMA ratios is observed where TTA-UC is maximal. Such ratio varies slightly in the two series of experiments shown here, which can be understood as follows. At fixed polymer concentration, generation of the excited singlets of the chromophores increases with increasing AnMMA ratio. The decrease in UC intensity after AnMMA ratio of 8.8% reflects the predominence of intra-chain quenching of the excited singlets. In contrast, when the concentration of the AnMMA unit in the polymers is fixed, the polymer concentration decreases, leading to the reduced generation of the excited singlets, as the AnMMA ratio increases. The effect on both generation and quenching of the excited singlets results in a smaller optimal AnMMA ratio of ~4%.

We therefore suggest that, when designing and synthesizing polymeric emitters to be used in the TTA-UC systems to achieve high UC efficiency, it is important to consider the distance between the adjacent chromophores to avoid self-quenching of the excited singlet of the emitter, other than simply increasing the number of emitting chromophores per polymer chain.

4.5 Conclusion

In summary, we reported the design and synthesis of a series of Poly(AnMMA-co-MMA) through RAFT with different AnMMA ratios, resulting in tunable inter-chromophore distances. These polymers can serve as emitters, with PtOEP as sensitizer, in TTA-UC systems. TTA-UC intensity of the Poly(AnMMA-co-MMA)/PtOEP mixtures displays
interesting dependence on the AnMMA ratio in the polymer. It increases initially with increasing AnMMA ratio, and decreases after the AnMMA ratio is above an optimal value, ultimately disappearing when AnMMA ratio reaches 40%. Interactions between chromophores on the same polymer chain play the key role in affecting the TTA-UC intensity in these systems. It is critical to minimize intra-chain chromophore quenching in order to achieve high UC intensity.

4.6 References


Chapter 5. Synthesis amphiphilic block copolymer to stabilize silver nanoparticles in hybrid photosensitizer.

5.1 Abstract

A novel hybrid photosensitizer was made by integrating amphiphilic block copolymer poly(N-isopropylacrylamide-b-styrene) (PNIPAAm-b-styrene) stabilized silver nanoparticles (Ag NPs) with hematoporphyrin (HP) to simultaneously enhance singlet oxygen production. Reversible addition-fragmentation chain-transfer (RAFT) polymerization was used as a method to build the block polymer. After reduction by sodium borohydride, PNIPAAm-b-styrene can stabilize Ag NPs via Ag-S bonds. HP was trapped by polystyrene block through hydrophobic interaction. PNIPAAm block worked as a hydrophilic block to increase the solubility of HP in aqueous solution. This hybrid photosensitizer was demonstrated to enhance singlet oxygen production.

5.2 Introduction

Firstly observed in 1924, singlet oxygen has drawn intense attention for various applications in recent decades. The ground state molecular oxygen ($^3\Sigma^-$) has a unique triplet spin electronic state while the two low-lying singlet excited states $^1\Delta_g$ and $^1\Sigma_g^+$, have 95 and 158 kJ mol$^{-1}$ above the triplet state $^3\Sigma_g^-$, respectively.$^1$ The transition from $^1\Delta_g$ to $^3\Sigma_g^-$ is spin forbidden, while the transition from $^1\Sigma_g^+$ to $^1\Delta_g$ is spin allowed. Thus, the lowest excited electronic state of molecular oxygen - $^1\Delta_g$ oxygen, which commonly referred to as singlet oxygen, has a relatively longer lifetime compared to $^1\Sigma_g^+$ oxygen. The $^1\Delta_g$ to $^3\Sigma_g^-$ transition at ~1270 nm is observed which can be used as direct proof for existence of singlet oxygen due to the energy difference between singlet oxygen and
ground state molecular oxygen. As highly reactive species, singlet oxygen can be used in various fields such as synthesis of fine chemicals, treatment of wastewater, blood sterilization, and photodynamic therapy of cancer (PDT).

