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Synthetic approaches to novel highly functionalized polythiophenes

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Synthetic approaches to novel highly functionalized polythiophenes

By

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A thesis submitted to the graduate faculty

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Chapter 1: Introduction to Conducting Polymers and Polythiophene

1.1. Conjugated Polymers

π-Conjugated polymers, PCPs, have gained significant attention since their discovery in 2001. PCPs are unique among all polymers due to their backbone, which is comprised of alternating double and single bonds. These extended π-conjugated systems result in delocalization of the electrons along several monomer units, and thus these materials can be regarded as intrinsic semiconductors. For this reason, a large amount of research is ongoing in efforts to develop these materials for use in applications that currently employ traditional semiconductors. PCPs have several potential advantages over classical inorganic semiconductors, including good mechanical strength, ease of processing and an unlimited number of accessible chemical structures (Figure 1), whereas inorganic semiconductors, are limited to Si, Ge and Group III-V and Group II-VI alloys. Thus, it may be possible to tailor the properties of PCPs via chemical modification. The main motivation for the development of devices based on PCPs is the premise that these materials, like other polymers, are relatively inexpensive to produce and can be easily cast or molded into a desired shape from solution or melt. Moreover, these materials may be the key to smaller electronics as we approach the size limit in the manufacturing of silicon-based microchips. Unfortunately, due to the strong interactions between the π-electrons, unsubstituted PCPs tend to be insoluble at higher molecular weights making them difficult to process.[1]
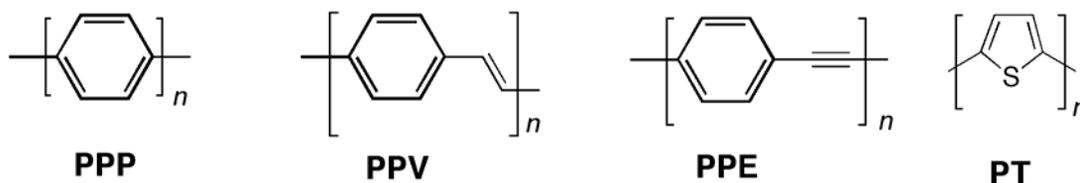
Figure 1. Four common types of conjugated polymers.

1.2. Poly(*p*-Phenylene)s

Poly(*p*-phenylene)s, PPPs, are being developed for use in organic light emitting diodes, OLEDs.[2] OLEDs have numerous advantages over standard displays, including higher brightness, low power consumption, the ease of production, a large viewing angle of 160°, and the ultrathin and rollable design.[3] PPPs are blue light emitters, which makes them valuable as this is currently the most difficult color to produce and sustain.[4] Like most conjugated polymers, unsubstituted PPPs are insoluble in common organic solvents. Typically conjugated polymers are functionalized with long alkyl chains to improve their solubility. Side chains improve the solubility of PCPs by increasing the entropy of dissolution and by screening the interaction between the rod-like main chains.[3] Functionalization improves the solubility of PPPs at the expense of the conjugation of the polymer backbone resulting from the twisting out of plane caused by these bulky side groups.[5] To resolve this issue, PPPs are often synthesized with methylene bridges to force planarity on the backbone.[6]

1.3. Poly(*p*-Phenylene Vinylene)s

Since the discovery of electroluminescence in poly(*p*-phenylene vinylene)s, PPVs,[2b] they have become one of the most widely studied classes of conjugated polymers.[7] Undoped PPVs are very low conducting polymers (10^{-13} S/cm),[8] but when doped, PPVs conductivity can range from 10^{-3} S/cm (iodine doped)[9] up to 100 S/cm

(H_2SO_4 doped).[10]   However, PPVs have low charge carrier mobility, which makes them useless as a conductive material for commercial devices, thus limiting them to OLED applications.[11]   PPVs emit green-yellow light when used as the active layer in OLEDs. Typically they are synthesized using two approaches: direct and precursor routes. Direct routes are used only for the formation of soluble materials, while the precursor routes are used to make soluble and insoluble polymers.   It is possible to create polymers that emit red, blue, yellow, and green light by varying the substituents on the polymer backbone. Additionally, it is possible to control the emission color of the PPV by copolymerization. For example, when the PPV is copolymerized with other aromatic rings, such as benzenes or pyridine, the results are red shifted emissions.[12]

1.4. Poly(*p*-Phenylene Ethylene)s

Poly(*p*-phenylene ethynylene)s, PPEs, have been explored for use in OLEDs, but do not perform as well as PPPs and PPVs.[13] They are more oxidatively stable than PPVs, which hinders their uses as organic semiconductors. PPEs are very good photodiodes and have been used in organic transistors.[14]   Another interesting property of PPEs is their optical responses to changes in their environment, which gives them potential for use as polymer-based sensors.[13] Variation of functional groups on PPEs allows for detection of a number of different analytes, including heavy metals,[15] bacterial toxins,[16] and *E.Coli*.[17]

1.5. Polythiophenes

Polythiophenes, PTs, have excellent thermal stability (42% weight loss at 900 °C) and good conductivity (3.4 x 10^{-4} - 1.0 x 10^{-1} S/cm when doped with iodine) making them an important class of conjugated polymer. Polythiophene was first synthesized in 1980[18,19] via oxidative coupling using $FeCl_3$. The resultant polymer was insoluble and

unprocessible.[20,21] The reason for the poor solubility was due to the strong π-stacking between the aromatic rings.[22] It was also discovered that many samples were contaminated with ionic impurities from the synthesis, which interfered with the conjugation.[23] Despite the lack of processability, the environmental stability, thermal stability and high electrical conductivity of PT-films still make them a highly desirable material.[24]

In an effort to increase the solubility of polythiophenes, the synthesis of poly-(3-alkylthiophenes), P3ATs, were examined. It has been shown that polythiophenes with alkyl groups larger than butyl can be readily processed from solution or melt, while still maintaining the conductivity of the polymer.[25,26,27] Upon doping with iodine, these poly-(3-alkylthiophenes), maintain electrical conductivities ranging from 0.1 to 10 S / cm.[24] While the methods used for chemical synthesis eliminated 2,4-couplings between two alkyl thiophenes, these syntheses did not consider the placement of the alkyl groups along the polymer backbone. It was later found that the substitution arrangement plays a major role in the properties of the polymer.

1.5.1. Regioregular vs Regioirregular

Since poly-(3-alkylthiophenes) are not symmetrical molecules, the fashion in which the rings are coupled together becomes an issue. If one considers the simple case of coupling two thiophene rings through the 2- and 5-positions on the rings, it is apparent that three relative orientations are possible (Figure 2).[28]. The first of these is 2,5' or head-to-tail coupling (HT), the second is 2,2' or head-to-head coupling (HH), and the third is 5,5' or tail-to-tail coupling (TT).[29] The situation become more complex when one

considers the coupling of three thiophene rings, which leads to a mixture of four chemically distinct triad regioisomers.
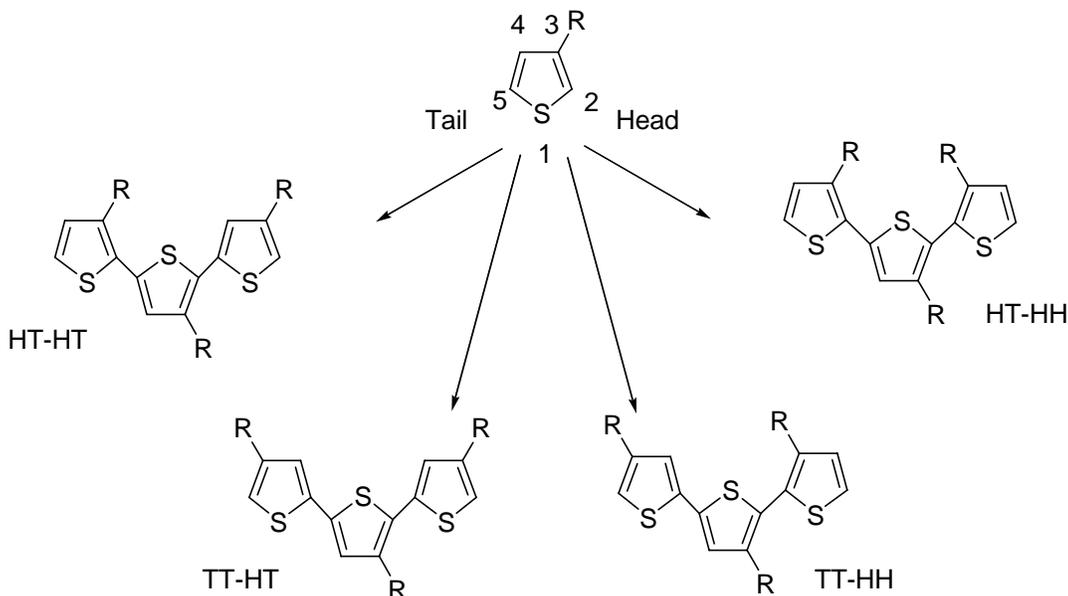

Figure 2. Regioisomers of polythiophene triads.

Previous syntheses did not invoke regiochemical control of the monomer units. When P3ATs were prepared without regiochemical control, they contained mixtures of the different coupling types. Polymers of this type are referred to as regioirregular, and they contain unfavorable HH couplings causing a sterically-driven twist of the thiophene rings. This increases the torsion angle between the rings, resulting in a loss of conjugation (Figure 3).[24,30] The increase of the torsion angles also leads to greater band gaps with consequent destruction of high conductivity and other desirable properties. It has also been demonstrated that regioirregular polythiophenes cannot properly π-stack, thereby impacting the polythiophenes electronic properties.[31]
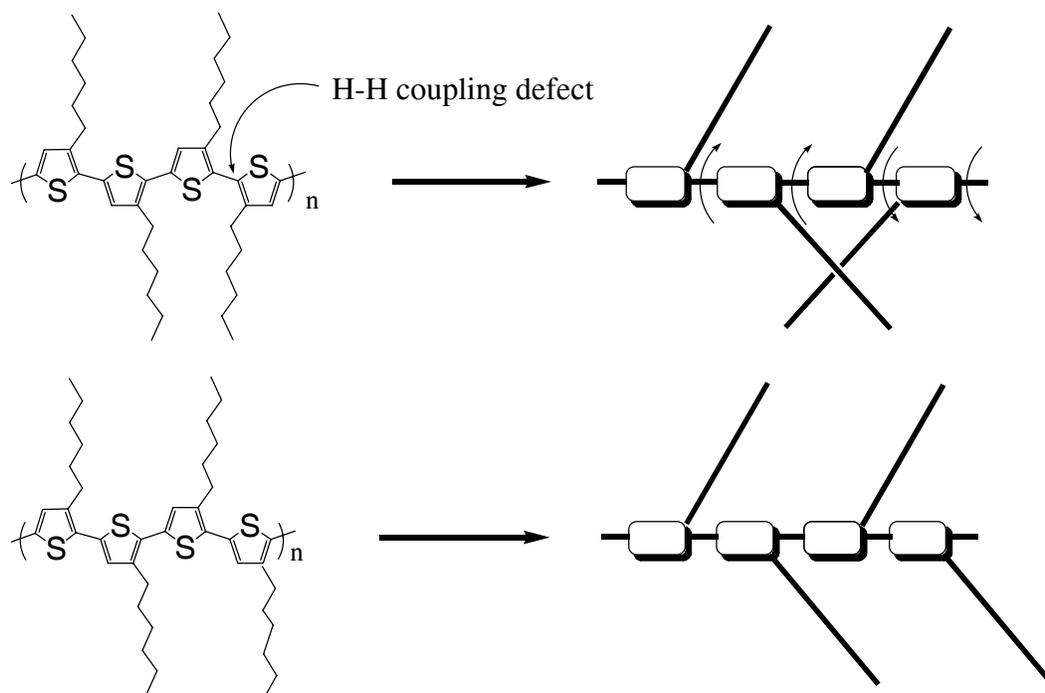
Figure 3. Regioirregular (top) vs. regioregular (bottom).

In contrast, P3AT can also be prepared containing only HT couplings. These polymers are known as regioregular or head-to-tail coupled P3ATs. Regioregular poly(3-alkylthiophene)s (rr-P3ATs) are among the most widely studied conducting polymers. Potential and practical applications include chemical and optical sensors,[32] electrochromic devices,[18] field effect transistors,[33] and solar cells.[34] rr-P3ATs have environmental stability, organic solubility, high conductivity and electron mobility, making them a versatile conducting polymer. These polymers adopt the lowest energy conformation when the rings are nearly coplanar. Regioregularity provides planar polymer backbones that can self-assemble in 3-dimensions. This allows for efficient inter- and intra-chain conductivity pathways, leading to highly conductive polymers (Figure 4). Due to the fact that regioregular polythiophenes minimize steric crowding,

the stacking ability of this conformation is much greater. HH and TT polymers have to twist to reach the lowest energy conformation, thus interrupting the π–delocalization.

