Graduate Theses and Dissertations

Iowa State University Capstones, Theses and Dissertations

2009

Synthesis of novel telechelic regioregular polythiophenes

Robyn Lynn Laskowski
Iowa State University

Synthesis of novel telechelic regioregular polythiophenes

by

Robyn L. Laskowski

A thesis submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Chemistry (Organic Chemistry)

Program of Study Committee:

Malika Jeffries-EL, Major Professor

Nicola Pohl

Zhiqun Lin

Iowa State University

Ames, Iowa

2009

Table of Contents

CHAPTER 1:

Introduction to Conducting Polymers and Polythiophenes

1.1 Thesis Organization

This thesis is divided into three chapters. Chapter 1 is a general introduction to the subject of conjugated polymers. It explains the background information needed to understand the chemistry behind polymers, with particular interest shown to poly(3-alkylthiophene)s. Chapter 2 summarizes the chemistry and synthesis of various alkene end-functionalized poly(3-hexylthiophene)s. Chapter 3 covers the synthesis of alkyne end-functionalized poly(3-hexylthiophene)s, with a major emphasis on "click" chemistry.

1.2 Introduction

Almost four decades ago, Hegger, Shirakawa, and MacDiarmid discovered the first known polymer capable of being electrically conductive, polyacetylene.[1] This breakthrough has spawned a dramatic increase of interest in the study of π-conjugated polymers (PCPs) for use in a variety of semiconducting applications. The use of polyacetylene has been limited due to its poor solubility and air sensitivity that limits its potential uses as a semiconductor. However, since the initial discovery a variety of different structures have been investigated.

Since the discovery of the high conductivity of polyacetylene, other PCPs have been studied extensively, such as poly(*para*-phenylene)s (PPP)[3], polypyrrole (PPy)[4], poly(*para*-phenylene vinylene)s (PPV)[5], poly(*para*-phenylene ethylene)s (PPE)[6],

polyaniline (PANI)[7], and polythiophene (PT)[2], (Figure 21). However, these unsubstituted PCPs have strong interactions between the π-electrons, which have a tendency to make higher molecular weight polymers insoluble.[8]
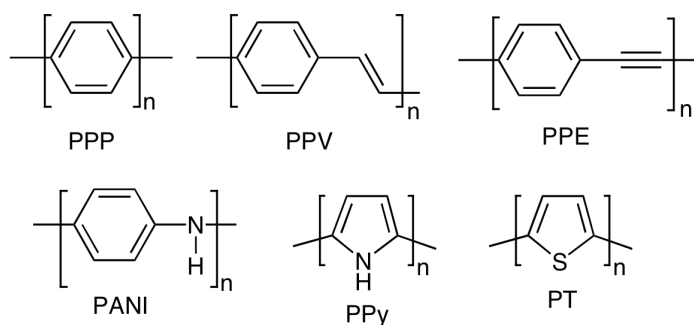
Figure 1: Commonly studied PCPs

The characteristic vital to conducting polymers is its backbone, comprised of a semi-infinite π system that extends throughout the monomer units. This extended system allows for directional conductivity along the backbone chain, producing an inherent semiconductor (Figure 2).[2]

PCPs have several advantages in comparison to their inorganic semiconductor counterparts including: a large number of accessible structures, which provides a means to tuning their properties and processing via a variety of solution based technologies, which reduces processing cost [9]. Given these characteristics, PCPs have a mounting interest for organic electronic applications, including photovoltaic cells[10,11], light-emitting diodes[12], and field-effect transistors[13].

CONDUCTORS

10^7

10^6 Copper Metal

10^5 regioregular Poly(alkylthiophene) doped with I_2

10^4 Polyaniline doped with I_2

10^3 Poly(p-phenylenevinylene) doped with I_2

       Poly(p-phenylenevinylene) doped with AsF_5

10^2

10 Poly(pyrrole) doped with I_2

0

SEMI CONDUCTORS

S/cm
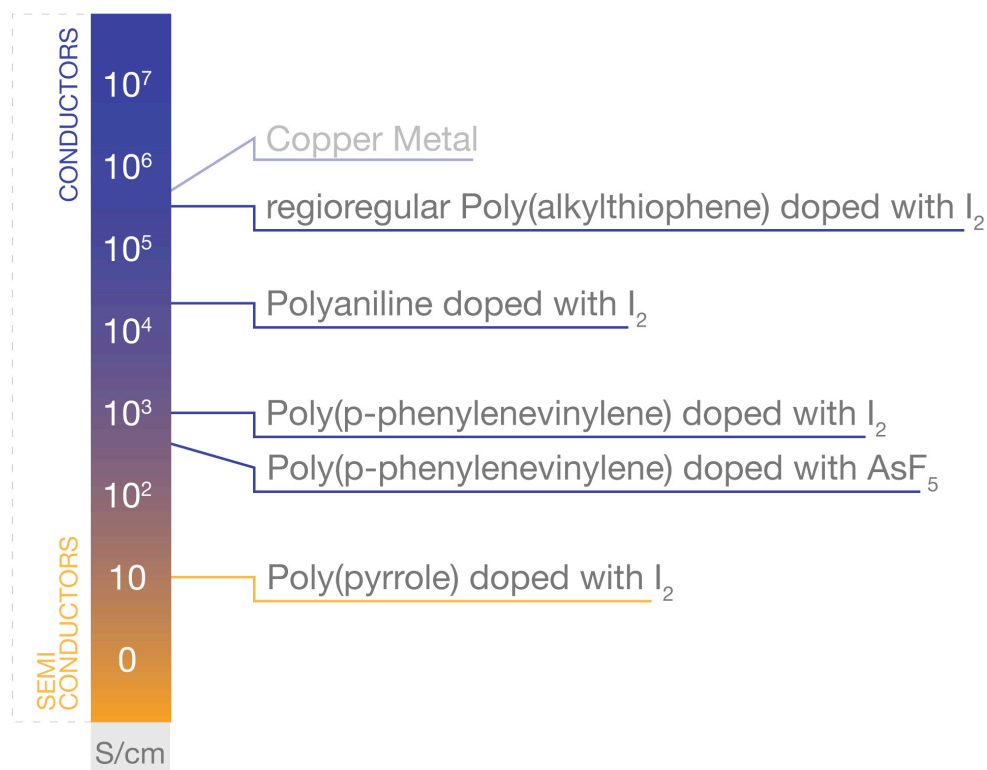
Figure 2: Conductivities of various doped conjugated polymers

1.3 Polythiophene

Polythiophene (PT) and its derivatives are among some of the most widely studied conjugated polymers. This is due to their the outstanding thermal stability (42% weight loss at 900°C), electrical conductivity (3.4 x 10^{-4} to 1.0 x 10^{-1} S/cm when doped), and environmental stability.[14] Polythiophene was first synthesized in the early 1980s via metal-catalyzed polycondensation polymerization of 2,5-dibromothiophene or the oxidative polymerization of thiophene.[15,16] These methods produced polymers that do not melt.[17] Synthetic studies of the polymerization have been performed, primarily by Yamamoto to optimize the reaction[18,19], by varying the amounts of magnesium[20],

solvent[19,21], type of catalyst used[18-20,22], concentration of same monomer[20], type of halogen bound to the monomer[18,20-23], temperature[18,22], reaction time[18], and. However, these variances only lead to minor improvement in the obtained sample.[17] High purity PTs have been synthesized using 2,5-diiodothiophene as the monomer. [24] Extensive washing of the isolated polymer resulted in a high purity PT, with approximately 50 ppm of Mg and Ni remaining in the polymer sample.[17] However, the resulting polymer was only soluble in anisole, limiting its use.