Photosensitization is one of the convenient and controllable means to generate singlet oxygen. Among various photosensitizer, porphyrins and their analogues draw tremendous attention because of their biological properties. These photosensitizers generally lack cytotoxicity in the absence of light, which is crucial in clinical applications. PDT to treat cancer patients is the most important application for photosensitized singlet oxygen and it has been widely applied. In the PDT process, visible light, photosensitizer, and oxygen are three components which need to be combined to generate lethal agents to inactivate tumor cells. It is widely accepted that it is the singlet oxygen responsible for this photobiological activity since it’s the primary cytotoxic agent. As a consequence of localization of sensitizer in the tumor, PDT enables the destruction of tumor without hurting normal tissue. Compared with conventional cancer therapies such as chemotherapy and radiation which also damage healthy tissue along with tumor cells, photodynamic therapy provides a way of targeted treatment of tumor cells with minimal side effects.

Since oxygen and light are usually limited factors in photodynamic therapy, to increase singlet generation, the efficiency of photosensitizer is of great importance. In order to fulfil this goal, a lot of ways have been tried to enhance the singlet oxygen production efficiency. Previous study showed that the singlet oxygen production can be increased when the photosensitizer molecule is close to metal nanoparticle surface. The resonance coupling between photosensitizer and metal can be reflected by the spectral
overlap between the absorption band of photosensitizer and the plasmon resonance band of metal nanoparticles. However, to kill deep tumors is still challenging for common photosensitizers due to the difficulty of penetration. Near-infrared (NIR) light (700-2500 nm) can penetrate biological tissues such as skin and blood more efficiently than visible light because these tissues can scatter and absorb less light at longer wavelengths. But most photosensitizers absorb visible light between 400 to 700 nm, and those lights have very limited penetration ability though tissues. Recently, a lot of research focuses on synthesizing or modifying organic photosensitizers to tune the absorption band at NIR region. Nevertheless, most of those sensitizers need multiple steps to synthesize and the singlet oxygen production efficiency was limited. Therefore, a photosensitizer, with higher singlet oxygen production efficiency at NIR absorption region is intensively needed for practical applications.

5.3 Experimental

Materials

All chemicals were purchased from Sigma-Aldrich at the highest available purity and used as received unless otherwise stated. N-isopropylacrylamide (NIPAAm) was recrystallized in hexane. 2,2'-azobis(2-methylpropionitrile) (AIBN) was recrystallized in MeOH. 2-(dodecylthiocarbonothioylthio)-2-methylpropionic acid (DDMAT) was synthesized according to previous paper. 1H and 13C NMR measurements were performed in CDCl3, with Si(CH3)4 standard, using a 400 MHz Bruker Ultrashield (100 MHz for 13C). 1H NMR and 13C NMR spectra were analyzed with MestReNova software. Molecular weights of polymers were determined using an Agilent 1100 Series HPLC
equipped with a DMF mobile phase and Optilab rEX differential refractometer (light source=658 nm) (Wyatt Technology Corporation) detector.

**Synthesis of poly(N-isopropylacrylamide) (Macro-CTA)**

NIPAAm (12.00 g, 0.106 mol), DDMAT (0.193 g, 0.53 mmol) and AIBN (4.34 mg, 0.026 mmol) were added to 48 mL 1,4-dioxane in a round-bottom flask equipped with septum and stir bar. The reaction flask was sealed with a rubber septum and purged with N₂ for 30 min. The reaction was allowed to proceed at 60 °C for 3 h and stopped by exposure the reaction to air. The residue was then precipitated in cold ether three times to afford 6.00 g yellow solids. Polymer was characterized using gel permeation chromatography: Number-average molecular weight (Mₙ) = 15.9 KDa, Dispersity (D) = 1.25.

**Synthesis of poly(N-isopropylacrylamide-b-styrene) (P(NIPAAm-b-styrene))**

1.00 g Macro-CTA, styrene (2.95 mL, 25.7 mmol) and AIBN (0.78 mg, 4.67 × 10⁻³ mmol) were added to 15 mL 1,4-dioxane in a round in a round-bottom flask equipped with septum and stir bar. The reaction flask was sealed with a rubber septum and purged with N₂ for 30 min. The reaction was allowed to proceed at 80 °C for 3 h and stopped by exposure the reaction to air. The residue was then precipitated in cold ether three times to afford yellow solids (0.97 g). Polymer was characterized using GPC: Mₙ = 20.5 KDa, D = 1.65. Sodium borohydride (NaBH₄) was used to reduce trithiocarbonylthio groups to thio group from the prepared polymers. 0.80 g NaBH₄ and 0.80 g polymer were dissolved in 30 mL THF and 10 mL water was added. The reaction was allowed to proceed at 25 °C overnight. The residue was then precipitated in cold ether three times to afford the final polymer as white power (0.50 g). Polymer was characterized using
GPC: $M_n = 20.1$ KDa, $D = 1.98$.