Stacked Polythiophenes
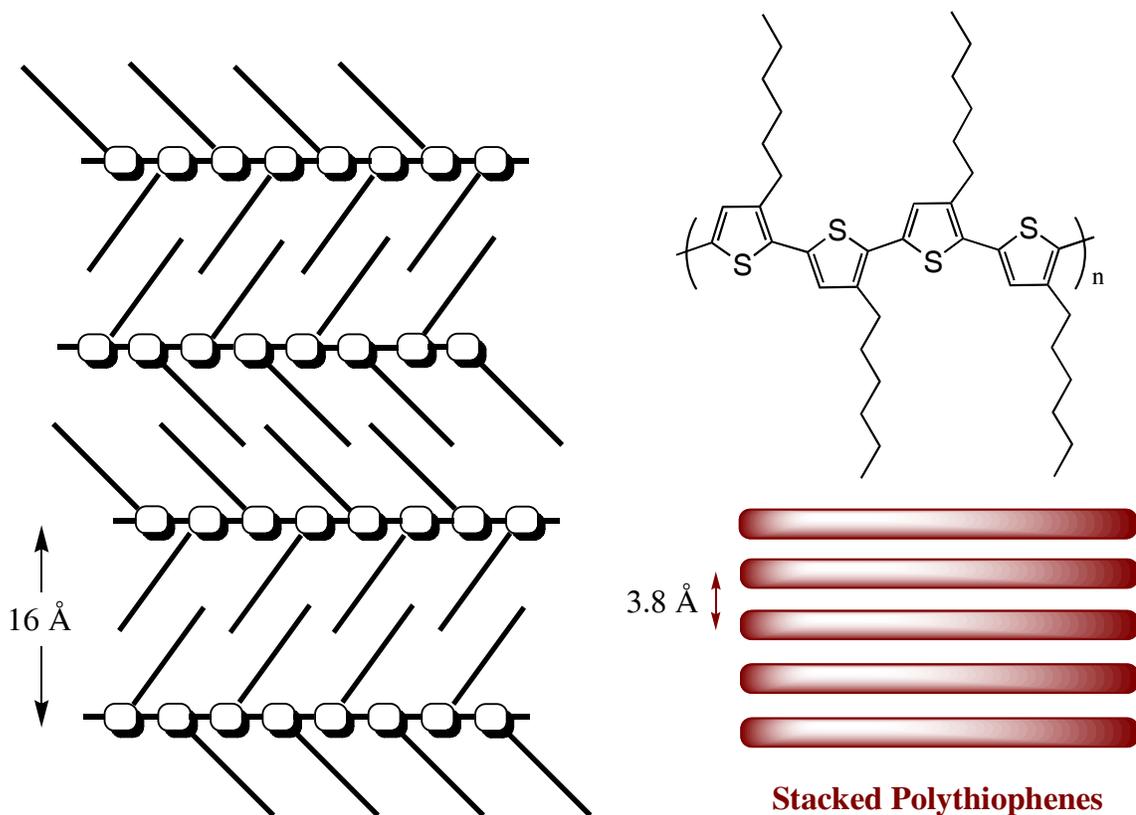
Figure 4. Three dimensional self-assembly of rr-P3HTs.[24]

1.5.2. Synthesis of rrP3ATs

Typically, regioregular P3ATs typically are produced by the McCullough, Rieke, and GRIM methods (Schemes 1-3). These methods all produce comparable PAT's. However, the Rieke method offers the advantage of tolerating a variety of different functional groups, because it employs organozinc reagents. The McCullough and GRIM methods are limited to use with groups that are stable to organolithium and organomagnesium reagents.[24] All of these methods are based on Kumada cross-coupling using catalytic amounts of $Ni(dppp)Cl_2$.[35-37]
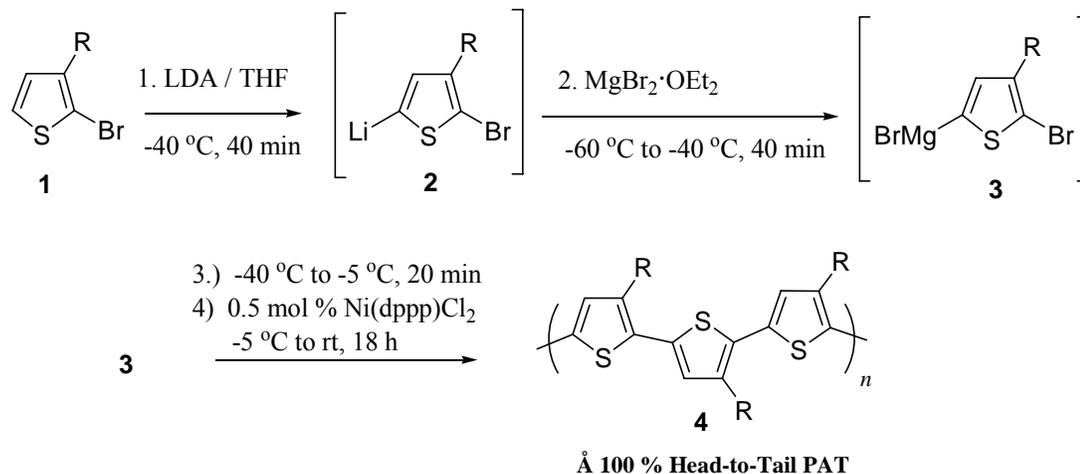
Scheme 1. McCullough Method
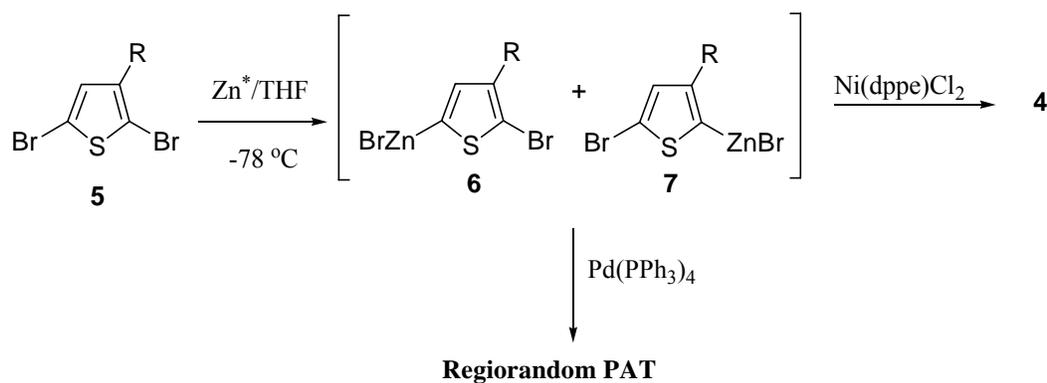
Scheme 2. Rieke Method
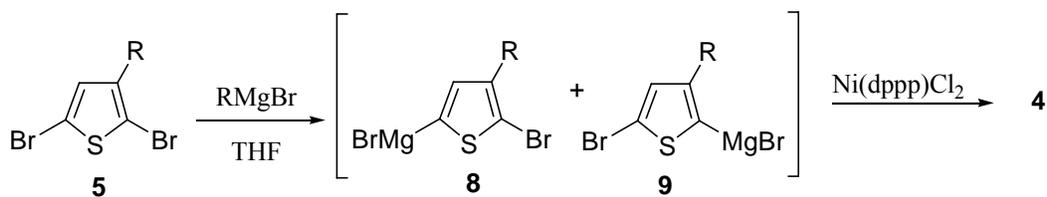
Scheme 3. Grim Method

The McCullough method produces the key intermediate 2-bromo-3-alkyl-5-(bromomagnesio)thiophene (**3**) by treating 2-bromo-3-alkylthiophene with lithium diisopropylamide at -78 °C (Scheme 1). Metal halogen exchange yields the target intermediate. The disadvantage of this approach is the sensitivity to the important cryogenic temperature changes.

Scheme 2 outlines the Rieke method, which creates the organometallic intermediate by treating 2,5-dibromo-3-alkylthiophenes with highly reactive "Rieke Zinc" (Zn*).[38] This reaction produces a mixture of the isomers, 2-bromo-3-alkyl-5-(bromozincio)thiophene (**6**) and 2-bromozincio-3-alkyl-5-bromothiophene (**7**). The ratio of these isomers is dependant upon the reaction temperature. Thus, cryogenic conditions must still be employed. The use of a nickel cross-coupling catalyst, Ni(dppe)Cl$_2$, yields a regioregular HT-PAT, as a result of steric hindrance at the metal center. Whereas the use of a palladium cross-coupling catalyst, Pd(PPh$_3$)$_4$, yields a completely regiorandom polymer.[31]

In the Grignard metathesis or GRIM method, 2,5-dibromo-3-alkylthiophene (**5**) is treated with 1 equivalent of a Grignard reagent to form a mixture of isomers 2-bromo-5-bromo-magnesio-3-alkylthiophene (**8**) and 2-bromo-magnesio-5-bromo-3-alkylthiophene (**9**) in an 85:15 ratio (Scheme 3).[39] This ratio appears to be independent of reaction time, temperature, and Grignard reagent used. As with the Rieke method, the use of a nickel cross-coupling catalyst, Ni(dppp)Cl$_2$, yields regioregular P3AT.

1.5.3. Post Polymerization Functionalization

One problem with rr-P3ATs is the difficulty associated with separating starting materials from the products. This can be limiting in their uses as block-copolymers and

further functionalization of side chains. This difficult separation results in the need for high yielding reactions with side products that can be removed in methanol or hexanes. Based upon these requirements, Click chemistry seemed like an ideal reaction.

Click chemistry is a chemical philosophy introduced by K. Barry Sharpless in 2001 which produces substances quickly and reliably by joining small units together. The inspiration for this philosophy is found in nature, which also generates substances by joining small modular units. Click chemistry was originally developed for use in the synthesis of drugs and peptides. Currently it is being exploited in a variety of areas, such as combinatorial chemistry, protenomics, DNA research, and polymer chemistry.[40]   In general, a Click reaction must meet the following set of criteria: the reactions must proceed in high yields, tolerate a wide range of functional groups, have inoffensive by-products, be purified by non-chromatgraphic techniques, have simple reaction conditions (unaffected by water or oxygen), and a solvent that is easily removed.   It is also preferable that there be a large thermodynamic driving force greater than 84 kJ/mol for a fast reaction with a single reaction product. A distinct exothermic reaction makes a reactant "spring loaded".[40] One type of Click reaction that is being widely used is the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition (Figure 5).[41]
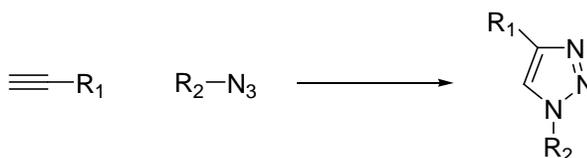

Figure 5. Huisgen 1,3-dipolar cycloaddition.

Traditionally, this involves the formation of a triazole from an azide and acetylene with Cu(I) and a base. Recently, Click reactions have been used for the synthesis of a

number of different macromolecules including block copolymers,[42] polymer brushes,[43] and dendrimers.[44] They have also been used to functionalize the side chains of conjugated polymers.[45] The utilization of Click chemistry toward the synthesis of complex polymers requires some adaptation as most of these reactions cannot be performed in water, because of the insolubility of the polymers. Reactions have been carried out in a number of solvents, such as methanol, DMF, and THF. Catalysts used include CuBr/PMDEA,[40] $CuSO_4$/sodium ascorbate,[40] and $CuBr(PPh_3)_3$/DIPEA.[44] The goal of this research was to utilize Click chemistry to form new block copolymers with P3AT and polystyrene, polybutyl acrylate and polyethylene glycol. We also attempted to prepare new rr-P3HT carbohydrate functionalized side chains.

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**Chapter 2: Investigation of New Methods for the Synthesis of Block Copolymers
Based on Click Chemistry**

2.1. Introduction

2.1.1. Block Copolymers

Polymers are macromolecules that are comprised of one or more different monomers. Many different types of polymers can be prepared from the same monomer, depending on the order in which they are coupled together. For example, consider two monomers "A" and "B", where the polymerization of monomer A with itself (or B with itself) produces a homopolymer. Alternatively, A and B can be coupled together to produce three different copolymers: alternating copolymer, statistical copolymer, and random copolymer. All of these polymers contain mixtures of the monomers A and B. In the alternating copolymer, the monomers are polymerized alternating A and B (ABABAB). Statistical copolymers are determined by reactions kinetics to form polymers that often contain sections of the A monomer followed by sections of the B (AABBBBAABBAABBBBAAABB).