1.4 Poly(3-alkylthiophenes)

In an effort to surmount the insolubility of PTs, Elsenbaumer synthesized a new class of PTs with flexible alkyl side chains, poly(3-alkylthiophene)s (P3ATs) in 1985. [25,26] Shortly thereafter, other groups reported both chemical and electrochemical preparation of P3ATs.[27] Introduction of these flexible alkyl chains along the backbone of a previously insoluble polymer was found to drastically increase its solubility.[28] Similarly, P3ATs with alkyl groups larger than butyl can be easily processed from solution or melt, while maintaining the overall conductivity of the polymer.[27]

PTs developed via Kumada cross-couplings[29-32] of Grignard reagent or oxidative coupling of thiophenes lead principally to coupling of the thiophene units in the 2 and 5 positions (Figure 3). PTs synthesized with linkages in the 2 and 5 positions benefit greatly by allowing the conjugation of the π-orbitals to extend down the polymer chain and form quinoidal type resonance structures when oxidized. This results in dense chain packing and extensive π orbital overlap. While this produces PTs with high conductivities, it also causes the PTs to be very insoluble and not easily processable.[27]
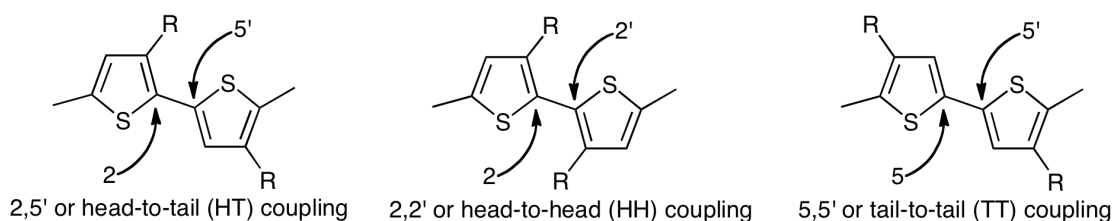
Figure 3: Regioisomeric couplings of 3-alkylthiophenes[33]

3-Alkylthiophene is not a symmetric molecule, therefore, poly(3-alkylthiophenes) can bond into three different relative orientations (Figure 3). The first coupling linkage of the two thiophene rings is a 2,5' linkage, also known as the head-to-tail coupling (HT). The second coupling, known as head-to-head (HH), is 2,2' coupling. Finally, tail-to-tail (TT) is a 5,5' coupling of the thiophene rings. [27,33] The head-to-head and tail-to-tail couplings cause twisting in the thiophene rings, therefore, increasing the torsional angle. Consequently, this disruption of the π-conjugation results in loss of conductivity and a larger band gap. Polymers with HH and TT couplings have no regiochemical control and are then referred to as regioirregular.

Similarly, regioregular, head-to-tail P3ATs can obtain a low energy planar conformation that can self-assemble. This aggregation coerces main-chain conformational order as well as supramolecular orientations.[14] Richard McCullough studied regioregular poly(3-hexylthiophene), rr-P3HT, using X-ray scattering and found the polymer chains form a well-defined lamellar structure with an interlaying backbone spacing of 16.0 ± 0.2 Å (Figure 4) and a π-stacking distance between the thiophenes on the ring of 3.81 ± 0.2 Å.[14] The inter- and intra-chain conductivity pathways are more efficient for regioregular

than regioirregular P3HT, which leads to a highly conductive polymer.[27]
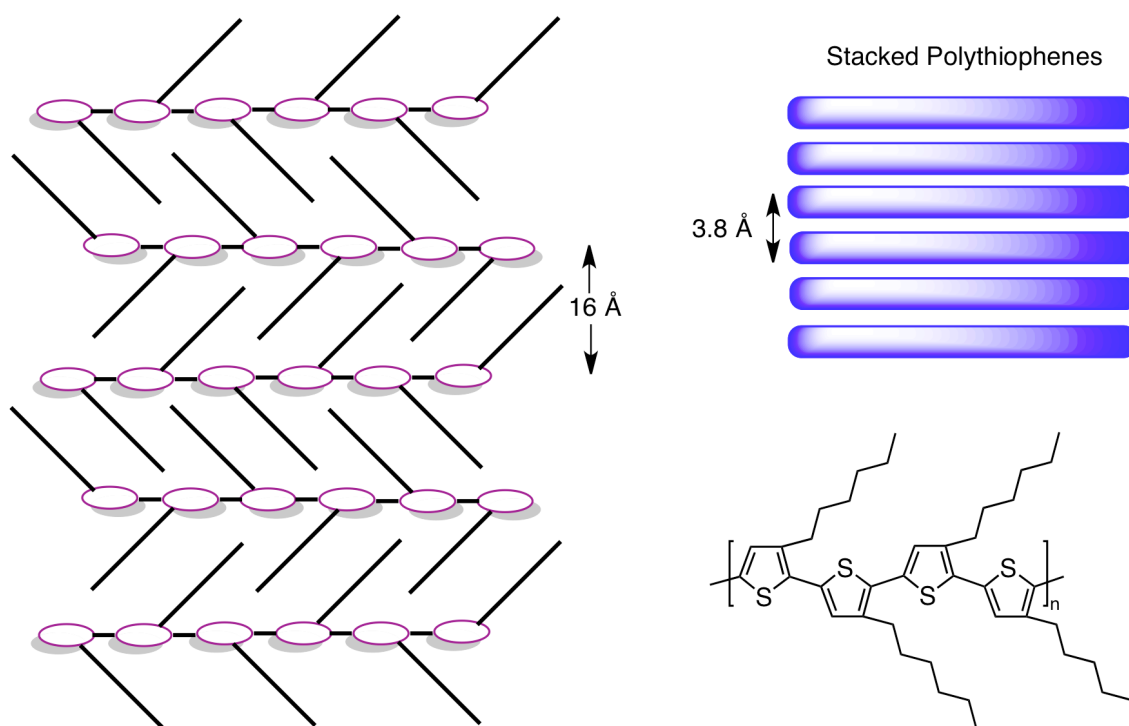
Figure 4: Self-assembly of regioregular P3ATs[17]

1.4.2 Synthesis of Regioregular Poly(3-alkylthiophenes)

Consequently, P3ATs polymerized via Kumada cross-couplings compared to those of previously reported PTs, were found to produce only 50-80% head-to-tail couplings. McCullough reported the first synthesis of regioregular head-to-tail coupled P3HT early in 1992.[34,35] This synthetic pathway regiospecifically generates a key intermediate, 2-bromo-5-(bromomagnesio)-3-alkylthiophene, by selective metal halogen exchange of lithium with 2,5-dibromo-3-alkylthiophene. This intermediate is polymerized with catalytic amounts of Ni(dppp)Cl$_2$, using Kumada cross-coupling methods to give P3ATs with 98-100% HT-HT couplings (Scheme1).[17]

Method	X, Y	Step 1	M (ratio)	Step 2	HT Regioregularity
McCullough	H, Br	i) LDA/THF, -40°C, 40min ii) MgBr, -OEt₂ (ZnCl₂), -60 to -40°C, 40min	MgBr(ZnCl) (~98:~2)ᵃ	Ni(dppp)Cl₂ "-5 to 25°C, 18h	98-100%
Rieke	Br, Br	Zn*/THF, -78°C to rt, 4h	ZnBr (90:10)	Ni(dppe)Cl₂, 0°C to rt, 24h	97-100%
Stille	H, I	i)LDA/THF, -80 to-40°C, 1h ii)Bu₃SnCl, -80°C to rt	SnBu₃ (99:1)	Pd(PPh₃)₄	>96%
Suzuki	H, I	i) LDA/THF, -40°C, 40min ii) B(Ome)₃, -40°C to rt iii) 2,2-dimethyl-1,3-propanediol, rt, 30mins	(99:1)	Pd(OAc)₂, K₂CO₃ THF, EtOH, H₂O refulx 16h	>96%
GRIM	Br, Br	R'MgXᵇ/THF, rt or reflux, 1h	MgX' (~85:~15)	Ni(dppp)Cl₂, rt or reflux, <1h	>99%

Scheme 1: Typical methods for the synthesis of regioregular P3ATs[33]

Shortly thereafter, Rieke also proposed a synthesis of HT-P3AT using a similar coupling approach that differs primarily in the organometallic intermediate formed.[36,37] 2,5-Dibromo-3-alkylthiophenes are treated with Rieke Zinc[38], Zn*, a highly reactive metal. This reaction produces a mixture of isomers—2-bromo-3-alkyl-5-(bromozincio)thiophene and 2-(bromozincio)-3-alkyl-5-bromothiophene. Cryogenic temperatures are a necessity, however, as the ratio of isomers varies with specific reaction temperatures. The use of Ni(dppp)Cl₂ yields regioregular HT-P3AT, whereas palladium cross-coupling using Pd(PPh₃)₄ yields a regiorandom polymer (Scheme 1).