5.4 Results and discussion

Scheme 1. a) Synthesis of Macro-CTA; b) copolymerization with styrene using this macro-CTA and subsequently reduction reaction.

P(NIPAAm-b-styrene) was synthesized using RAFT polymerization. Compared with other polymerization methods, RAFT has its own advantages since it’s controllable and easy to perform with a broad range of monomers. NIPAAm was chosen as the comonomer since its thermoresponsive hydrophilic property. DDMAT was used as chain transfer agent to afford the polymer with a trithiocarbonylthio group which can be further reduced to thio group. This polymerization was performed in 1,4-dioxane with AIBN as initiator (Scheme 1(a)). This macro-chain transfer agent (macro-CTA) was then characterized with both NMR and GPC (NMR spectrum was shown in Figure 1).
Then styrene was copolymerized using this macro-CTA to afford an amphiphilic polymer with $M_n = 20.5$ KDa, $D = 1.65$ (shown in Scheme 1 (b)). Mole fraction was calculated from NMR (shown in Figure 2). By integrating the peak around 4 ppm (proton from NHCH(CH$_3$)$_2$) and the peak around 6.5-7.1 ppm (proton from benzene ring), NIPAAm mole fraction was determined as 70.7%.

**Figure 1.** $^1$H NMR spectrum of poly(N-isopropylacrylamide)
P(NIPAAm-b-styrene) stabilized silver nanoparticles were synthesized directly in water/ethanol (30/70) by using sodium borohydride as a reducing agent and P(NIPAAm-b-styrene) as a capping agent through the Ag-S chemical bonds. Hematoporphyrin, as an organic photosensitizer, has very poor solubility in water. Polystyrene as the hydrophobic block, thus can trap this photosensitizer via hydrophobic interactions. As shown in Figure 3, the long hydrophilic PNIPAAm chains not only prevent hematoporphyrin from escaping the hybrids, but also improved the solubility of hematoporphyrin in water. The loading efficiency of photosensitizer in the hybrids is 34.7 μg/mg by measuring the UV-Vis absorption spectra. The photosensitizer leakage test has been monitored in water and phosphate buffer solution (pH=7.4) (PBS) for continuous 5 days, respectively. The results imply that photosensitizer has very little leakage in water. And the slow leak of hematoporphyrin for the samples in PBS is due to the higher solubility of hematoporphyrin in PBS.
Figure 3. Illustration of synthesis and structure of Ag@P(NIPAAm-b-styrene)@HP hybrids.

TEM image was taken to characterize the size of those nanoparticles. As shown in Figure 4a, Ag NPs have an average size of 25 nm. The normalized UV-Vis spectra of silver nanoparticles, the free HP and the hybrids were shown in Figure 4b. The polymer coated Ag NPs has only one strong absorption peak at ~ 400 nm in accordance with the position of typical silver nanoparticle plasmon band. The free HP exhibited a typical Soret band (397 nm) where the silver plasmon peak lies and four weak Q bands (450-650nm). Hence, The UV-Vis spectra display significant spectral overlap between the Ag NPs plasmon resonance band and HP absorption band.
Figure 4. (a) TEM image of Ag@PNIPAAm-b-styrene@HP hybrids, (b) normalized UV-Vis spectrum of Ag@PNIPAAm-styrene NPs, HP and Ag@PNIPAAm-b-styrene@HP hybrids.