A block copolymer can be formed when one or more homopolymers are linked to a different homopolymer.[1] Due to differences in the stiffness of the polymer chains, these materials have been known to phase separate to create a number of different nanostructures: spherical, cylindrical and lamellar.[2] In general terms, the separation that occurs in block copolymers can be related to an oil and water analogy: each of the copolymer's blocks wants to separate from the other due to differences in their structure, but the repulsion of the different segments are limited due to the chemical bond between the two. The copolymer adapts a conformation to minimize these interactions. As a result different morphologies can be obtained by varying the ratio of the two blocks.

Polymer structures are of interest because of their ability to form well-defined molecular architectures composed of micro domains of polymer A and polymer B.[3]   Thus, the potential exists to control the properties of the bulk system by varying the ratio and type of the polymer blocks.

Block copolymers have four factors that affect the phase behavior: molecular architecture (linear versus branched), choice of monomer, composition and degree of polymerization. Molecular architecture affects the morphology of the polymer and can influence other physical properties as well.   The choice of monomers matters when looking at the A-A, B-B interactions vs. the A-B interactions. Composition refers to the volume fraction of each component in the block copolymer, while degree of polymerization refers to the number of monomer units in the individual blocks. Favorable mixing conditions usually occur when both monomers can hydrogen bond.

The three classes of block copolymers most commonly examined are linear, star, and branched. Linear polymers are composed of two or more different linear polymers. Star polymers have linear polymer "arms" that are attached through a central core. Branched polymers have one or more different branching points leading to an irregular structure. Star block copolymers are the best defined of the three and can be prepared with specific composition, molecular weight, and low molecular weight distributions.[2]

2.1.2. Rod-Coil Block Copolymers

While most polymers adopt a flexible, coil conformation in solution, there are some which are rigid and stiff due to their structure. Rod-coil block copolymers are a special case of block copolymers, where one of the polymer blocks in the system is a persistent rod in solution and had a significantly stiffness than the other block.[3]   While

coil-coil block copolymers can give a variety of multi-phase supramolecular structures, rod-coil block copolymers typically adopt an organized stacked macromolecular assembly driven by the stiffness of the rod segment in addition to strong $\pi-\pi$ interactions. As a result, rod-coil block copolymers form ordered structures, even at low molecular weights, due to the difference in stiffness between the two blocks.[3]   These ordered structures can form on the scale of a few nanometers.[4]   Rod-coil block copolymers have been used for membrane structural proteins or DNA gels and artificial membranes.[5] Block copolymers containing conjugated polymers are technologically important since these materials can be used for control over the morphology of multi-component active layers in LEDs and photovoltaics.[5]

Two approaches which are commonly used for synthesizing block copolymers: "graft from" and "graft to" methods illustrated in Figure 1.
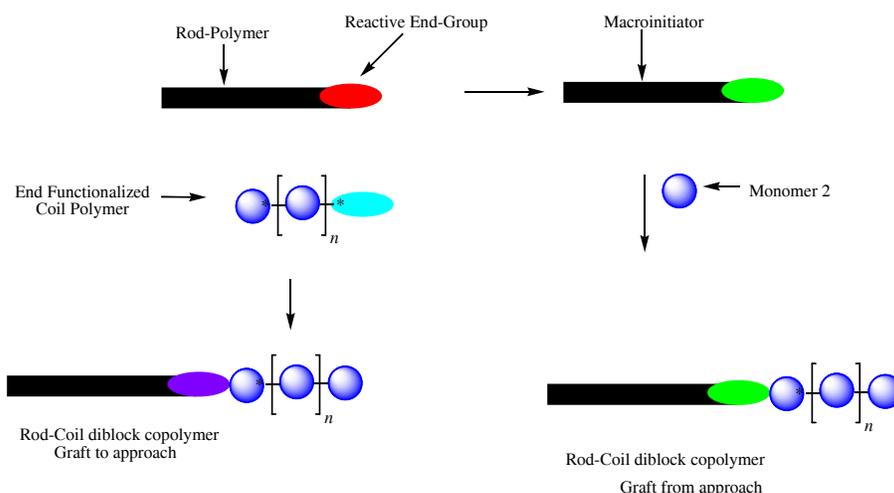

Figure 1. Two common synthetic routes for block copolymers.

The graft from method employs an end group functionalized homopolymer referred to as a macroinitiator, which can be used to initiate the polymerization of the

second block. The addition of the second monomer and subsequent polymerization results in the formation of the block copolymer. The graft to approach requires the synthesis of two homopolymers with functionalized end groups and then coupling them together. For the synthesis of rod-coil block copolymers containing conjugated polymers, both the graft from and the graft to approaches are limited by the difficulty in synthesizing conjugated polymer with functionalized ends resulting in a broad range of low molecular weight block copolymers. Previous work using end functionalized polythiophenes demonstrated that a macroinitiator could be used for the polymerization of methyl acrylate[6] as shown in Scheme 1. While the copolymer synthesis was successful, once the molecular weight of the copolymer reached 13,000 D the polymerization slowed and the poly dispersity index (PDI) increased substantially with time.[6]
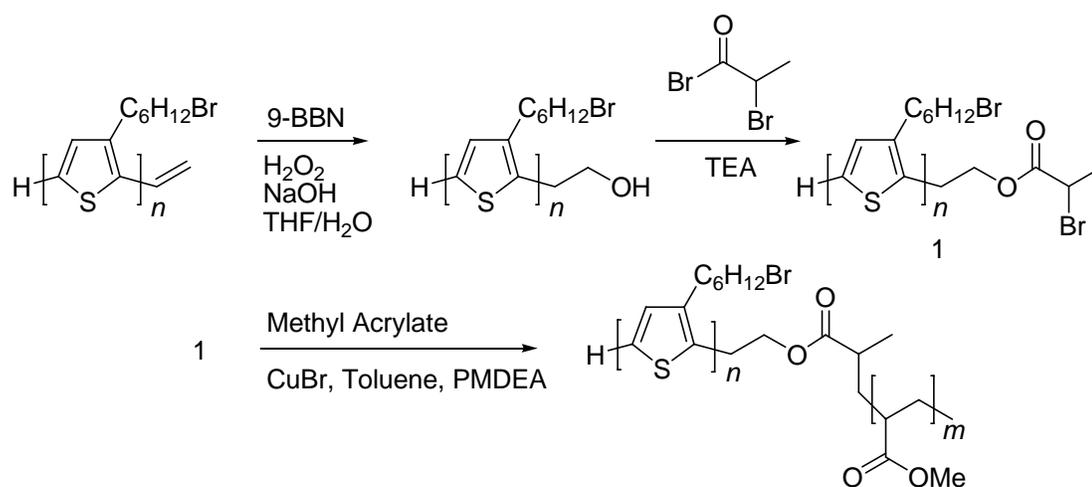

Scheme 1. Synthesis of P3AT Diblock Copolymers via ATRP Chemistry**.**

The advantage of the graft to approach is that it allows for greater control of the PDI of the block copolymers, since it is predetermined by the PDI of both starting

homopolymers. This approach has been successfully used for the synthesis of polythiophene-block-polystyrene,[7] polyphenylene-vinylene-*b*-polyisoprene[5] and polystyrene-*b*-polyphenylene vinylene.[8] The synthesis of polythiophene-block-polystyrene, polyphenylene-vinylene-*b*-polyisoprene and polystyrene-*b*-polyphenylene vinylene involves the coupling of a living polymer to an end functionalized conjugated polymer, thus they were limited to systems that are polymerized anionically. The goal of this research is to utilize the ease and versatility of click chemistry to synthesize rod-coil block copolymers via a graft to method. Our approach is based on two previously established reactions, namely end group functionalization of regioregular polythiophene to produce ethynyl terminated rod homopolymer[9] and the atom transfer radical polymerization (ATRP) of vinyl monomers (styrene, methyl acrylate, and butyl acrylate) to yield a bromine-terminated coil homopolymer.[10]

2.2. Results and Discussion

An ethynyl terminated poly-(3-alkylthiophene) (P3HT) was prepared by the GRIM reaction according to Scheme 2.
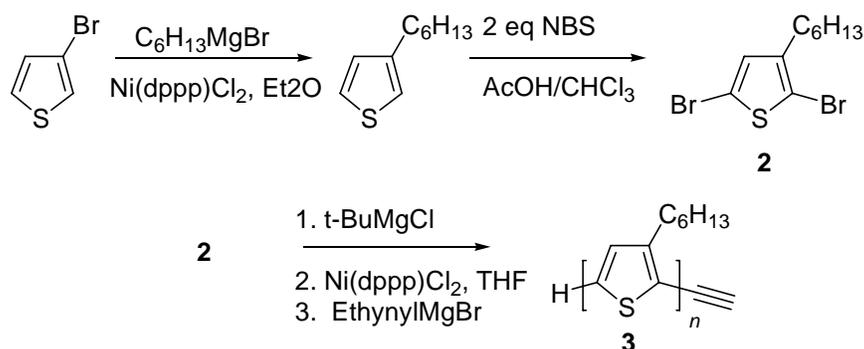
Scheme 2. Synthesis of Ethynyl Terminated Polythiophene

Following this scheme, the polymer was obtained with a number averaged molecular weight (M_n) of 4429 and a polydispersity index (PDI) of 1.55. Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) was employed to determine the end-group composition of the ethynyl P3HTs. This method was used because of its ability to ionize and analyze macromolecules with minimal fragmentation in the mass spectrometer. It has been established previously that terthiophene was the best matrix for use with P3ATs.[11] In general, the end group composition of the polythiophenes can be determined by multiplying the molecular weight of the repeating unit and adding the molecular weight of the end groups. For poly(3-hexylthiophene) the equation would be $166.2n$ + EG1 +EG2, where 166.2 is the molecular weight of 3-hexylthiophene, n is the number of repeating units and EG1 and EG2 are the molecular weights of the corresponding end groups. This technique allows for identification of the peaks within $\pm$ 5Da, which is the expected error due to isotope effects.[12]

The MALDI-TOF spectra of the ethynyl P3AT shown in Figure 2 indicates three different populations exist in the sample, one major and two minor. The major peak corresponds to a polymer bearing an ethynyl group on one end and a bromine group on the other (ethynyl/Br), one minor peak correlates to a polymer with an ethynyl group on one end and a hydrogen on the other (ethynyl/H), and the last minor peak can be attributed to a polymer with two ethynyl groups (ethynyl/ethynyl).
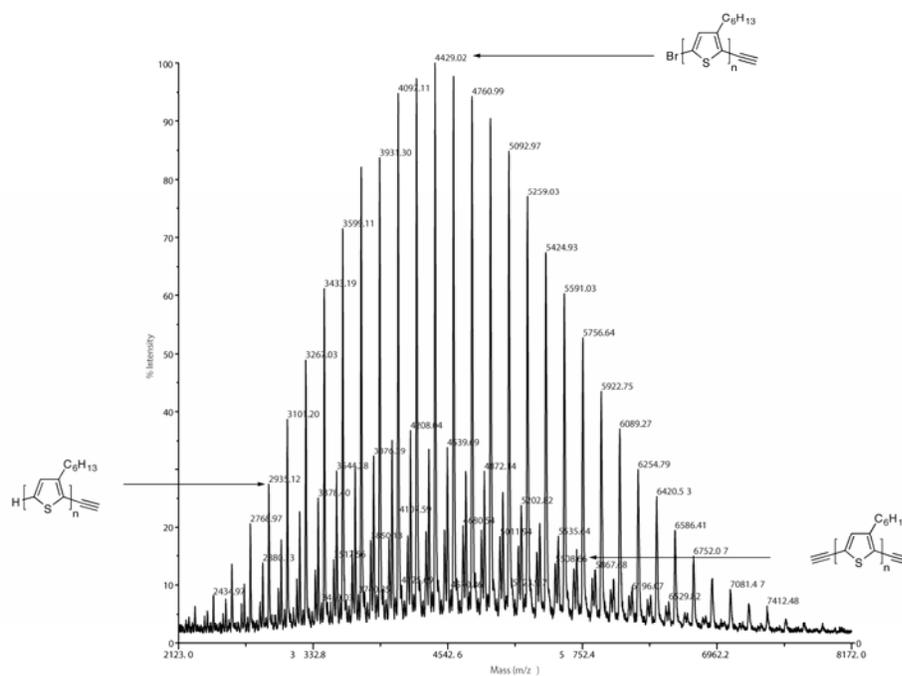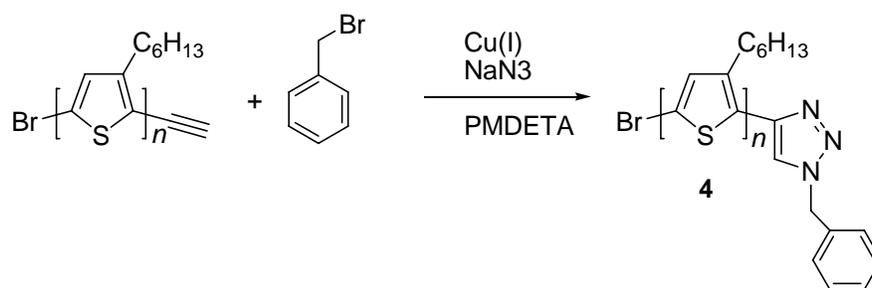
Figure 2. MALDI-TOF spectrum of ethynyl terminated P3HT.