In 1999, the Grignard metathesis, or GRIM, method was first reported.[40,43,44] This method eliminated the need to use cryogenic temperatures and reactive metals. 2,5-dibromo-3-alkylthiopene was treated with one equivalent of a Grignard reagent to yield

both 2-bromo-5-(bromomagnesio)-3-alkylthiophene and 2-(bromomagnesio)-5-bromo-2-alkylthiophene in an 85:15 ratio, regardless of reaction time, temperature, and Grignard reagent used. Ni(dppp)Cl$_2$ was once again used as the catalyst to yield regioregular P3ATs (Scheme 1).

Additionally, work was also done by using palladium-catalyzed approaches to synthesizing P3ATs. Iraqi et. al. used Stille[39] type palladium-catalyzed cross-couplings to synthesize P3ATs with 3-hexyl-2-iodo-5-(tri-*n*-butylstannyl)thiophene as a stable, isolatable intermediate.[40] This monomer is then purified prior to polymerization. However, some of the tri-butyl tin groups can potentially be cleaved. Separation of the tin and iodo end functionalized polymers is possible, allowing for additional reactions to be available (Scheme 1). In another example, Guillerez[41] used palladium-catalyzed Suzuki[42] type cross-couplings to synthesize P3ATs. 2-iodo-3-octylthiophene was treated with trimethylborate to generate the boronic acid, and then converted to the boronic ester. Polymerization was achieved by coupling the ester on itself. Its compatibility with a larger array of functional groups provided an alternative to the Rieke and McCullough methods (Scheme 1).

There are advantages and disadvantages to the methods discussed above. The Rieke method is capable of tolerating a wide array of different functional groups because it utilizes organozinc reagents, unlike the McCullough and GRIM methods that limit the functionality because the groups must be stable to organolithium and organmagnesium. The GRIM method allows for polymerization to be completed at room temperature or at reflux. Given the ease of polymerization, the GRIM method is widely utilized.
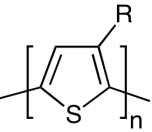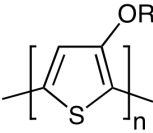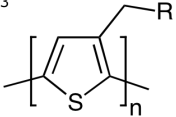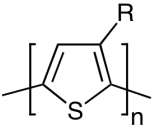
1.4.3 Side-Chain Functionalized Polythiophenes

The original purpose for the introduction of various side chains on PT was to improve solubility and processability. Through this process, numerous other functionalized side chains were then studied to fine-tune the properties of the polymer or potentially manipulate the polymer for use in a sensor (Table 1).

Electron-donating groups that contain heteroatom such as alkoxy or alkyl thio groups, placed in the 3 position are shown to decrease the band gap by raising the level of the HOMO levels, leading to low oxidation potential and a stable conducting state. Poly(3,4-ethylenedioxythiophene), PEDOT, is arguably the most widely studied alkoxy substituted PT. P3ATs containing ester groups and other carbonyl containing electron-withdrawing groups were also synthesized, but were found to increase the band gap.[45]

Once polymerization is complete, functionalization at the gamma position can further tune the properties of the polymer to those desired. This has been predominantly achieved by using protecting groups at the end of the side chains, which allow utilization of functional groups that may not withstand polymerization conditions. Tetrahydropyranyl, trimethylsilyl, phosphonic esters, and bromohexyl side chains have all been employed in previous works.[45]

Table 1: Summary of Side-Chain Functionalized PATs[46]

Entry	R=	Polymer	Entry	R=	Polymer
1	C_4H_9 C_6H_{13} C_8H_{17} $C_{12}H_{25}$ $C_{14}H_{29}$ $C_{18}H_{37}$ $C_5H_{10}OCH_3$ $C_6H_{12}OCH_3$ $C_{10}H_{20}OCH_3$ $(C_6H_5)C_8H_{17}$		3	$(CH_2CH_2O)_3CH_2CH_3$ $CH_2O(CH_2CH_2O)_2CH_3$ $(CH_2CH_2O)_2CH_3$ OC_6H_{13}	
			4	$(CH_2CH_2O)_mCH_3$ $(CH_2CH_2O)_7CH_3$ $CH_2CH(CH_3)(OC_2H_5)_4OCH_3$	
2	$O(CH_2CH_2O)_2CH_3$ $OCH_2CH_2OCH_3$ OCH_3 SCH_3		5	$(CH_2)_5(CF_2)_4F$ $(CH_2)_{11}(CF_2)_4F$ C_8F_{17}	
			6	C_4H_9 C_6H_{13} C_8H_{17} $C_{12}H_{25}$	

1.5 Block Copolymers

Polymers are large macromolecules consisting of many monomers that are covalently linked together to form long, linear chains. In the simplest case, all the monomers are the same resulting a homopolymer.[45] At the next level of complexity, a polymer can be comprised of two (or more) different monomers, designated as "A" and "B" in Figure 1. The monomers can be linked together in a random sequence, resulting in a random copolymer. Alternatively, the monomers can be arranged in blocks, resulting in a block copolymer. Block copolymers may have two, three, or more blocks. Such polymers are known as diblock copolymers, triblock copolymers, etc. (Figure 5).
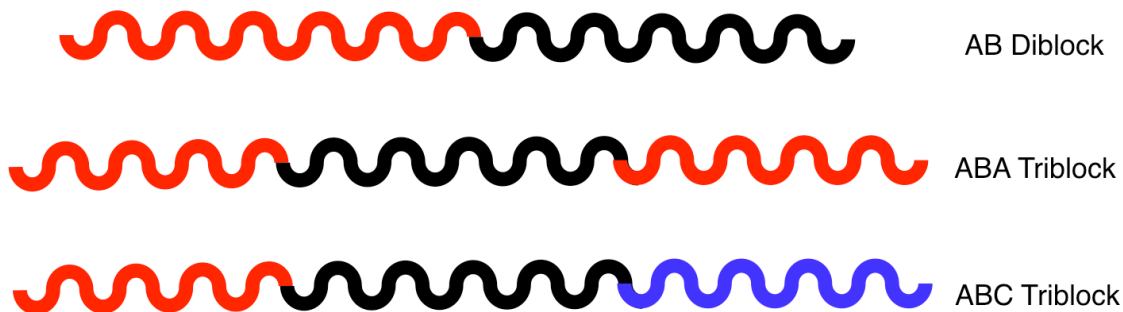
Figure 5: Variations of Different Block Copolymers

Block copolymers have four factors that determine the phase behavior: the molecular architecture (linear vs. branched vs. star), choice of monomer, composition, and the degree of polymerization.[47,48] The molecular architecture directly correlates to the morphology of the polymer and can also affect other physical properties. The monomers are selected when looking at the interactions between both the A blocks and the B blocks. Interactions between the different blocks tend to favor structures where similar blocks of the block copolymers cluster near each other. Thus, a polymer melt consisting of AB block copolymers will tend to organize itself in a way so that the A-blocks from different copolymer chains are near each other, the B-blocks are near each other, and the A and B blocks are as far away from each other as possible, consistent with the constraint that the A and B blocks of each individual copolymer are covalently linked together. This organization of the A and B blocks into different domains is referred to as microphase separation. The chemical differences between the A and B blocks need not be large. Composition then refers to the volume fraction of each constituent (A and B) in the block

copolymer. The degree of polymerization relates to the number of monomer units in each of the individual blocks.