The singlet oxygen production was directly monitored by measuring its phosphorescence. Phosphorescence spectra of Ag NPs, HP and the hybrids with the same amount of Ag NPs or HP were shown in figure 5. Hybrids containing 10 μM HP shows the strongest excitation peak at ~ 395 nm. The intensity for this peak of the hybrids is obviously stronger than that of free HP, which proved enhanced singlet oxygen production. The excitation spectrum from the hybrids is also broadened for the measurable 300 to 800 nm region. In order to verify the singlet oxygen production with broad-spectrum excitation, three different wavelengths were chosen: 395 nm – the excitation wavelength for free HP, 500 nm – the wavelength of the peak at the shoulder from hybrids and 625 nm – the wavelength at NIR region to excite all samples as shown in Figure 5 (b)-(d). The phosphorescence spectrum in Figure 5 (b) displayed that the hybrid has stronger emission peak than pure HP with the 395 nm excitation, which is consistent with the excitation spectra. Under the irradiation of 500 nm, the
phosphorescence intensity demonstrates that the hybrids can still generate significant amount of singlet oxygen. In contrast, the phosphorescence intensity for the free HP is much weaker. We also measured the phosphorescence emission under the 625nm light excitation. In this case, the hybrids still showed an emission peak at 1290 nm with the relative intensity around 1.6, as the free HP cannot show any obvious signal. Those phosphorescence spectra convince us that the combining of HP and silver nanoparticles enhanced the singlet oxygen production with broad-spectrum excitation.

**Figure 5.** Phosphorescence excitation spectra of Ag@PNIPAAm-styrene NPs, HP and Ag@PNIPAAm-styrene@HP NPs (a), and emission spectra under 395 nm (b), 500 nm (c) and 625 nm (d) excitation (HP concentration is 10 μM).

5.5 Conclusion
In summary, we synthesized the amphiphilic block copolymer P(NIPAAm-b-styrene) to stabilized Ag NPs. This hybrid system provides a facile method to absorb HP onto Ag NPs and also increase its solubility in water. Due to the strong resonance coupling between Ag NPs and HP, the quantum efficiency of singlet oxygen production was enhanced. Phosphorescence spectra demonstrated the singlet oxygen excitation region was much broadened compared to the free photosensitizer. It opens a new strategy to fabricate photosensitizer to be used in clinical applications.

5.6 References


Chapter 6. Synthesis and electrospinning of self-immolative polymers

6.1 Abstract

A self-immolative polymer containing a polyurethane backbone was synthesized with a tert-butyl group as trigger. Removal of the butyl end group with trifluoroacetic acid:dichloromethane (TFA:DCM) solution initiated a head to tail depolymerization. Electrospinning was used to fabricate nanofibers and different TFA:DCM ratios were tested to obtain optimal conditions for depolymerization. The depolymerization process was monitored by gel permeation chromatography (GPC). Scanning electron microscopy (SEM) was used to characterize nanofibers. These electrospun nanofibers have potential application in drug delivery.

6.2 Introduction

Self-immolative polymers (SIPs) comprise a kinetically stable polymer chain where the chain end is able to respond an external stimulus. The external stimuli can trigger a head to tail depolymerization.\(^1, 2\) This architecture has drawn attention in recent years due to the triggered deconstruction of the polymers. However, the "self-immolative" concept can traced back to 1981 when Carl and coworkers synthesized a novel connector linkage for prodrug design.\(^3\) As shown in scheme 1, the drug and trigger were linked together via a self-immolative connector. After a sequence of hydrolytic steps, the drug was released. This concept is applicable for higher molecular weight molecules too. A self-immolative oligomer was fabricated as spacer to link a peptide substrate with doxorubicin (DOX), which was released when treated with plasmin.\(^4\) Self-immolative
dendrimers, as even higher molecular weight molecules, were also developed according to a similar strategy.\textsuperscript{5, 6}

![Scheme 1. Reaction scheme for self-immolative connector.](image)

SIPs can be depolymerized through elimination, providing a spontaneous and irreversible disassembly process. Polymer was depolymerized to fragments through a cascade of electronic elimination processes (shown in Figure 1). The elimination reaction is driven by an increase in entropy, coupled with the irreversible formation of thermodynamically stable products such as CO\textsubscript{2}.

![Figure 1. Example of elimination process.](image)

The elimination process can be triggered by enzyme-mediated, redox-mediated, acid/base-mediated or photo-mediated cleavage.\textsuperscript{7-11} The benefits of a controllable degradation upon specific trigger conditions has resulted in SIPs becoming a powerful tool in applications such as drug delivery, biological and chemical sensors, and degradable nanoscale materials.\textsuperscript{12-15}
Figure 2. a) Release of p-nitroaniline; b) release of 6-aminoquinoline.