The next step was to evaluate the efficiency of click reactions of the ethynyl P3HT using model reactions with benzyl bromide shown in Scheme 3.

Scheme 3. Ethynyl P3HT Click Model Reaction

Benzyl bromide was selected because it is structurally similar to the end group of polystyrene, which is to be used as the coil portion in the block copolymer. The click reaction was first attempted using an in-situ approach where CuBr, PMDETA, sodium

azide, and benzyl bromide were added to a solution of the ethynyl terminated P3HT in THF. These reaction conditions were selected based on previous work on click reactions of polystyrene.[13] Unfortunately, the reaction was unsuccessful, due to the poor solubility of the sodium azide and CuBr in the reaction mixture. The reaction conditions were then modified, by changing the solvent to DMF. However, the polymer was insoluble in this solvent, even with heating.

A subsequent reaction was performed, where the sodium azide and CuBr were initially dissolved in a few hundred micro liters of water. This solution was then added to a solution of the polymer dissolved in THF. As a result of all the ionic components in the water, it beaded on the bottom of the vial, and was immiscible with THF. A second attempt was made to dissolve the salts in DMF, then add this solution to a mixture of the ethynyl terminated P3HT dissolved in THF. Unfortunately, this again lead to the polymer precipitating out of solution.

The next approach was to change the catalyst from CuBr/sodium azide to $CuSO_4$/sodium ascorbate, for better solubility, however this also failed again due to the lack of solubility of $CuSO_4$. The catalyst was changed again to a $CuBr(PPh_3)_3$/DIPEA system. The addition of 10 equivalents of sodium azide to the mixture was enough to drive the reaction to completion, yet the results were not reproducible. This failure was attributed to the lack of solubility of the sodium azide, therefore eliminating sodium azide during the click reaction was explored.

The in-situ conversion of benzyl bromide to the corresponding benzyl azide seemed to be the limiting factor due to the insolubility of sodium azide in THF. By first forming the benzyl azide, then carrying out the click reaction, the model compound was

obtained. According the MALDI-TOF spectrum shown in Figure 3, almost all of the starting material was consumed (95%). Specifically, the peaks attributed to ethynyl/H and ethynyl/Br terminal groups were gone and new peaks corresponding to the benzyl triazole/H or benzyl triazole/Br terminal groups appeared. For example, the new peak formed at 4563.78 corresponds to $n=26$ with a benzyl triazole and a bromine for end groups.
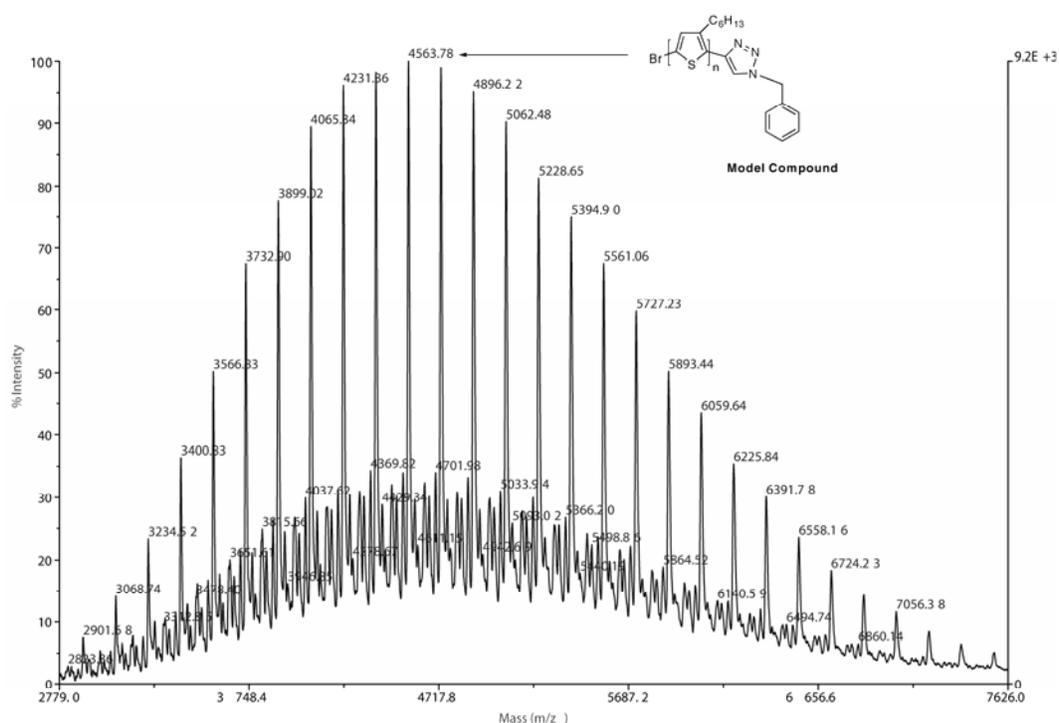

Figure 3. MALDI-TOF spectrum of Click test reaction.

Interestingly, it was found that the minor population of peaks previously credited to a P3HT bearing two ethynyl groups looked relatively unchanged. This was later reasoned that the two ethynyl groups were coupled to each other forming a diacetylene. After recognizing this, it was decided to use a protecting group on the alkyne. Since the

starting material was readily available, a protected propynyl system was proposed, illustrated in Scheme 4.
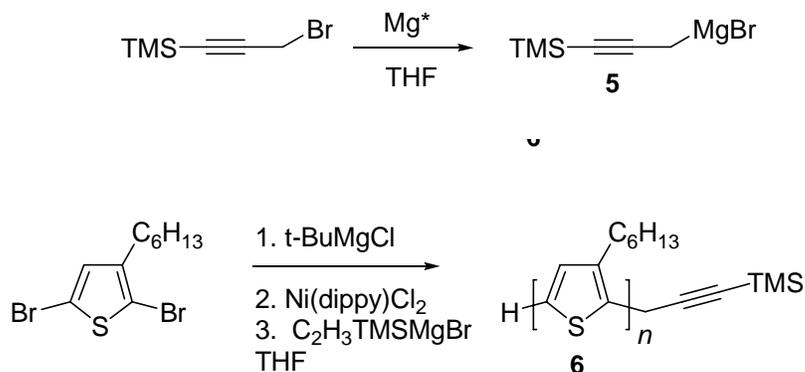
Scheme 4. Synthesis of Protected Acetylene Grignard and Corresponding P3HT

The activated Rieke magnesium (Mg*) was prepared by the reduction of anhydrous $MgCl_2$ using lithium and naphthalene in THF.[14] Rieke magnesium was used instead of standard magnesium metal because the Rieke metal does not contain trace impurities found on the surface of standard magnesium. These impurities decrease the end capping reaction yields. The polymerization was carried out similar to Scheme 2, but in this instance the propargyl Grignard was added to end cap the polymer. This approach was successful as the resultant polymer was cleaner, as shown in Figure 4. The polymer contains two populations H/propargyl-TMS and Br/ propargyl-TMS, the latter being the major product.
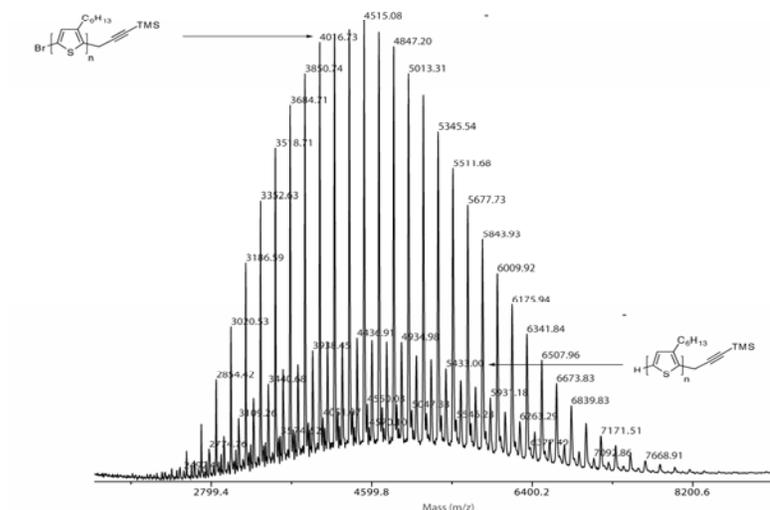
Figure 4. MALDI-TOF spectrum of end capped propynyl-TMS P3HT.

After the successful synthesis of ethynyl and propargyl-TMS terminated P3HTs rod portions, the next step was the preparation of the polystyrene coil portion. The synthesis of azide terminated polystyrene from the corresponding bromine terminated polymer has been reported in the literature[15] (Scheme 5).
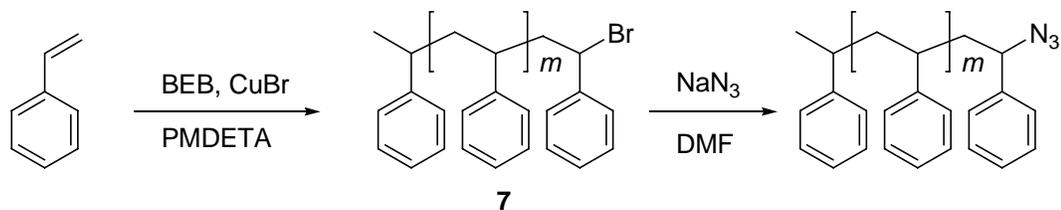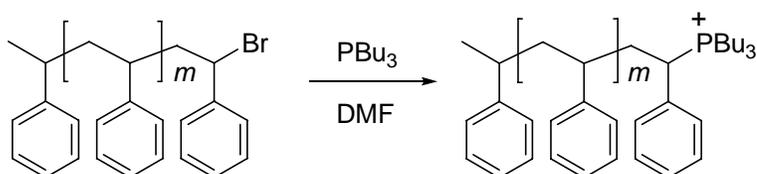

Scheme 5. Synthesis of Azide Terminated Polystyrene

A detailed procedure for the ATRP reaction of styrene proved to be elusive. While the ratios of the reagents varied depending on the target molecular weight, the

critical missing information was temperature and reaction times. After a variety of different attempts using different temperatures, solvents, and reaction times, it was found that a bulk ATRP synthesis worked best. This method produced a low molecular weight bromine terminated polystyrene of approximately 2900 with a PDI of 1.2. The reaction conditions were adjusted to yield a high molecular weight bromine terminated polystyrene of 7700 with a PDI of 1.1. Before moving on to the click reaction, we wanted to confirm the presence of bromine end group. However, MALDI-TOF of polystyrene was difficult to accomplish with a bromine end group, due to lack of ionization, the sample could not be used as it was. Instead an analytical sample of the styrene with bromine end groups was reacted with tributyl phosphine, which can easily be cationized in the MALDI allowing for end group analysis shown in Scheme 6.[16] Figure 5 is the MALDI-TOF spectrum of tributyl phosphine terminated polystyrene.