The three classes of block copolymers that were mentioned previously are the most commonly studied (Figure 6). Linear block copolymers (**A**) are composed of two or more different linear polymers. Branched block copolymers (**B**) have one or more branching points that lead to an irregular structure. Star block copolymers (**C**) have linear polymers attached to a central core. These polymers are the best defined of the three because preparation can be done with specific composition with low molecular weights.[47]
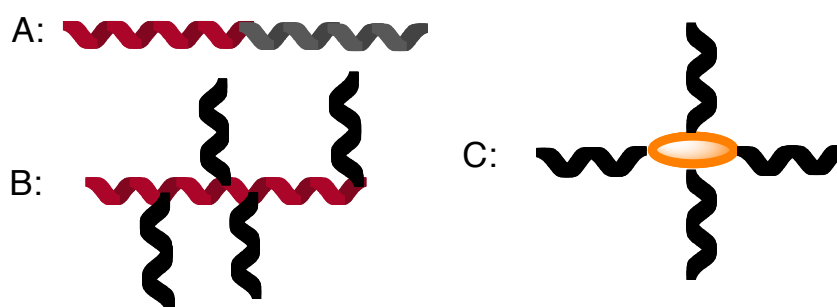
Figure 6: A) Linear B) Branched C) Star Block Copolymers

1.5.2 Rod-Coil Block Copolymers

Most polymers can adopt a coil conformation in solution that is very flexible, however, there is another subclass of polymers that are rigid and stiff due to their structure. Rod-coil block copolymers are a polymeric system wherein one of the polymer blocks is in a permanent rod conformation in solution that has significant stiffness compared to the flexible coil block.[49] The stiffness of the rod portion of the rod-coil block copolymer typically forces the polymer into an organized, stacked, macromolecular

assembly. As a result, rod-coil block copolymers form very ordered structures due to the flexibility differences between the blocks even at low molecular weights, which can form even on the scale of several nanometers.[50,51]

General Methods of Diblock Copolymer Synthesis
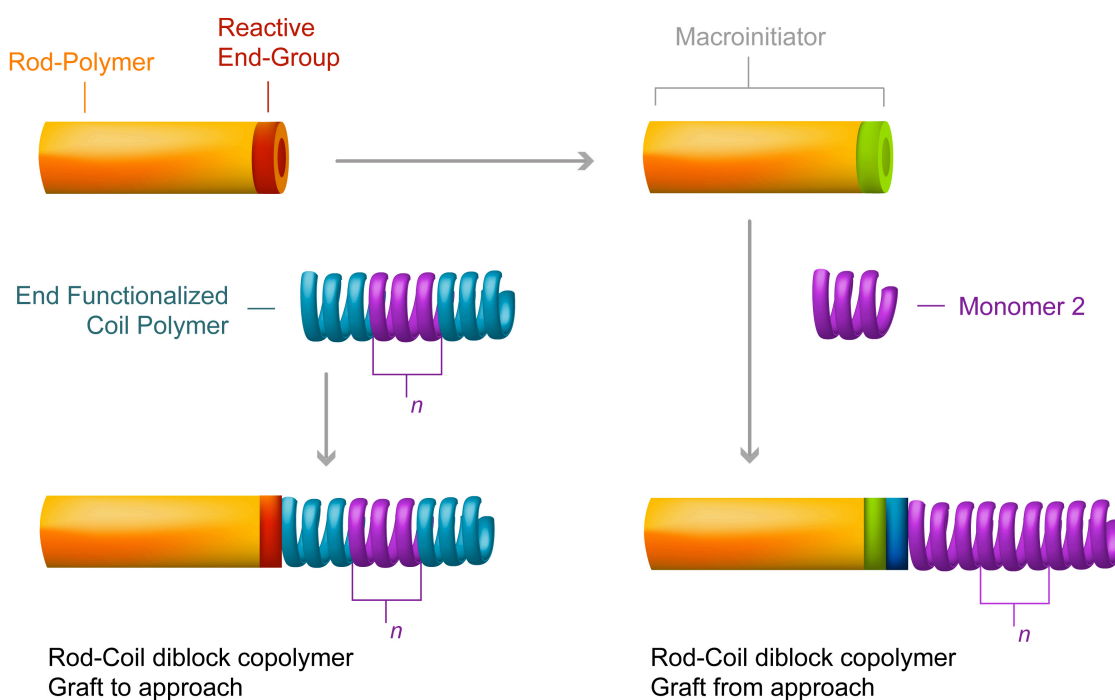
Figure 7: Synthetic Routes for Block Copolymers

Two approaches to synthesizing rod-coil block copolymers are commonly employed: the "graft from" and "graft to" methods, as seen above in Figure 7. The "graft from" approach utilizes an end-group functionalized homopolymer, commonly referred to as a macroinitiator. Polymerization of the second block is initiated from the macroinitiator. Addition of the second monomer unit followed by successive polymerization yields the resulting diblock copolymer. The "graft to" approach requires

the synthesis of two homopolymers that have functionalized end groups that can be coupled together. Both the "graft from" and "graft to" approaches has been used to create rod-coil block copolymers where one or both of the blocks is a conjugated polymer. This approach has been very successful in synthesis of polyphenylene-vinylene-*b*-polyisoprene[51] and polystyrene-*b*-polyphenylene vinylene[52] block copolymers, while the "graft from" approach has produced polyphenylene-vinylene-*b*-fullerene[52], polythiophene-*b*-perylene diimide[53], poly(3-hexylthiophene)-*b*-fullerene[54], and poly(3-hexylthiophene)-*b*-poly(perylene bisimide acrylate)[55], and poly(3-hexylthiophene)-*b*-poly(acrylate) block copolymers.[56]

The graft from approach has been quite limited by the ability to synthesize conjugated polymers with functionalized end groups. The "graft to" approach has an advantage of allowing for greater control of the PDI since each homopolymer's PDI is predetermined prior to coupling each of the blocks together. However this "graft from" approach offers the advantage of versatility and compatibility with a number of techniques such as ATRP, RAFT, and anionic polymerizations.

1.6 Conclusion

The "graft to" approach that was previously mentioned has also been successfully used to graft vinyl-terminated P3HT to quantum dot surfaces by work done in collaboration with our group. It was hypothesized that these conducting polymer-quantum dot nanocomposites would facilitate an electronic interaction that could be utilized for assembling one-layer solar cells.[60] Therefore, the goal of this research was to synthesize various end-functionalized regioregular polythiophenes to utilize the "graft to" and "graft

from" methods to synthesize diblock copolymers that could be used make other nanocomposite materials.

1.7 References

(1)   Chaing, C. K., Fincher, C.R. Jr., Park, Y.W., Heeger, A.J., Shirakawa, H., Louis, E.J., Gau, S.C., MacDiarmid, A.G. *Physical Review Letters* **1977**, *39*, 1098-1101.

(2)   Roncali, J. *Chemical Reviews* **1992**, *92*, 711.

(3)   Schluter, A. D. In *Handbook of Conducting Polymers*; 2 ed.; Skotheim, T. A. E., R.L.; Reynolds, J. R., Ed.; Marcel Dekker, INC. : New York, 1998, p 209-224.

(4)   Curran, D., Grimshaw, J., Perera, S. *Chemical Society Reviews* **1991**, *20*, 391-404.

(5)   Moratti, S. C. In *Handbook of Conducting Polymers*; 2 ed.; Skotheim, T. A. E., R.L.; Reynolds, J. R., Ed.; Marcel, Dekker, INC. : New York, 1998, p 343-362.

(6)   Bunz, U. W. F. In *Handbook of Conducting Polymers*; 3 ed.; Skotheim, T. A., Reynolds, J. R., Ed.; CRC Press: Boca Raton, FL, 2007.

(7)   Genies, E. M., Boyle, A., Lapkowski, M., Tsintavis, C. *Synthetic Metals* **1990**, *36*, 139-82.

(8)   *Conjugated Polymers: Theroy, Synthesis, Properties, and Characteristics*; 3 ed.; Skotheim, T. A., Reynolds, J. R., Ed.; CRC Press: Boca Raton, FL, 2007.

(9)   Osaka, I.; SauvÈ, G.; Zhang, R.; Kowalewski, T.; McCullough, R. D. *Advanced Materials* **2007**, *19*, 4160-4165.

(10)   Liu, J., Tanaka, T., Sivula, K., Alivisatos, A.P., Frechet, J.M.J. *Journal of the American Chemical Society* **2004**, *126*, 6550-6551.

(11)   Cheng, Y. J., Yang, S.H, Hsu, C.S. *Chemical Reviews* **2009**, *ASAP*.

(12)   Andersson, M. R., Thomas, O., Mammo, W., Svensson, M., Theander, M., Inganas, O. *Journal of Materials Chemistry* **1999**, *9*, 19933-1940.

(13)   Torsi, L., Tafuri, A., Cioffi, N., Gallazzi, M.C., Sassella, A., Sabbatini, I., Zambonin, P.G. *Sensors and Actuators B: Chemical* **2003**, *93*, 257-262.

(14) McCullough, R. D., Jeffries-EL, M.J. In *Handbook of Conducting Polymers*; 3 ed.; Skotheim, T. A. R., J. R., Ed.; CRC Press: Boca Raton, FL, 2007.

(15) Yamamoto, T., Sanechika, K., Yamamoto, J. *Journal of Polymer Science, Polymer Letters Edition* **1980**, *18*, 9.

(16) Lin, J. W. P., Dudek, L.P., *Journal of Polymer Science, Polymer Chemical Edition* **1980**, *18*, 2869.