P-nitroaniline and 6-aminoquinoline are two common outputs (sometimes called “reporters”) which can be released by deconstruction of SIPs (shown in Figure 2).\textsuperscript{11, 12} Both reporters can be detected either through UV-vis spectrometry or photoluminescence spectrometry. Due to the fact that SIPs can amplify release of covalently bound molecules when the trigger is activated, SIPs are suitable for sensor applications. A self-immolative comb-polymer was developed to fulfill this goal.\textsuperscript{16} Shabat’s group developed a SIP containing 4-nitroaniline as a reporter molecule (shown in Figure 3). Initiated by piperidine, these SIPs depolymerized and released multiple reporters to amplify the outputs.
Figure 3. Piperidine initiated depolymerization of SIPs to release multiple copies of the 4-nitroaniline reporter units.

When reporter molecules such as $p$-nitroaniline and 6-aminoquinoline are replaced by a pharmaceutical agent, SIPs can be used for drug delivery. SIPS are able to “hold” anticancer drugs until they reach tumor cells, preventing exposure of cytotoxic drugs to normal cells. Shabat’s group reported using SIPs as prodrug vectors. 4-Hydroxybenzylalcohol was used as a self-immolative linker between the amino group of DOX and diethylenetriamine. Gillies and coworkers illustrate the possibility to synthesizing self-immolative block copolymers with a PEO end capper, which can modify the hydrophobicity of self-immolative block. This amphiphilic block copolymers can self-assemble into nanoparticles in aqueous solution. Microcapsules were also prepared using a self-immolative polycarbamate backbone to control the release rate of prodrugs. Self-immolative spacer, oligomers, linear polymers and dendrimers have been shown to be promising materials in drug delivery and sensing applications due to their ability to receive and translate a signal into an amplified response as well as controllable degradation. In our work, we have fabricated high surface-area fibers of a
self-immolative polymer that possess fast degradation rates and have potential applications in drug delivery system.

6.3 Experimental

Materials

All chemicals were purchased from Sigma-Aldrich at the highest available purity and used as received unless otherwise stated. $^1$H and $^{13}$C NMR measurements were performed in CDCl$_3$, with Si(CH$_3$)$_4$ standard, using a 400 MHz Bruker Ultrashield (100 MHz for $^{13}$C). $^1$H NMR and $^{13}$C NMR spectra were analyzed with MestReNova software. Molecular weights of polymers were determined using an Agilent 1100 Series HPLC equipped with DMF containing 0.1% LiBr as mobile phase and Optilab rEX differential refractometer (light source=658 nm) (Wyatt Technology Corporation) detector. Scanning electron microscopy (SEM) investigations were carried out on a XL30-ESEM instrument operating at energy of 20 and 30 Kev.

Synthesis of Phenyl (4-(hydroxymethyl)phenyl)carbamate

The monomer was synthesized according to a literature procedure.$^{18}$ 4-aminobenzyl alcohol (4.00 g, 32.5 mmol) was suspended in a 60 mL mixture of tetrahydrofuran (THF):saturated sodium bicarbonate (sat. NaHCO$_3$):water (ratio 2:2:1), and phenylchloroformate (4.16 mL, 33.1 mmol) was added dropwise over 5 min. The reaction proceeded under room temperature overnight. When completed, ethyl acetate was added and the organic phase was washed twice with saturated NH$_4$Cl solution. The solvents were removed by rotary evaporation and the crude product was further purified by column chromatography on silica gel (30:70 ethyl acetate: hexane as mobile phase),
yielding the desired product as a white solid (6.69 g, 85%). This product was identified by spectral comparison with literature data.\textsuperscript{11} \textsuperscript{1}H NMR (400 MHz, d\textsubscript{6}-DMSO): δ(ppm) 10.20 (1H, s), 7.45 (4H, m), 7.19 (5H, m), 5.07 (1H, t, J = 5.6 Hz), 4.43 (2H, d, J = 5.6 Hz). \textsuperscript{13}C NMR (100 MHz, d\textsubscript{6}-DMSO): δ(ppm) 62.9, 118.6, 122.3, 125.8, 127.5, 129.8, 137.6, 150.9, 152.1.