Scheme 6. Synthesis of Terminated PBu$_3$ Polystyrene

Figure 5. MALDI-TOF spectrum of terminated PBu₃ polystyrene.
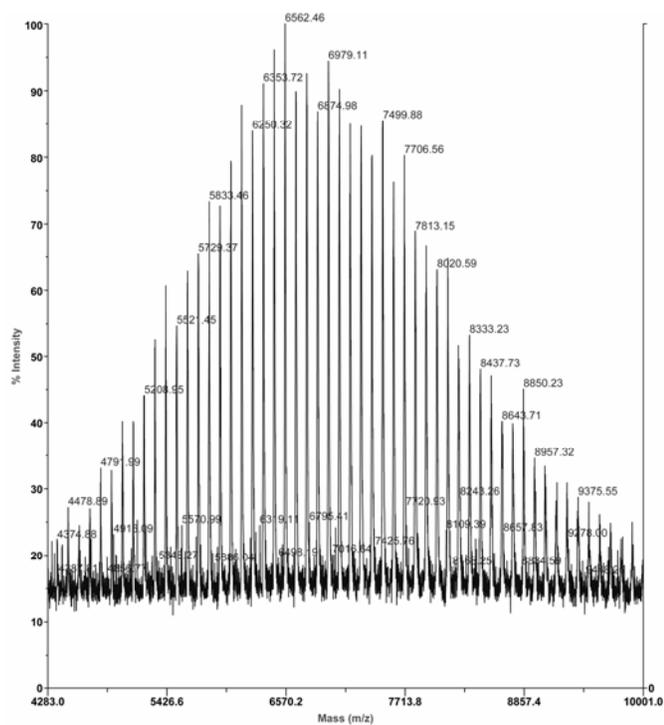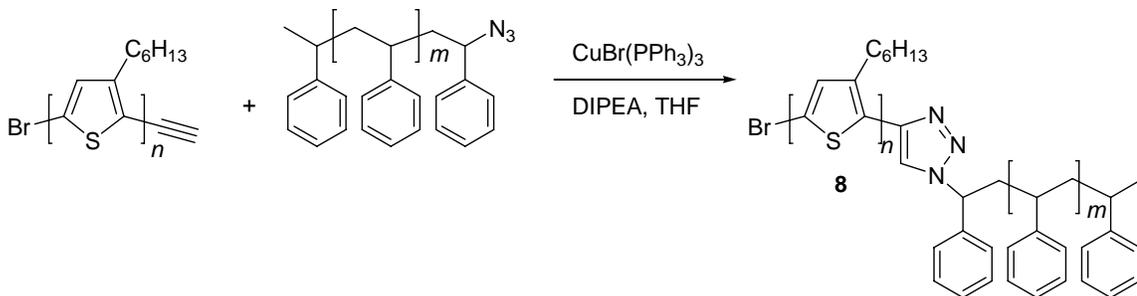
Once the presence of a bromine end-group was confirmed, the polystyrene was then converted to the corresponding azide by reacting it with sodium azide in DMF overnight. Next, the azide terminated polystyrene was reacted with the ethynyl terminated P3HT shown in Scheme 7.[9]

Scheme 7. Click Reaction of Ethynyl Terminated P3HT and Azide Terminated Polystyrene

After work-up, the two starting materials and the product were analyzed by Gel Permeation Chromotography (GPC). This was often considered the most convenient technique for measuring molecular weight and molecular weight distribution because of the simplicity, availability, and low relative cost.[17]

A variety of detectors can be used to customize the GPC based on research needs. Typically GPCs come with three detectors: refractive index, light scattering, and a viscometer. Polythiophenes do not work well with light scattering detectors, so a UV/Vis detector was used for this study. GPC works by correlating the hydrodynamic volume of coil polymers to that of molecular weight. Molecular weights are determined by comparison against a set of polystyrene standards. Conjugated polymers, like polythiophene, adopt a rod-like conformation, thus they pass through the system more quickly, leading to an increase of molecular weight.[18]
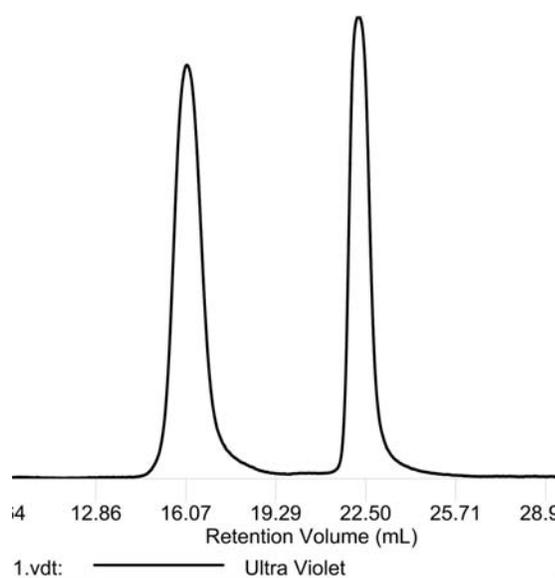

Figure 6. UV-Vis GPC trace of bromine terminated polystyrene.

The GPC trace of polystyrene (Figure 6) indicates the presence of residual unreacted styrene from the bulk polymerization, which corresponds to the peak at 22.5

retention volume. However, it seems to have no net effect on the click reaction. This trace was obtained by monitoring at 256 nm, which is near the absorbance maximum for polystyrene. To monitor the ethynyl terminated P3HT, detector wavelength was changed from 256 nm to 456 nm, which is the absorbance maximum for P3HT. The ethynyl terminated polythiophene starting material was analyzed at this wavelength and is shown in Figure 7.
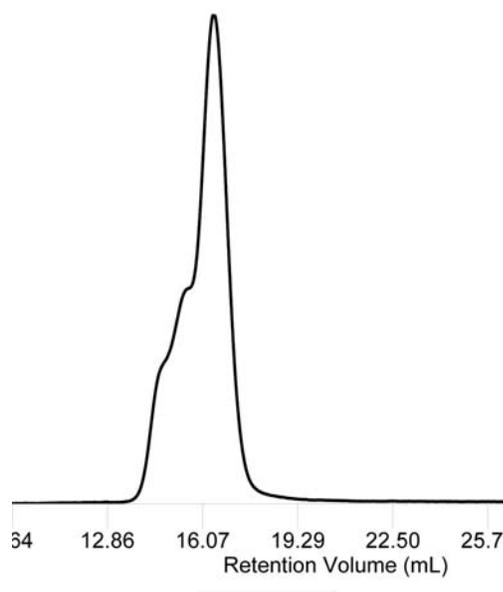
Figure 7. UV-Vis GPC trace of ethynyl terminated P3HT monitored at 456.

The shoulder on the trace is attributed to one of two possible scenarios. The first possibility is agglomeration of the polythiophene on the column causing an increase in molecular weight. The second could be due to a large PDI, with numerous mass ranges. After reexamining the MALDI-TOF spectrum and observing no peaks above the 8000 mass range, the shoulder is assigned to the first scenario. An overlay was then done of the ethynyl P3HT starting material and the block copolymer, which is shown in Figure 8.

It can be clearly seen that the block copolymer has a greater molecular weight than the polythiophene segment. Since this was taken at 456 nm wavelength, where styrene does not absorb, it is fair to rule out the possibility of a blend of the homopolymers. Thus the new high molecular weight polymer must contain P3HT.
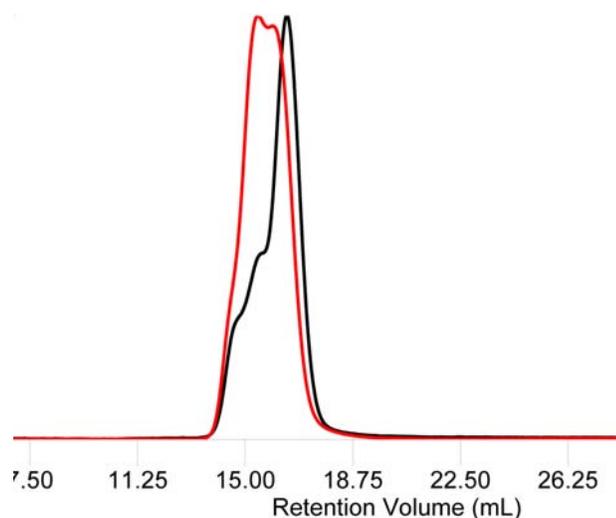
Figure 8. Overlay of block copolymer and P3HT.

Although the synthesis of the polythiophene/styrene block copolymer was successful, there were a few problems associated with it. The first issue was that the styrene protons overlapped with the polythiophene protons in the NMR spectrum, rendering it useless as a characterization tool. Second, since polystyrene contains aromatic rings, the analysis of the block copolymer can be complicated by π-stacking interactions. The third problem is the proximity of the two peaks on the GPC trace. It is difficult to determine whether it was 100% block copolymer or a mixture of products and reactants. After further analysis, it could be determined that the aforementioned GPC trace was actually overlapping peaks consisting of about 60% block copolymer 40%

polythiophene. The problems associated with polystyrene gave cause to investigate two new coil polymers, polyethylene glycol (PEG) and polybutyl acrylate (PBA). These polymers were chosen for three reasons: they do not have any peaks that overlap with the aromatic peaks of P3HT in the proton NMR spectrum,   they are not aromatic, and therefore would be no interference of the P3HT π-stack, and they could increase resolution of the GPC.

PEG was selected for the ease of separation from the starting material. The 2000 M.W. polyethylene glycol mono methylether was converted to the corresponding azide via the tosylated intermediate shown in Scheme 8.[19]   After conversion to an azide terminated PEG, the click reaction with propynyl-TMS terminated P3HT was carried out as shown in Scheme 9. Two reactions, using 10 equivalents of the PEG were set up and run for two and four days respectively.
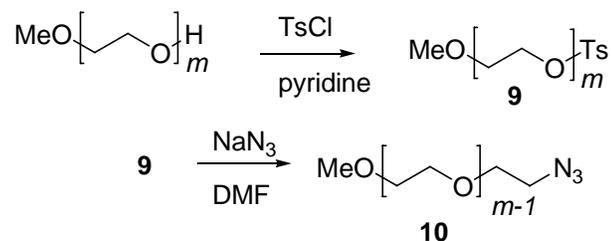
Scheme 8. Conversion of Hydroxy Terminated PEG to Azide Terminated PEG
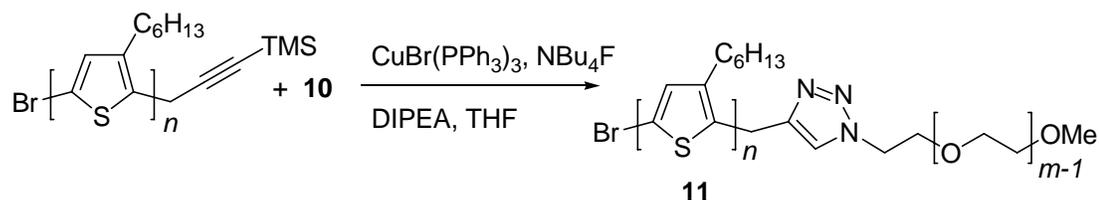
Scheme 9. Click Reaction of Propynyl-TMS Terminated P3HT and Azide Terminated PEG.

Each reaction was washed with methanol and chloroform and examined by GPC and NMR spectroscopy. The GPC of the block copolymer showed another distinct UV shift for the polythiophene (Figure 9).
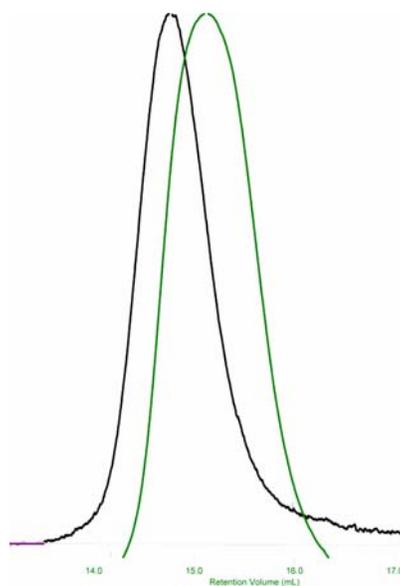
Figure 9. GPC overlay of propynyl-TMS P3HT and PEG block copolymer.