(17) McCullough, R. D. In *Handbook of Oligo- and Polythiophenes*; Fichou, D., Ed.; Wiley-VCH: Weinheim, 1999, p 1-44.

(18) Yamamoto, T., Morita, A., Miyazaki, Y., Maruyama, T., Wakayama, H., Zhou, Z.H, Nakamura, Y., Nanbara, T., Sasaki, S., Kubota, K. *Macromolecules* **1992**, *25*, 1214.

(19) Yamamoto, T., Osakada, T., Wakabayashi, T., Yamamoto, A. *Makromolekulare Chemie Rapid Communications* **1985**, *6*, 671.

(20) Hotz, C. Z., Kovacic, P., Khoury, A. *Journal of Polymer Science - Polymer Chemistry Edition* **1983**, *21*, 2617.

(21) Colon, I., Kwiatkowski, G.T. *Journal of Polymer Science - Polymer Chemistry Edition* **1990**, *28*, 367.

(22) Yamamoto, T., Maruyama, T., Zhou, Z.H., Miyazaki, Y., Kanbara, T., Saneckika, K. *Synthetic Metals* **1991**, *41*, 345.

(23) Kobayashi, M., Chen. J., Chung, T.C., Moraes, F., Heeger, A.J., Wudl, F. *Synthetic Metals* **1984**.

(24) Souto Maior, R. M., Hinkelmann, K., Eckert, H., Wudl, F. *Macromolecules* **1990**, *23*, 1268.

(25) Elsenbaumer, R. L. J., K.-Y.; Miller, G. G.; Eckhardt, H.; Shacklette, L. W.; Jow, R. In *Electronic Properties of Conjugated Polymers*; Kuzmany, H. M., M.; Roth, S., Ed.; Springer: Berlin, 1987.

(26) Jen, K. Y., Miller, G.G., Elsenbaumer, R.L. *Journal of the Chemical Society Chemcial Communication* **1985**, *17*, 1346-1347.

(27) McCullough, R. D. *Advanced Materials* **1998**, *10*, 93-116.

(28)   Ballauff, M. *Angewandte Chemie, International Edition English* **1989**, *28*, 253-367.

(29)   Miller, G. G., Elsenbaumer, R.L. *Journal of the Chemical Society Chemcial Communication* **1986**, *17*, 1346-1347.

(30)   Elsenbaumer, R. L. J., K.-Y.; Oboodi, R. *Synthetic Metals* **1986**, *15*, 169.

(31)   Tamoa, K., Sumitani, K., Kumada, M. *Journal of the American Chemical Society* **1972**, *94*, 4376.

(32)   Kodama, S., Naajima, I., Kumada, M. *Tetrahedron* **1982**, *38*, 3347.

(33)   Osaka, I., McCullough, R.D. *Accounts of Chemical Research* **2008**, *41*, 1202-1214.

(34)   McCullough, R. D., Lowe, R.D.; *Journal of the Chemical Society, Chemcial Communication* **1992**, *1*, 70-72.

(35)   McCullough, R. D., Lowe, R.D., Jayaraman, M., Anderson, D.L. *Journal of Organic Chemistry* **1993**, *58*, 904-912.

(36)   Chen, T. A., Rieke, R.D. *Journal of the American Chemical Society* **1992**, *114*, 10087-10088.

(37)   Chen, T. A., Wu, X., Rieke, R.D. *Journal of the American Chemical Society* **1995**, *117*, 223.

(38)   Rieke, R. D. *Accounts of Chemical Research* **1977**, *10*, 301-306.

(39)   Stille, J. *Angewandte Chemie, International Edition English* **1986**, *25*, 508-524.

(40)   Iraqi, A., Barker, G. *Journal of Materials Chemistry* **1998**, *8*, 25-29.

(41)   Guillerez, S., Bidan, G. *Synthetic Metals* **1998**, *93*, 123-126.

(42)   Suzuki, A. *Journal of Organometallic Chemistry* **1999**, *576*, 147-168.

(43)   Loewe, R. S., Khersonsky, S.M., McCullough, R.D. *Advanced Materials* **1999**, *11*, 250-253.

(44)   Loewe, R. S., Ewbank, P.C., Liu, J., Zhai, L., McCullough, R.D. *Macromolecules* **2001**, *34*, 4324.

(45)   Osaka, I., McCullough, R.D. *Accounts of Chemical Research* **2008**, *41*, 1202-1214.

(46)   McCullough, R. D., Jeffries-EL, M.J. In *Handbook of Conducting Polymers*; 3 ed.; Skotheim, T. A. R., J. R., Ed.; CRC Press: Boca Raton, FL, 2007.

(47)   Odian, G. *Principles of Polymerization*; 3 ed.; John Wiley: New York, 1991.

(48)   Bates, F. *Science* **1991**, *251*, 898.

(49)   Fournier, D., Hoogenboom, R., Schuber, U.S. *Chemical Society Reviews* **2007**, *36*, 1369-1380.

(50)   Lee, M., Cho, B., Zin, W. *Chemical Reviews* **2001**, *101*, 3869.

(51)   Olsen, B., Seglaman, R. *Materials Science Engineering R* **2008**, *62*, 37-66.

(52)   Olsen, B., Seglaman, R. *Macromolecules* **2005**, *38*, 10127.

(53)   van der Veen, M., de Boer, B. Stalmach, U., van de Wetering, K., Hadziioannou *Macromolecules* **2004**, *37*, 3673-3684.

(54)   Zhang, Q., Cirpan, A., Russell, T., Emerick, T. *Macromolecules* **2009**, *42*, 1079-1082.

(55)   Yang, C., Lee, J., Heeger, A., Wudl, F. *Journal of Materials Chemistry* **2009**, *19*, 5416-5423.

(56)   Sommer, M., Lang, A., Thelakkat, M. *Angewandte Chemie International Edition* **2008**, *47*, 7901-7904.

(57)   Iovu, M., Jeffries-EL, M., Sheina, E., Cooper, J., McCullough, R. *Polymer* **2005**, *46*, 8582-8586.

(58)   Jeffries-EL, M., Sauve, G., McCullough, R. *Macromolecules* **2005**, *38*, 10346-10352.

(59)   Craley, C. R., Zhang, R., Kowalewski, T., McCullough, R., Stefan, M. *Macromolecular Rapid Communication* **2009**, 11-16.

(60)   Iovu, M., Craley, R., Jeffries-EL, M., Krankowski, A., Zhang, R., Kowalewski, T., McCullough, R. *Macromolecules* **2007**, *40*, 4733-4735.

CHAPTER 2:

Living Synthesis of Polythiophenes

## 2.1 Introduction: Mechanism of the Nickel-Catalyzed Cross-Coupling Reaction

As mentioned in the previous chapter, regioregular P3ATs can be functionalized in a variety of ways. End-functionalized P3ATs have been easily synthesized using the GRIM method, as first mentioned in 2004.[1] This chapter will detail a variety of syntheses of alkene end-functionalized P3ATs.

The exact mechanism for metal-catalyzed cross-coupling polymerizations was not completely understood until recently.[2] Originally, it was believed polymerization occurred via a step-growth mechanism because nickel-catalyzed dehalogenative polymerizations are technically viewed as a polycondensation reaction. Within the past few years, it has been proposed that the mechanism actually proceeds via a chain-growth mechanism, instead of the accepted step-growth mechanism. The chain-growth mechanism is considered to be a quasi-living system and allows for narrower molecular weight distributions.