**Synthesis of self-immolative polymer**

Phenyl (4-(hydroxymethyl)phenyl)carbamate (4.00 g, 16.4 mmol) and dibutyltin dilaurate (DBTL) (0.49 mL, 0.82 mmol) were added via a syringe to dry dimethylformamide (DMF) (8 mL), which was preheated to 110 °C under N\textsubscript{2} atmosphere. The reaction mixture was stirred for 15 min after which t-butanol (7.77 mL, 81.2 mmol) in 8 mL DMF was then added. The reaction mixture was stirred for additional 30 min and was then allowed to cool to room temperature. The polymer was precipitated from cold methanol, filtered, and dried under vacuum. Polymer was obtained as a yellow powder (3.00 g yield 75 %). Polymer was characterized using gel permeation chromatography (GPC): Number-average molecular weight (\(M_n\)) = 16 000 g/mol, Dispersity (\(D\)) = 4.7.

**6.4 Results and discussion**

The synthesis of the self-immolative polymer (SIP) followed similar methods to both Moore’s and Shabat's groups.\textsuperscript{11, 18} The self-immolative polymer contains a polyurethane backbone terminated with \textit{tert}-butyl group as the trigger (shown in Scheme 2). Cleavage of the \textit{tert}-butyl end group initiates a head to tail depolymerization via 1,6-elimination and decarboxylation reactions. The size of the polymer was controlled by multiple factors including the concentration of the monomer, temperature, and time of the
polymerization. Our polymer was characterized using GPC and found to possess a number average molecular weight ($M_n$) of 16 000 g/mol and dispersity ($D$) of 4.7. This is a broad dispersity, but it is reasonable for a condensation polymerization.\textsuperscript{19, 20}

![Scheme 2. a) Synthesis of Phenyl(4-(hydroxymethyl)phenyl)carbamate; b) synthesis of self-immolative polymer (SIP).](image)

Polymers were exposed to conditions known to remove Boc groups (TFA/CH$_2$Cl$_2$ 1:1) in order to trigger the depolymerization reaction. The depolymerization of the linear polymers was monitored using GPC. As shown in Figure 4, we set one sample as control experiment which was not exposed to TFA/CH$_2$Cl$_2$ 1:1 solution. Another sample was immersed in the trigger solution for 24 hours. From the GPC trace we can see, the polymer peak shifted to right, which means low molecular weight species were generated. The polymer showed a large molecular weight reduction with the $M_n$ changing from 16 000 g/mol to 1 800 g/mol.
Figure 4. GPC trace for depolymerization test of SIP.

The self-immolative polymer was fabricated into fibers using electrospinning. We used coaxial electrospinning with polyacrylonitrile (PAN) with a concentration of 10 wt % in DMF as the core solution and the SIP with a concentration of 30 wt % in DMF as sheath solution. This core-sheath structure ensures the SIP at the outer layer and PAN as support at inner layer. Figure 5 shows the SEM image of these fibers.
Figure 5. SEM image of electrospun fibers using the self-immolative polymer in the sheath with PAN as the core.

We tested trigger solutions with different TFA:DCM ratios (shown in Figure 6 (a)) from 1:1000 to 1:1 and took SEM images of each sample (shown in Figure 6(b)) in order to find the best condition for depolymerizing the electrospun fibers. From the SEM images we can see when the TFA:DCM ratio is 1:10, the fiber structure starts to be destroyed. Therefore, TFA:DCM 1:20 is the best degradation conditions for the fastest depolymerization of SIP without breaking the structures of nanofibers.

![Figure 6. a) Electrospun fibers in different trigger solution; b) SEM images of electrospun fibers under different trigger solution.](image)

We used this optimized depolymerization condition to characterize the degradation of the SIP electrospun fibers. After immersing the fibers in a TFA:DCM 1:20 solution for 10
min, there is an obvious reduction in $M_n$ observed in the GPC traces (shown in Figure 7). Table 1 shows the $M_n$ and $D$ for both PAN and SIPs. PAN does not change a lot after contacting with trigger solution while SIPs have an obvious reduction in $M_n$. Due to the large surface area of the electrospun fibers, our self-immolative materials show faster degradation rate compared to other systems. From the GPC traces, our degradation happened in the first 10 min when contacting with trigger solution while self-immolative microcapsules and bulk SIPs need more than 48 hours to depolymerize. The core-shell structure of nanofibers provides a vector to deliver drugs. If the drug was dissolved in core solution while SIPs as sheath solution, before depolymerization, the drug can be delivered to target position. Then triggered by certain condition, the core species can be released upon depolymerization of SIPs.