The extent of polymerization was determined using NMR spectroscopy. Figures 10 and 11 show the products obtained from two different reactions with reaction times of 48 and 96 hours, respectively. The expected integration ratio for the two peaks should be approximately 1:3 for aromatic thiophene proton vs. the PEG protons, based on the

molecular weight of the polymers. After 48 hours only approximately only 10% of the

P3HT appeared to have reacted with the PEG. After doubling the reaction time to 96

hours, there was only a slight increase in the amount of reacted PEG.
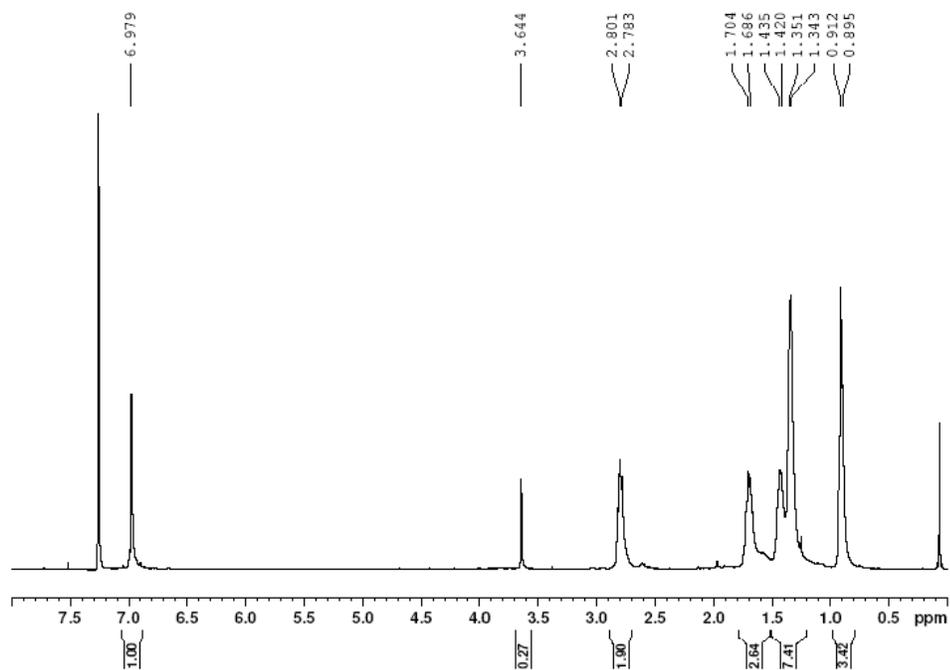
Figure 10. Proton NMR spectrum of the PEG/P3HT Click reaction after 48 hours.
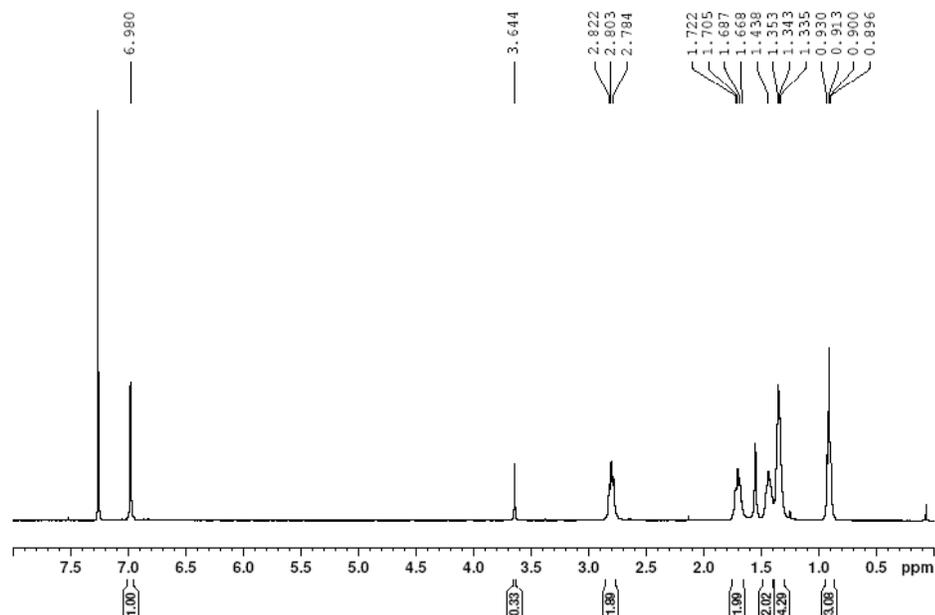
Figure 11. Proton NMR spectrum of the PEG/P3HT Click reaction after 96 hours.

The synthesis of polybutyl acrylate (PBA) is illustrated in Scheme 10. PBA was synthesized using ATRP chemistry,[20] with a molecular weight of 6400 D and the PDI was 1.18. The product was converted to the corresponding azide using a literature procedure.[9]
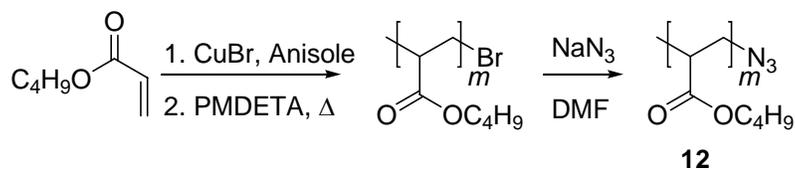
Scheme 10. Synthesis of an Azide Terminated Polybutyl Acrylate

It was anticipated that by using a sample that would not π-stack with the polythiophene, a higher percentage of block copolymer would be obtained. Moreover, since the proton peaks for the PBA would show up in a different portion of the ^{1}H NMR,

analysis would be easier. A click reaction was set up for 48 hours, illustrated in Scheme 11. The change in retention time between the starting materials, and product was again negligible in GPC (Figure 12).
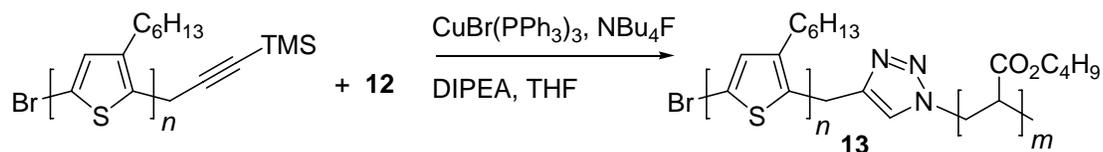
Scheme 11. Click Reaction of Propynyl-TMS Terminated P3HT and Azide Terminated PBA
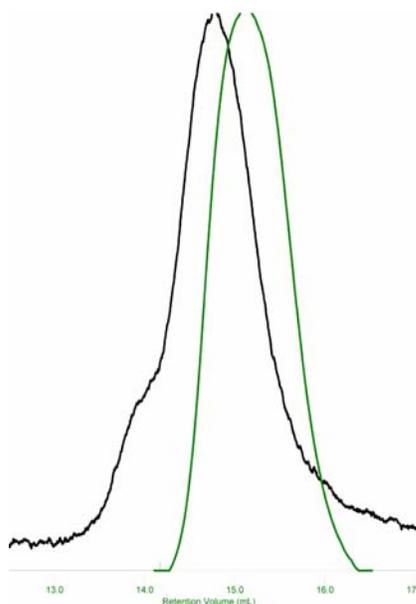
Figure 12. GPC overlay of the starting P3HT and PBA block copolymer.

2.3. Conclusions

    The synthesis of a rod-coil block copolymer is of interest because of the ability to control the nanoscale morphology. Previous work using rr-P3HT in a graft from method did produce rod-coil block copolymers; however, the drawback of increasing molecular weight distribution left room for improvement. Utilizing click chemistry in a graft to

approach was somewhat successful. It was possible to form the block copolymer in up to 60% block copolymer yields. Yet, block copolymer synthesis requires yields approaching 100% due to the inability to separate the thiophene homopolymer from the block copolymer. As a result of the different behavior of the coil segment and the rod segment in the GPC column, polymers with larger differences in molecular weight need to be prepared to achieve sufficient separation. Additionally, it was found that the GPC system used needs to be modified to increase sensitivity in the molecular weight range of 5,000-60,000.

2.4. Experimental Methods

All reactions were preformed under prepurified nitrogen or argon, using oven-dried glassware. Tetrahydrofuran (THF) was dried using an Innovative Technologies purification system. Anhydrous Magnesium Chloride, lithium wire, Napththalene, Ni(dppp)Cl$_2$, tert-butylmagnesium chloride, ethynyl magnesium bromide, were purchased from Aldrich Chemical Co. and used without further purification. 2,5-dibromo-3-hexylthiophene **1** was synthesized according to the literature procedures from 3-hexylthiophene.[10,21] 3-Bromo-1-trimethylsilyl-1-propyne was purchased from GFS Chemicals and used without further purification.

Azide terminated PEG was prepared from the corresponding tosyl[19] terminated PEG.[9]

Bromine terminated PBA was prepared according to literature procedures.20 Mn = 6400, PDI = 1.18

Instrumentation.

^{1}H NMR spectra were recorded using a Varian 400 MHz instrument. MALDI-TOF MS (Voyager-DE STR BioSpectrometry) workstation by Biosystems was used to

record spectra in linear mode, in which samples were irradiated under high vacuum using a nitrogen laser (wavelength 337 nm, 2ns pulse). The accelerating voltage was 20 kV, and the grid voltage and low mass gate were 92.0% and 1000.0 Da., respectively. The matrix used for all samples was 2,2': 5,2"-Terthiophene (Aldrich). GPC measurements were carried out on a Viscotek GPC Max 280 separation module equipped with two 5µm I-gel columns connected in series (guard, HMW and LMW) with a variable λ absorbance UV detector, online viscometer and refractive index detector. Analyses were performed at 30 °C using THF as the eluent, and the flow rate was 1.0µL/min. Calibration was based on polystyrene standards obtained from Viscotek.

Synthesis of 3-magnesium-bromo-1-trimethylsilyl-1-propyne: To a 25 mL Schlenk flask 0.4765 g (0.005 mol) $MgCl_2$, 0.135 g (0.00103 mol) naphthalene, 6 mL of THF and 0.072g (0.0105 mol) Li wire were added. The reaction mixture was stirred vigorously for 24 hours at RT. After 24 hours the Grignard was taken up in a syringe and added dropwise to the polymerization reaction as described for general method.

Typical End-Capping Reaction.[10] In a three neck round bottom flask 2,5-dibromo-3-hexylthiophene **1** (1.63g, 5.0 mmol) was dissolved in THF (10 mL) and stirred under N2. *tert*-Butylmagnesium chloride (2.5 mL, 5.0 mmol) was added via syringe and the mixture was stirred at room temperature for 2 hours. The reaction mixture was then diluted to 50 mL with THF and $Ni(dppp)Cl_2$ (1.75-2.25 mol%) was added in one portion. The mixture was stirred for 10 minutes at room temperature, and the Grignard reagent (20-30 mole % of monomer) was added via syringe to the reaction mixture. The mixture was stirred for an additional 2 minutes and then poured into methanol to precipitate the polymer. The polymer was filtered into an extraction thimble and then washed by Soxhlet extraction

with methanol, hexanes, and chloroform. The polymer was isolated from the chloroform

extraction.

GPC: M_n: 4429, PDI: 1.5; MALDI-MS: *m/z*: 4429.02 [M+] (calcd: 4426.20, DP of 26,

ethynyl/Br end groups).

Synthesis of Ethynyl Terminated P3HT Clicked with Benzyl Bromide: To a 20 mL

scintillation vial 0.085 g (0.021 mmol) of poly 3-hexyl thiophene ethynyl end capped,

0.025 g (0.385 mmol) NaN_3, 0.010g (0.011 mmol) $CuBr(PPh_3)_3$, 200 μL of DIPEA, 10

mL of THF and .5 mL of Benzyl Bromide were added. The vial was capped and stirred

at 40°C for 16 hours. The reaction mixture was the precipitated into 100 mL of methanol

and filtered through a cellulose thimble. Soxhlet extraction was performed using hexanes

and chloroform. MALDI-MS: *m/z*: 4563.45 [M+] (calcd: 4559.20, DP of 26, Clicked

Benzyl/Br end groups)

 Synthesis of Ethynyl Terminated P3HT Clicked with Benzyl Azide: To a 20 mL

scintillation vial 0.105 g (0.0267 mmol) of poly 3-hexyl thiophene ethynyl end capped,

0.0013 g (0.00140 mmol) $CuBr(PPh_3)_3$, 40 μL of DIPEA, 10 mL of THF and 50 μL of

Benzyl Bromide were added. The vial was capped and stirred at 40°C for 48 hours. The

reaction mixture was the precipitated into 100 mL of methanol and filtered through a

cellulose thimble. Soxhlet was performed extraction using hexanes and chloroform.

MALDI-MS: *m/z*: 4563.78 [M+] (calcd: 4559.20, DP of 26, Clicked Benzyl/Br end

groups)

Synthesis of Low Molecular Weight Bromine Terminated Polystyrene: To a 25 mL

Schlenk flask 10 mL (0.087 mol) of styrene and 0.152 g (0.00087 mol) of CuBr was

added. Argon was bubbled through the mixture for 45 min. PMDETA 0.180 mL

(0.000435) was added and stirred for 15 min. The bubbling Ar was removed and the reaction mixture was heated to 100 °C. 1-bromoethyl benzene 0.594 mL (0.00435 mol) via syringe and mixture was stirred for 5 hours. The Schlenk flask was then opened to air and 15 mL of THF was added. The organics were then passed through a neutral alumina column and precipitated into 100 mL of methanol. M_n = 2900, PDI = 1.2

Synthesis of High Molecular Weight Bromine Terminated Polystyrene: To a 100 mL Schlenk flask 50 mL (0.437 mol) of styrene and 0.314 g (0.00219 mol) of CuBr was added. Argon was bubbled through the mixture for 45 min. PMDETA 0.457 mL (0.00219) was added and stirred for 15 min. The bubbling Argon was removed and the reaction mixture was heated to 100 °C. 1-bromo ethyl benzene 0.800 mL (0.00437 mol) via syringe and mixture was stirred for 6 hours. The Schlenk flask was then opened to air and 15 mL of THF was added. The organics were then passed through a neutral alumina column and precipitated into 100 mL of methanol. M_n = 7700, PDI = 1.1

Synthesis of Diblock Ethynyl P3HT/HMW Polystyrene: To a 20 mL scintillation vial 0.110 g (0.028 mmol) of ethynyl end capped poly-(3-hexylthiophene), 0.212 g (0.031 mmol) of azide terminated polystyrene, 0.002 g (0.00215 mmol) of $CuBr(PPh_3)_3$, 40 μL of DIPEA, and 10 mL of THF were added. The vial was capped and stirred at 40°C for 60 hours. The reaction mixture was the precipitated into 100 mL of methanol and filtered through a cellulose thimble. Soxhlet extraction was performed using methanol, hexanes, and chloroform.