Yokozawa[3] presented studies that provided evidence that the chain-growth mechanism was probable by showing the molecular weight, M_n, values increased proportionately to the conversion of the monomer. This suggested an initiator species propagates the polymerization.[3,4] Yokozawa explained that the oxidative addition of the polymer could occur selectively because it is kinetically faster or thermodynamically more

stable than the oxidative addition to the monomer, given the decrease in electron density on the thiophene ring in a polymer chain.[5]

Independently, McCullough also showed that the mechanism is chain growth and the degree of polymerization of P3AT increases with monomer conversion. This can be predicted by the molar ratio of nickel catalyst to the monomer.[6,7] The proposed mechanism was verified using the two different monomers found in both the McCullough and GRIM methods. It was proposed that the polymer chain and the metal catalyst exist as an associative pair via formation of a π-complex, restricting polymerization to one end of the polymer chain.[8,9] The proposed mechanism is shown below in Scheme 1.
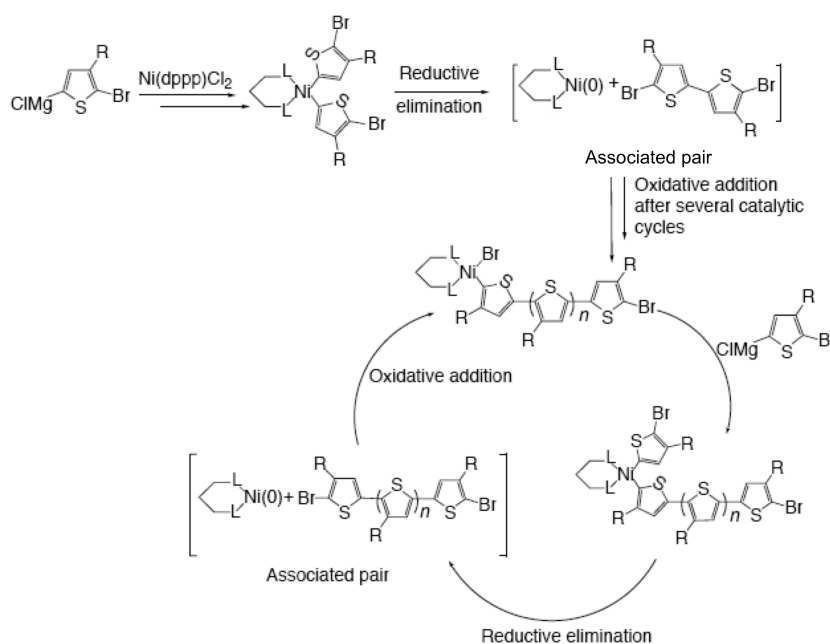

Scheme 1: Proposed mechanism for the nickel initiated cross-coupling polymerization[8,10]

Understanding the mechanism of these living polymerizations is critical to understand and facilitate in the control of not only the molecular weights of the system, but also in control of the possible end-group modifications.

2.2 End Functionalized Polythiophenes

Side chain functionalization[11] of PTs has been the major focus of studies, since the late 1980s, while end group functionalization is a somewhat more recent development field within the realm of PTs that constitutes approximately only 10% of the research completed. Two approaches of modification have been used routinely—*in situ* method and postpolymerization method. Janssen first utilized the *in situ* method combining it with the McCullough method of polymerization, but it gave a mixture of HH terminated PT and mono- and dicapped polymers.[12]

McCullough also reported an alternative pathway using the GRIM method.[10,13] As mentioned previously, the GRIM method of polymerization follows a living mechanism. In this pathway, the nickel catalyst is still affixed to the P3AT. Therefore, addition of another Grignard reagent will terminate the polymerization reaction and end cap the polymer. Addition of allyl, vinyl, or ethynyl Grignards will result in a mono-capped polymer, while alkyl or aryl Grignards will result in a dicapped polymer (Scheme 2). A major advantage of the *in-situ* method is that P3ATs can obtain a higher degree of functionality in one step that is highly versatile and efficient.
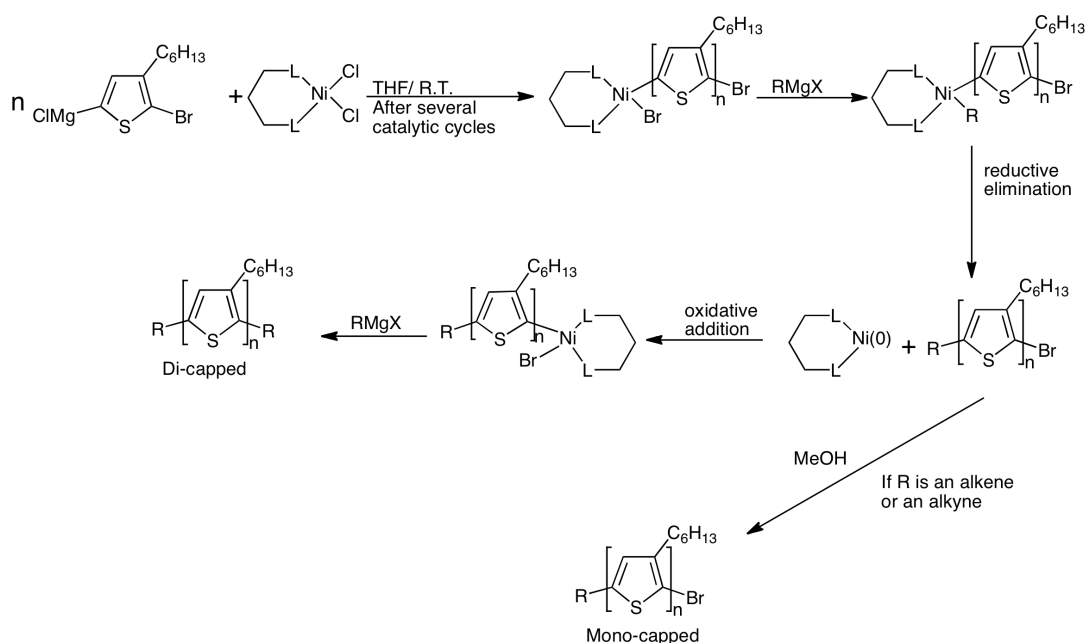
Scheme 2: End-Functionalization of P3ATs[8,10,14]

The postpolymerization method uses the H and Br terminal groups of P3ATs as a branch to further extend the synthesis and bring forth new functionality. Additional thiophene-based end groups can be added to the bromine end P3ATs[15], while conversion to a H/H terminated polymer has allowed for subsequent transformation to aldehydes.[2]

2.3 Results and Discussion

2.3.2 Synthesis Alkene End-Functionalized P3HTs

Both the vinyl (**1**) and allyl (**2**) terminated poly(3-hexylthiophene)s were synthesized using known literature procedures (Scheme 3)[16]. This was done not only to become familiar with GRIM polymerization techniques, but also to synthesize end-functionalized polymers that could also be modified post-polymerization to expand their uses. Each of the polymers were analyzed via gel permeation chromatography (GPC) and

matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS). GPC uses size-exclusion chromatography to determine the molecular weight (M_n) and PDI. MALDI-TOF is utilized to determine the end-group functionalization of P3ATs and M_n. This method is used because of its ability to ionize and analyze macromolecules with limited fragmentation within the mass spectrometer. Terthiophene has been recognized previously to be the best matrix to use with P3ATs[15]. Generally, the end-group constitution of the polythiophene can be determined using the following equation:

$$166.2n + EG1 + EG2 \qquad\qquad (1)$$

where 166.2 is the molecular weight of 3-hexylthiophene, n is the number of repeat units in the polymer, EG1 and EG2 are the molecular weights of the corresponding end groups. This calculates the projected molecular weights of the polymer within ±5 Da, which is due in part to isotope effects.[17]
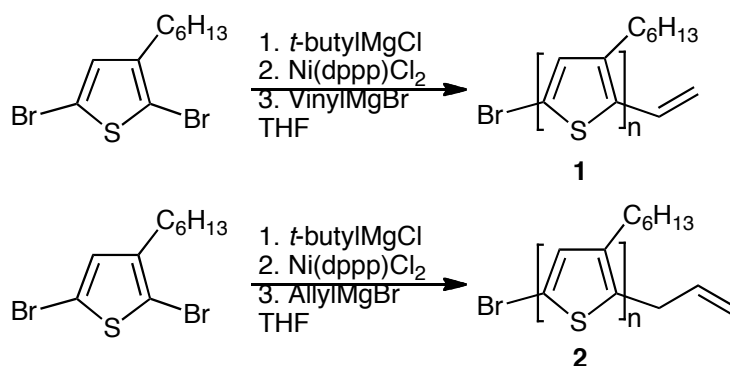
Scheme 3: Synthesis of vinyl and allyl-terminated P3HTs