![Figure 7. GPC traces for degradation test of electrospinning fibers.](image)

![Table 1. Detailed information about polymer degradation test.](image)
<table>
<thead>
<tr>
<th></th>
<th>$M_n$ (SIP) (g/mol)</th>
<th>$\mathcal{D}$ (SIP)</th>
<th>$M_n$ (PAN) (g/mol)</th>
<th>$\mathcal{D}$ (PAN)</th>
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<tr>
<td>0 min</td>
<td>$1.30 \times 10^4$</td>
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<tr>
<td>10 min</td>
<td>$2.31 \times 10^3$</td>
<td>1.699</td>
<td>$2.36 \times 10^6$</td>
<td>1.912</td>
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<tr>
<td>60 min</td>
<td>$2.29 \times 10^3$</td>
<td>1.169</td>
<td>$2.39 \times 10^6$</td>
<td>2.217</td>
</tr>
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</table>

### 6.5 Conclusion

We synthesized a self-immolative polymer containing polyurethane as backbone. By removing tert-butyl end group with TFA:DCM solution, a head to tail depolymerization occurred. Electrospinning was used to fabricate nanofibers which contain a core-shell structure. These electrospun fibers were demonstrated to rapidly release their contents upon activating the depolymerization. This provides various possibilities in different areas ranging from drug delivery to bio-imaging. We plan to use PAN/SIP as a sheath solution and add a dye with PVP as the core solution to further investigate release of core species after degradation of shell polymer.

### 6.6 References


This dissertation summarized the synthesis and characterization of self-assembling polymers via hydrogen bonding or hydrophobic effects. Firstly, linear supramolecular polymers were generated through H-bonding with N-alkyl urea peptoid oligomers as backbone. This N-alkyl urea peptoid oligomer served as precursor to simplify the synthetic process. Different functional groups were converted from one precursor by one or two steps. Quadruple hydrogen bonding system UPy group was incorporated to N-alkyl urea peptoid oligomers to obtain supramolecular polymers.

Secondly, UPy containing monomer was synthesized to form organogels. Three different monomers with different $T_g$ values were copolymerized with this UPy monomer via RAFT polymerization. Organogels were demonstrated to form in both chloroform and dichlorobenzene. Critical gelation concentration and mechanic properties of organogels were examined. By copolymerizing another pyrene containing monomer to with UPy monomer, fluorescent organogels were achieved which were suitable for potential up-conversion applications.

A series of Poly(AnMMA-co-MMA) through RAFT with different AnMMA ratios were synthesized, resulting in tunable inter-chromophore distances. These polymers can serve as emitters, with PtOEP as sensitizer, in triplet-triplet annihilation up-conversion (TTA-UC) systems. TTA-UC intensity of the Poly(AnMMA-co-MMA)/PtOEP mixtures displays interesting dependence on the AnMMA ratio in the polymer. It increases initially with increasing AnMMA ratio, and decreases after the AnMMA ratio is above an optimal value, ultimately disappearing. Interactions between chromophores on the same
polymer chain play the key role in affecting the TTA-UC intensity in these systems. It is critical to minimize intra-chain chromophore quenching in order to achieve high UC intensity. By taking advantage of hydrophobic effect, P(NIPAAm-b-Styrene) was made to fabricate a hybrid photosensitizer via RAFT polymerization. This amphiphilic polymer can stabilize Ag nanoparticles while the hydrophobic block can trap HP and hydrophilic block can increase the solubility of HP in aqueous solution. Due to the strong resonance coupling between Ag NPs and HP, the quantum efficiency of singlet oxygen production was enhanced resulting an enhanced ability of inactivation bacteria.

Self-immolative polymer was made with a polycarbamate backbone and tert-butyl end group which can respond to external stimulus by triggering a head-to-tail depolymerization. Electrospining was used to fabricate nano-scale fibers. Due to the increased surface area, these electrospun fibers were demonstrated to rapidly release their contents upon activating the depolymerization. It provides various possibilities in different areas ranging from drug delivery to bio imaging.