Synthesis of Diblock Ethynyl Terminated P3HT/LMW Polystyrene: To a 20 mL scintillation vial 0.101 g (0.0257 mmol) of ethynyl end capped poly-(3-hexylthiophene), 0.082 g (0.028 mmol) of azide terminated polystyrene, 0.0011 g (0.00118 mmol) of

CuBr(PPh$_3$)$_3$, 40 μL of DIPEA, and 10 mL of THF were added. The vial was capped and stirred at 40°C for 60 hours. The reaction mixture was the precipitated into 100 mL of methanol and filtered through a cellulose thimble. Soxhlet extraction was performed using methanol, hexanes, and chloroform.

Synthesis of Diblock LMW Propynyl Terminated P3HT/PEG: To a 20 mL scintillation vial 0.070 g (0.019 mmol) of propynyl TMS end capped poly(3-hexylthiophene), 0.075 g (0.0375 mmol) of azide terminated PEG, 0.003 g (0.00322 mmol) of CuBr(PPh$_3$)$_3$, 40 μL of DIPEA, 100 μL of N(Bu)$_4$F, and 10 mL of THF were added. The vial was capped and stirred at 40°C for 48 hours. The reaction mixture was the precipitated into 100 mL of methanol and filtered through a cellulose thimble. Soxhlet extraction was performed using methanol and chloroform.

Synthesis of Diblock HMW Propynyl Termiated P3HT/PEG: To a 20 mL scintillation vial 0.074 g (0.00779 mmol) of propynyl TMS end capped poly(3-hexylthiophene), 0.155 g (0.0779 mmol) of azide terminated PEG, 0.004 g (0.0043 mmol) of CuBr(PPh$_3$)$_3$, 40 μL of DIPEA, 100 μL of N(Bu)$_4$F, and 10 mL of THF were added. The vial was capped and stirred at 40°C for 48 hours. The reaction mixture was the precipitated into 100 mL of methanol and filtered through a cellulose thimble. Soxhlet extraction was performed using methanol and chloroform.

Synthesis of Diblock HMW Propynyl Terminated P3HT/PBA: To a 20 mL scintillation vial 0.074 g (0.00757 mmol) of propynyl TMS end capped poly(3-hexylthiophene), 0.080 g (0.00757 mmol) of azide terminated PBA, 0.004 g (0.0043 mmol) of CuBr(PPh$_3$)$_3$, 40 μL of DIPEA, 100 μL of N(Bu)$_4$F, and 10 mL of THF were added. The vial was capped and stirred at 40°C for 48 hours. The reaction mixture was

the precipitated into 100 mL of methanol and filtered through a cellulose thimble. Soxhlet extraction was performed using methanol and chloroform.

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CHAPTER 3: Toward the Development of Bioresponsive Polythiophenes

3.1. Introduction

Conducting polymers offer several advantages for use in sensor technologies including relatively low cost, their simple fabrication techniques, and the ability to be deposited on various types of substrates. In some systems, changes in the conducting polymer's environment can result in changes in the polymers properties that are measurable. In many cases, properties such as electron mobility, electrical conductivity, or fluorescence are amplified, providing increased sensitivity.[1] The synthesis of such systems is simplified by the need to produce polymers with an effective conjugation length of only 7-13 repeating units.[2] There are four types of conducting polymer sensors: conductometric, potentiometric, fluorescence and colorimetric. Conductomeric sensors display changes in electrical conductivity in response to analyte activity.[3] Potentiometric sensors rely on analyte induced changes in the system chemical potential by exploiting the reversible redox properties of PCPs in addition to their sensitivity to conformation and electrostatics.[4] Fluorescence sensors measure either amplification or it quenching of the conjugated polymer fluorescence in the presence of analytes. This response is a result of a variety of events such as changes in intensity, energy transfer, wavelength (excitation and emission) and lifetime. Thus it was possible to reach high levels of sensitivity using this approach.[5,6] Colorimetric sensors use changes in absorption spectra of the conjugated polymer for detection. Although the absorption properties of PCPs are determined by their structure, they are sensitive to the polymers conformation and thus can be changed in the presence of analytes. There are a variety of ways to tune the sensor to be analyte specific, including covalent or physical integration of receptors, imprinting the

conjugated polymers, and the electrostatic and chemical characteristics of the conjugated polymer.

The development of polymer sensors based on these concepts can be designed using two approaches: lock and key and sensor arrays. Lock and key sensors utilize a polymer which is functionalized with a specific receptor that induces a response for a specific analyte. To date, this approach has been largely applied to the development of biosensors for a number of different analytes such as Avidin,[7] amines,[8] viruses,[9] and bacteria.[9] The benefit of this approach is its increased selectivity, but it is not without limitations. For instance, the synthesis of such polymers is complicated, the polymer systems cannot handle matrix effects leading to false positives, and the polymers were inefficient for multi-analyte detection.

The second approach is non-specific sensor arrays, where a number of structurally different polymers are placed together to form an array. The polymers are not designed to respond to one specific analyte, rather they respond to many chemicals or chemical classes. Due to differences in structure, the polymers respond differently to the analytes. By looking at the response of the array as a whole analytes can be determined by its "fingerprint", or unique set of responses. Additionally, the combination of a variety of different polymers that detect different chemicals and chemical groups, and cross referencing them, makes it possible to identify analytes in the presence of complex matrixes. The advantage to this system is the relative ease of synthesis. However, the sensor array approach was well suited for chemical analytes, it is not suitable for the detection of biological molecules due to the lack of specificity.

Among PCPs, functionalized polythiophenes are an ideal choice for use as a sensor. When appropriately functionalized, polythiophenes can exhibit responses in the presence of a variety of stimuli, including biomolecules avidin, viruses[9] and DNA.[10,11] P3HT undergoes an optical transition when perturbed changing from a purple to a yellow color, due to the transition from planar to a non-planar conformation caused by side chain disordering. Additionally, the ability to synthesize polymers bearing a number of different substituents makes the development of arrays based on polythiophene feasible.

The goal of this project is to develop efficient methods for the synthesis of functionalized polythiophenes which bear selective receptor groups. Carbohydrates were selected due to the highly selective interaction with certain biomolecules. In particular, the main interest is in the interaction between α-D-mannose and *E*. Coli. Previous research has shown that polythiophenes bearing α-D-mannose can be used as a colorimetric detector for *E*. Coli.[9] However, this report used a polymer which was not regioregular, thus the degree of conjugation was reduced thereby reducing the optical response. Also there are a large number of steps involved in the synthesis, making it very inefficient. Since the polymerization uses Grignard reagents, which react with the hydroxyl groups on the sugar, the α-D-mannose can not be present on the monomer. The strategy was to synthesize a α-D-mannose with an ethynyl group (Scheme 1), a poly(3-hexylthiophene) bearing azide groups on the side chain (Scheme 2), and utilize click chemistry to form the responsive polythiophene (Scheme 3).
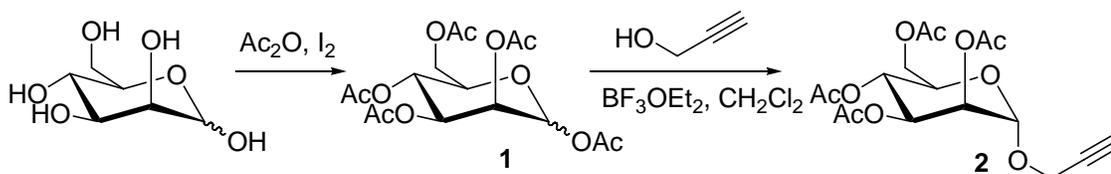
Scheme 1. Synthesis of Acetylated Mannose
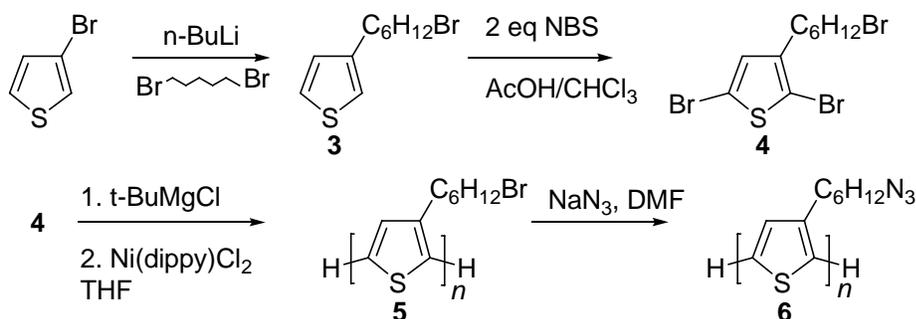
Scheme 2. Synthesis of Azide Terminated Side Chain Polythiophene
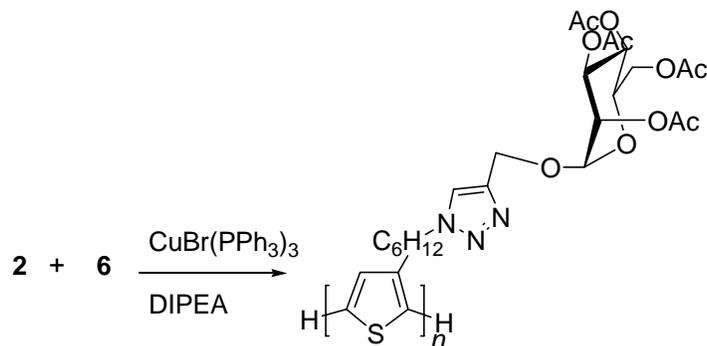
Scheme 3. Target Responsive Polythiophene Molecule

3.2. Results and Discussion

Following literature procedures, compounds **1** and **2** were prepared in good yields.[12,13] The second step was the synthesis of product **6,** which proved to be problematic in many ways. Yields in the range of 15-20% were routinely obtained for compound **3**, while the literature procedure[14] lacked a reported yield. For this reason a different route was investigated shown in Scheme 4.
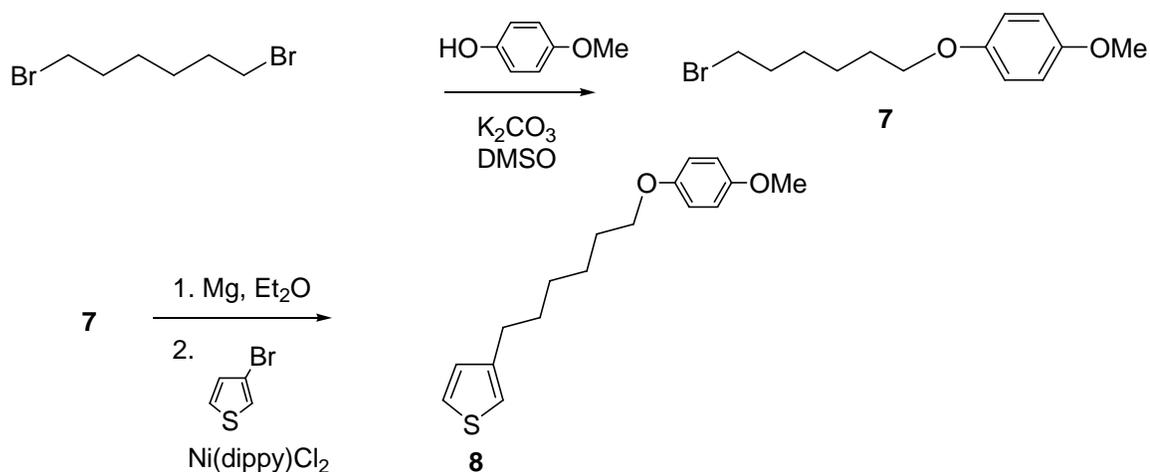
Scheme 4. Synthesis of Protected 3-(6-Bromo-Hexyl)Thiophene

Although this route increases the number of steps, the first step was reported to occur in good yield $(75\%)^{15}$, making this strategy a likely improvement. Product **7** was obtained in good yield (74%) as a low melting point solid, which can be purified by distillation. Product **7** was converted to the corresponding Grignard, and coupled with 3-bromo thiophene using Ni(dppp)Cl$_2$. Although product **8** was obtained in good yields (72%), it was not easily recrystallized, instead requiring purification by Kugel-Rohr air-bath distillation. The conversion of **8** to **1** occurred in decent yield (70%), however the extra steps needed in this route, resulted in only a slightly higher overall yield. For this reason the original method was revisited.