Through analysis of both the vinyl and the allyl-terminated P3HTs, it was determined that the vinyl-terminated P3HT had a higher percentage of H/vinyl terminated

and H/H terminated P3HT, resulting in higher PDIs than the allyl-terminated (Figures 1 and 2). Only the allyl-terminated P3HT was used in the following efforts to try and minimize the number of possible defects that could possibly form.
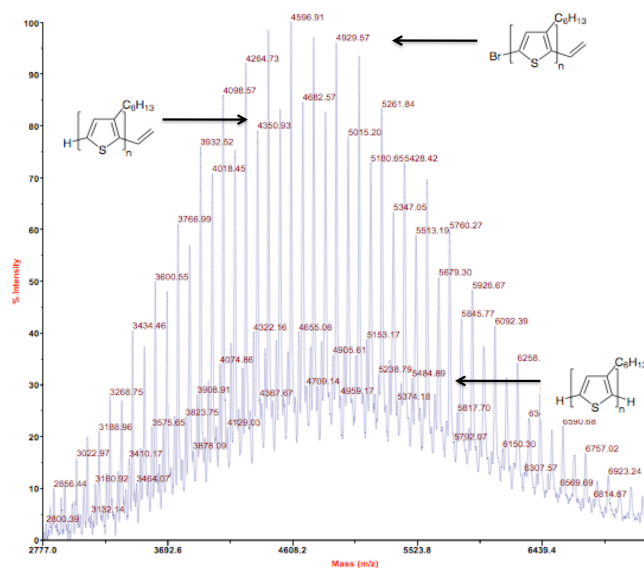

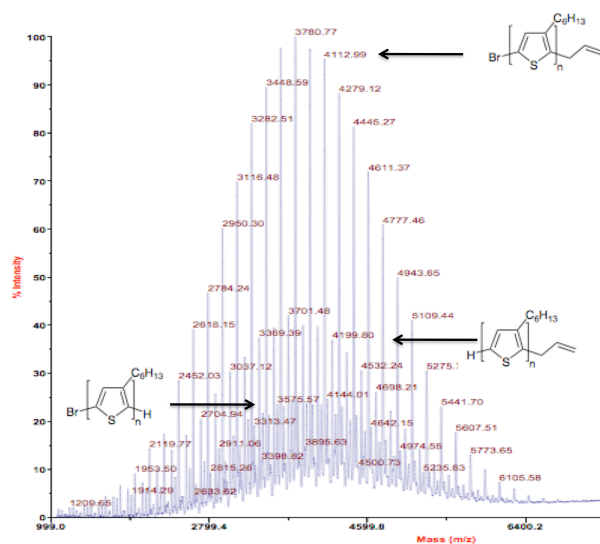**Figure 1:** MALDI-TOF of Vinyl-Terminated P3HT

Figure 2: MALDI-TOF of Allyl-Terminated P3HT

While becoming accustomed to polymerization syntheses, it was found that using the GRIM method one could control the molecular weights of the desired P3HT by varying the amount of Ni(dppp)Cl$_2$ used in the polymerization (Figure 3**).** Using this process, varying molecular weights of allyl-terminated P3HT.
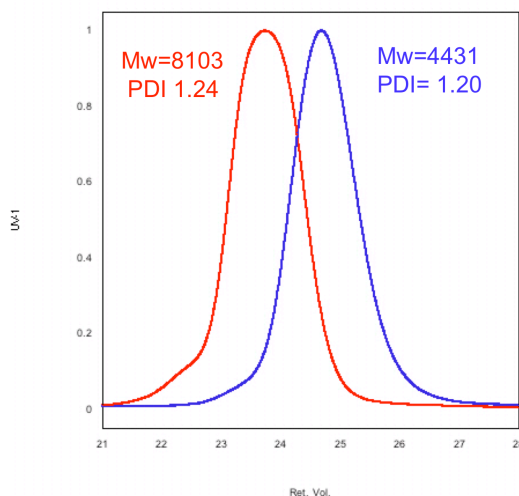
Figure 3: Varying Weights of Allyl-terminated P3HT

A further example of how the molecular weight of a polymer can be controlled using this process is given. A targeted, low molecular weight sample of *rr*-P3HT (13.5K) was given to the Lin group to study the self-assembly of regioregular conjugated polymers. *rr*-P3HT was a desirable material for this because it is soluble in many organic solvents and has excellent film-forming properties that have made it a good material for use as a printable conjugated polymer.[18] Also, the interchain π-π stacking of P3HTs would facilitate the formation of regular, controllable spacing that has been lacking in previous attempts at using evaporative self-assembly. It was found that when a doing controlled evaporation on an axially symmetric sphere, microscopic "snake-skin" like patterns

formed ellipsoids that contained bundles of P3HT nanofibers that formed from the strong intermolecular interactions of the P3HT polymer chains. This could have potential for creating highly useful materials and devices for applications in biosensors, photonics, and optoelectonics.[19] Further collaborations with the Lin group are currently being explored.

2.2.3 Thiol-Ene Coupling

As previously stated, allyl-terminated P3HTs are easily synthesized with little degradation and side products (H vs. Br/allyl terminated, H/Br terminated, etc.) (Figure 2 and 4).
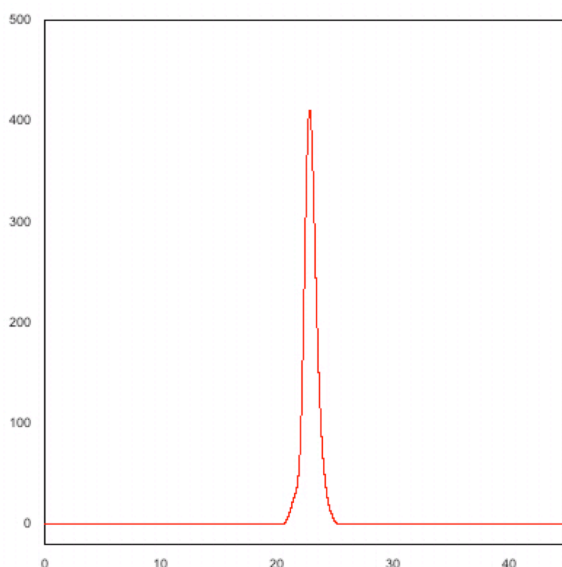

Figure 4: GPC of Allyl-Terminated P3HT

Given that the allyl-terminated polymer can be synthesized cleanly, it was believed that thiol-ene couplings could provide an easily accessible route to producing thiol containing end-functionalized polymers. These thiol containing end-functionalized P3ATs

could be utilized to produce "graft from" diblock copolymers by initalizing RAFT polymerizations from the end group. Thiol-ene coupling is a radical-based reaction between an alkene and a thiol that offers versatility through the incorporation of cross-linkers that also eases the photocurring in the presence of oxygen.[20,21] The cross-linking can be initiated either thermally or photochemically.[22,23] Inhibition by oxygen is not seen within the thiol-ene systems that are typically associated with other radical-based systems. It was proposed that developing thiol-end-functionalized P3HTs would open the possibility then using RAFT polymerization to synthesize a diblock copolymer.

Using the easily synthesized allyl-terminated P3HTs, several thiol-ene coupling reactions were attempted using a few different initiators at different wavelengths (Table 2 and Scheme 4).

Table 2: Attempts at Thiol-Ene Coupling Reactions

| P3HT	Thiol	Initiator	Temp.	Wavelength	Time
allyl	pentane-2-thiol	AIBN	55		4
allyl	pentane-2-thiol	TEMPO	55		4
allyl	pentane-2-thiol	AIBN	r.t.	254	2
allyl	pentane-2-thiol	TEMPO	r.t.	254	2
allyl	pentane-2-thiol	AIBN	r.t.	360	2
allyl	pentane-2-thiol	TEMPO	r.t.	360	2
allyl	pentane-2-thiol	DMPA	r.t	360	8
allyl	pentane-2-thiol	DMPA	r.t	360	48
allyl	1-thiolglycerol	AIBN	r.t	254	8
allyl	1-thiolglycerol	AIBN	r.t	360	8
allyl	1-thiolglycerol	TEMPO	r.t	254	8
allyl	1-thiolglycerol	TEMPO	r.t	360	8
allyl	1-thiolglycerol	DMPA	r.t	254	8
allyl	1-thiolglycerol	DMPA	r.t	360	8
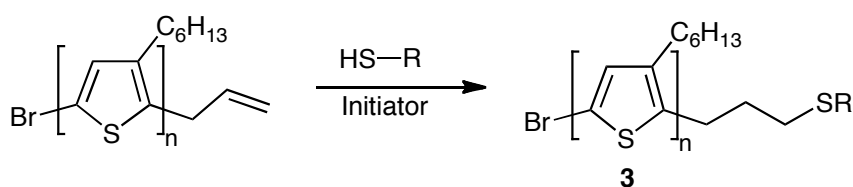
Scheme 4: Thiol-ene Reactions

Allyl-terminated P3HTs were initially reacted with pentane-2-thiol thermally and photochemically using azobis(isobutylnitroxide)(AIBN) and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) as the initiators at the stated wavelengths. However, analysis by MALDI-TOF proved that at best there was possibly only 10% conversion to the thiol end-fucntionalized P3HT. The thiol was then changed to 1-thiolglycerol because it would allow for further functionalization of the hydroxy groups if the thiol-ene reactions were completed. The reactions were then attempted with AIBN, TEMPO, and 2,2-dimethoxy-2-phenylacetophenone (DMPA), as the latter initiator was successful in the synthesis of fourth-generation dendrimers.[24] Nonetheless, once again these reactions did not produce any thiol containing end-functionalized P3HTs. It is hypothesized that changing the thiol once again to one that contains a carbonyl group alpha to the thiol would make the reaction more electronically favorable.