Several low yielding reactions were run to obtain an adequate amount of compound **3**, which was easily brominated to yield pure monomer **4,** that was then polymerized using the GRIM method. ^{1}H NMR spectroscopy indicated the formation of the regioregular polythiophene bearing bromine-terminated side chains. The next step in the reaction sequence was the conversion of polymer **5** to the azide, **6**, which was carried

out according to literature methods.[15]   In this report, the polymer **5** was dissolved in refluxing DMF and 10 equivalents of sodium azide were added. Again, contrary to the paper, the polymer seemed to be mostly insoluble in refluxing DMF, which was surprising since our polymer was of lower molecular weight that that used in the literature report. We then attemped the in-situ click reaction in THF, however it was also unsuccessful due to the poor solubility of the polymer. As a result of the consistent problems and numerous issues with this procedure another approach was examined.

A new target polymer was designed that would still utilize the click coupling reaction. In this approach, the thiophene was functionalized with an ethynyl terminated side chain (Scheme 5), and the corresponding azidial sugar (Scheme 6) was prepared. Since the reaction was to be carried out under GRIM reaction conditions, the alkyne was protected with a TMS group. The protected 5-hexynol **11** was obtained according to the literature procedure in good yield.[16]
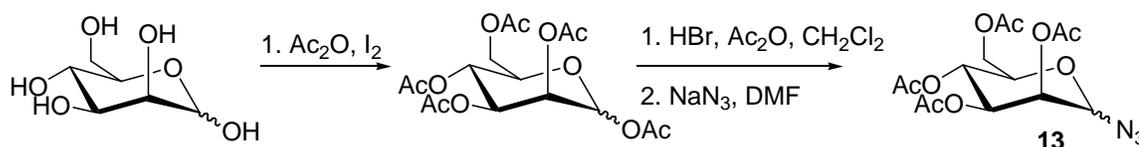

Scheme 5. Synthesis of Azidial Mannose.
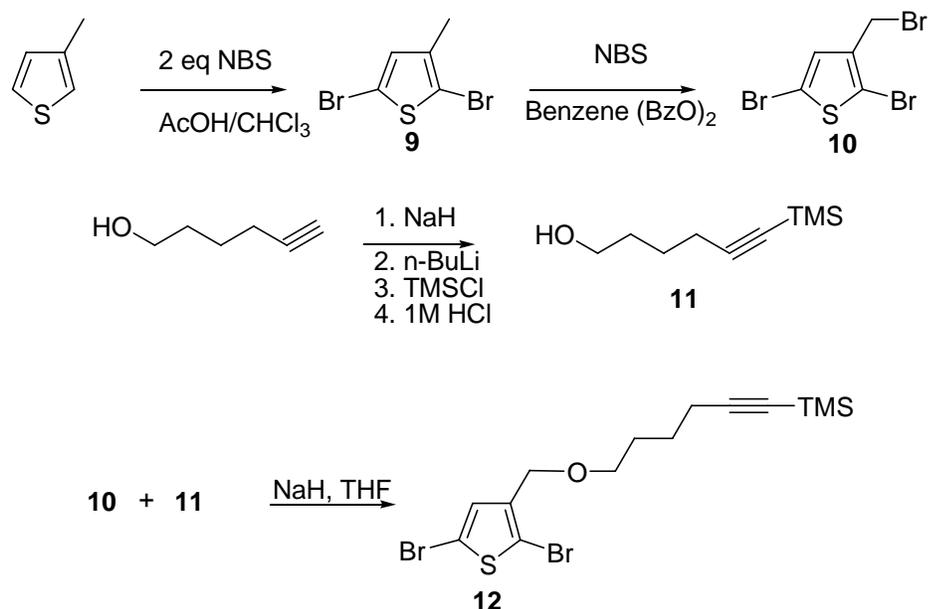
Scheme 6. Synthesis of Ethynyl Terminated Side Chain Thiophene

The carbohydrate **13** was prepared from carbohydrate **1,** which we previously synthesized according to the literature method.[17] There are several different routes reported in the literature for the synthesis of 2,5-dibromo-3-methylthiophene **10**. The reaction of 3-methyl thiophene and 3 equivalents of Br_2 at reflux under UV irradiation seemed promising as it eliminated the need to synthesize and isolate 2,5-dibromo-3-methylthiophene. Unfortunately, GC/MS indicated that the major product was 2,5-dibromo-3-(dibromomethyl)thiophene.[18] It was also found that using 1 equivalent of NBS with a catalytic amount of AIBN in CCl_4 at reflux failed to produce the product after 12 hours.[19] The GC/MS indicated that a large amount of 2,5-dibromo-3-methyl thiophene remained unreacted and some 2,5-dibromo-3-(dibromomethyl)thiophene was produced. However, it was found that refluxing the 2,5-dibromo-3-methylthiophene with 0.95 equivalents of NBS in benzene under light yielded the desired product 2,5-dibromo-3-bromomethylthiophene.

After distillation, the product was reacted with the TMS protected 5-hexyno1 with NaH and THF. Following work-up three peaks were seen in the GC-MS spectrum of the crude reaction mixture. These peaks were assigned to the desired product, the product without the TMS protecting group, and a third product which was unknown. The mass of the unknown compound was approximately equal to that of the starting alcohol. ^{1}H NMR spectra of the mixture indicated two TMS peaks, indicating that this compound had a TMS protecting group on it. The unknown compound is tenetively assigned to the cyclized hexyn-1-ol. A silica column was run first using hexanes to elute unwanted starting material, then 20:1 Hexane:Ethyl Acetate to obtain the product. GC/MS still indicated three peaks, therefore, a second column was ran using 40:1 Hexanes:Ethyl Acetate and collected in 4 mL fractions. Checking the fractions by TLC and MS, which indicated the deprotected product was removed, however all but two fractions contained the cyclized impurity. A trial, test-scale metathesis reaction was carried out to see if the cyclized product interfered with the reaction. After approximately 3 hours, the test reaction was quenched, and checked by GC-MS. Although there was a small indication of the start of a metathesis reaction, via loss of a halogen, the main component was starting material without the TMS protecting group (Scheme 7).
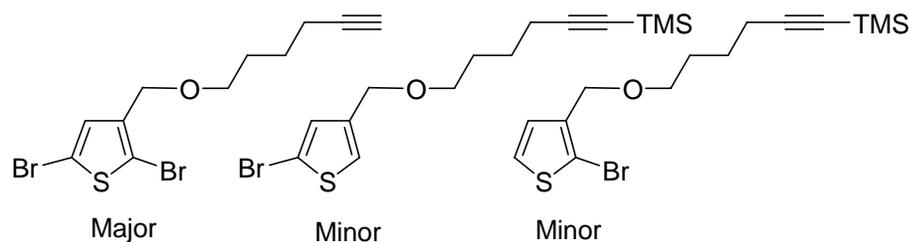
Scheme 7. Products of Test Metathesis Reaction

3.3. Future work

In light of the issues encountered in the pursuit of these functionalized polythiophenes, it becomes apparent that additional changes to the reaction scheme are necessary. The switch to the ethynyl-functionalized thiophene in contrast to the azide-functionalized polythiophene is a major improvement because of the improved solubility and eliminating the need to synthesize a potentially dangerous polymer. However, further modification the synthetic approach is required. The first change to this system should be the protecting group on the alkyne. Switching to a TIPS protection group should eliminate the deprotection during the metathesis. The formation of the cyclized product may be eliminated by using a shorter alkyne. Since a monomer with side chains that are at least 6 atoms long would be necessary to maintain solubiltiy, synthesis can accomplished by starting with 3-thiopheneethanol. The proposed synthesis is illustrated in Scheme 8.
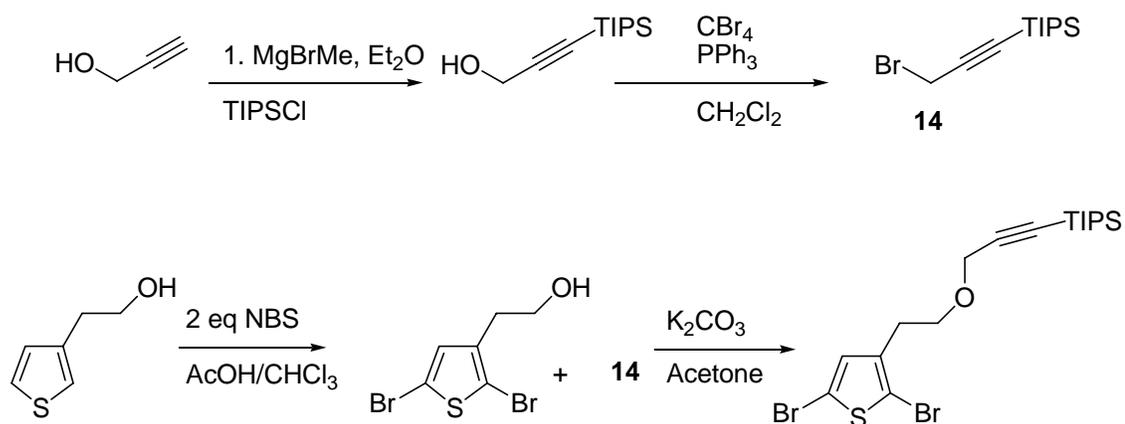
Scheme 8. Proposed Synthesis for TIPS protected alkynl monomer

The first step is to protect propargyl alcohol with TIPS, followed by bromination with CBr_4/PPh_3. Following previous methods, the thiophene ring would be dibrominated,

then coupled with the TIPS protected propargyl bromide using K$_2$CO$_3$/Acetone to produce the desired monomer.

3.4. Conclusions

Conducting polymers have much to offer the for development of sensors. With increased sensitivity, they still remain one of the most intriguing classes of sensor material. In particular, polythiophenes have a lot to offer the sensor field due to their chromatic response to analytes when properly functionalized. Click chemistry remains a very viable method to produce thiophene sensors, as long as all starting materials are soluble in the solvent. Although previously synthesized, producing 3-(6-bromo-hexyl)thiophene was relatively unsuccessful. Even after polymerization, conversion of the 3-(6-bromo-hexyl)thiophene to the corresponding azide was problematic due to the insolubility of the polymer. The new synthesis is able to provide the desired monomer, however the TMS protection did not withstand the metathesis reaction. Future work on the modified alkyne functionalized polythiophenes should resolve these issues.

3.5. Experimental Methods

3.5.1. General Methods

General methods remain the same as in chapter 2. α-D-mannose, 3-methyl thiophene, 4-methoxyphenol and 6-hexynol were purchased from Aldrich and used without further purification. 1,6-dibromohexnane was obtained from Acros and distilled before use.

3.5.2. Synthesis

1,2,3,4,6-Penta-*O*-acetyl-α-D-mannospyranoside (**1**)[13], 2-Propynyl 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (**2**)[14], 3-(6-bromohexyl)-thiophene (**3**)[15], 2,5-dibromo-3-(6-

bromohexyl)-thiophene (**4**)[15], Poly-3-(6-bromohexyl)-thiophene (**5**)[15], 1-(6-bromohexyloxy)-4-methoxyphenol (**7**)[16], 3-[6-(4-methoxyphenol)-hexyl]-thiophene (**8**)[16], 2,5-dibromo-3-methyl-thiophene(**9**)[15], 2,5-dibromo-3-bromomethyl-thiophene (**10**)[19], 6-(Trimethylsilyl)-5-hexyn-1-ol (**11**)[16], Azidial 2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranoside (**13**)[18], were prepared according to literature procedures were synthesized according to literature procedures.

Synthesis of **12**: To a 100 mL round bottom flask, 40 mL of dry THF was added along with 1.036 g (0.0259 mol) of 60% NaH. 5 mL of dry THF was added to 4.00 g (0.0235 mol) of **11** and was added via syringe to the reaction mixture. After 10 minutes, the evolution of H_2 stopped and a mixture of 5 mL THF and 8.67 g (0.0259 mol) of **10** were added via syringe dropwise. The mixture was stirred overnight. 5 mL of water was added dropwise, and the solvent was removed in vacuo. The residue was taken up in 50 mL CH_2Cl_2 and washed with 3 x 40 mL water. The organic layer was collection, dried with $MgSO_4$, filtered and removed in vacuo. The product was purified using a silica column with an initial eluent of hexanes, and a second eluent of 40:1 Hexanes:Ethyl Acetate. ^{1}H NMR 400 δ = 6.961 (s, 1H), 4.361 (s, 2H), 3.485 (t, 2 H), 2.220 (m, 2H), 1.687 (m, 2H), 0.878 (t, 2H).

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