2.2.4 Synthesis of Other End-Functionalized P3ATs

Allyl-terminated poly(3-decylthiophene) (P3DT) was desired to study the effects of different alkyl chains on the glass transition temperature (T_g). The decyl Grignard reagent was made using commercially available magnesium turnings and 1-bromodecane (**4**) (Scheme 5). The monomer (**6**) was then made by dibromination of the thiophene ring,

and the standard GRIM method was used to result in the allyl end-functionalized P3DT. Upon examination of the MALDI-TOF spectrum, it was found several times that the major product synthesized was H/Br terminated P3DT rather than the expected allyl-terminated.
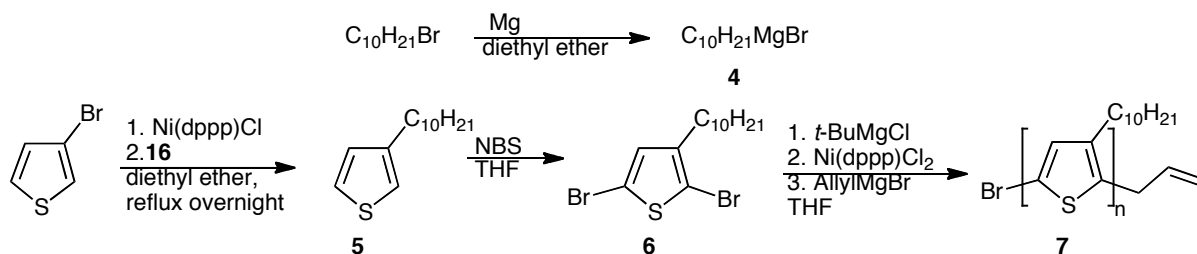
Scheme 5: Synthesis of P3DT

Numerous attempts were made at this synthesis with each one producing the same result. It was determined that it would be advisable to do a kinetic study of the polymerization and determine the effects of having a longer alkyl chain in the 3-position has. Several polymerizations were consequently attempted, with aliquots taken at specific time intervals to monitor the concentration of 2,5-dibromo-3-decylthiophene by gas chromatography-mass spectrometry (GC-MS). However, before complete analysis of the polymerization was completed, a kinetics study of this system was published.[25] A hypothesis was proposed that once the maximum conjugation was reached (which was stated as a repeat unit equally ten), electronic delocalization is favored, which would lead to decrease the reactivity of the intermediates formed during polymerization.[25]

A few other syntheses were attempted in an effort to increase the variance in the end-functionality of P3HTs. The hydroxypropyl-terminated P3HT (**8**) was toslyated using

*p*-toluenesulfonyl chloride to convert the hydroxyl group into a much better leaving group to proceed with an S_N2 reaction with sodium azide to produce an azidopropane-terminated P3HT (Scheme 6). Unlike other end-functionalized P3HT, using MALDI-TOF for analysis of an oxygen containing end-functionalization is difficult. A ^{1}H-NMR was obtained, however, there was no clear distinction that the azide was made, as the disappearance of the hydroxyl-proton was not clearly seen.
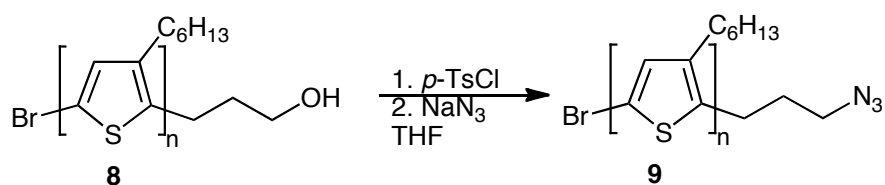
Scheme 6: Attempted Synthesis of an Azide-Terminated P3HT[26]

Lastly, the hydoxypropyl-terminated P3HT was also treated with sodium hydride to form the alkoxide anion. This was reacted further with propargyl bromide to construct a propargyl propyl ether (**10**, Scheme 7). Again, MALDI-TOF spectrum was difficult to obtain. A ^{1}H-NMR was also obtained, however, it would appear that the polymer had a large value of repeat units, so the peak correlated to the end-groups were very difficult to differentiate. Analysis using a 500 MHz ^{1}H-NMR is currently pending.
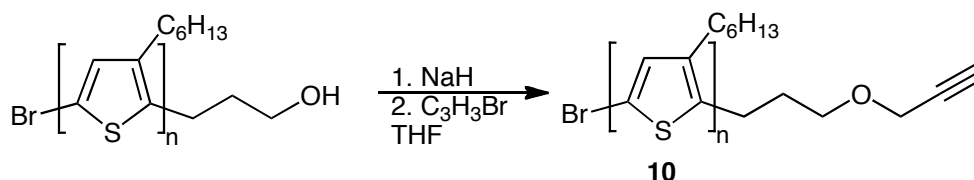
Scheme 7: Attempted Synthesis of Propargyl Propyl Ether End-Functionalized P3HT[27]

2.3 Conclusions

The ability to mono-cap P3ATs with various functional groups efficiently using Grignard reagents has opened the possibility of synthesizing an abundance of new materials given the ability of alkene and alkyne terminated polymers to be used as building blocks in the synthesis of diblock copolymers.[10] Alkene end-functionalized P3HTs, namely vinyl and allyl, were synthesized with success. Allyl-terminated P3HTs were utilized for further synthesis more often because if its ability to be synthesized cleanly. Thiol-ene coupling reactions were first attempted using a small variety of conditions and several thiols to determine if these systems would be useful to produce "graft from" diblock copolymers. However, there was no success using the aforementioned conditions and the allyl-terminated P3HT. Other synthetic modifications were also attempted, but the isolated polymer products were difficult to separate to confirm if the reactions were completed as hypothesized. Overall, while limited accomplishments were made, there are still vast possibilities for synthesis of novel diblock copolymers containing alkene end-functionalized P3HTs.

2.4 Experimental Methods

All reactions, when specified, were preformed under purified nitrogen or argon, using oven-dried glassware. Tetrahydrofuran (THF) was dried using an Innovative Technologies purification system. *tert*-Butylmagnesium cloride, vinylmagnesium bromide, allylmagnesium bromide, Ni(dppp)Cl$_2$, pentane-2-thiol, 1-thioglycerol, borane in THF complex, 30% hydrogen peroxide, AIBN, TEMPO, DMPA, 1-bromodecane, magnesium turnings, *para*-toluenesulfonyl chloride, sodium azide, sodium hydride,

propargyl bromide and diethyl ether were purchased from Aldrich Chemical Co. and used without further purification. *N*-Bromosuccinimide was purchased from Aldrich Chemical Co. and recrystalized prior to use. 2,5-dibromo-3-hexylthiophene was synthesized according to the literature procedures from 3-hexylthiophene.[28] *rr*-P3HT, allyl and vinyl-terminated poly(3-hexylthiophene) and allyl-terminated poly(3-decylthiophene) were prepared according to literature procedures.[1]

Instrumentation.

^{1}H NMR spectra were recorded using a Varian 400 MHz instrument. A MALDI-TOF MS (Voyager-DE STR BioSpectrometry) workstation by Biosystems was used to record spectra in the linear mode, where 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 30 °C using THF as the eluent and the flow rate was 1.0μL/min. Calibration was based on polystyrene standards obtained from Viscotek. A Rayonet mini-reactor was used containing 8 broadly emitting 4 Watt bulbs centered around 256 and 350 nm.

Attempted Thiol-Ene "Click" Reactions: To a 100 mL reaction vial, 0.15 mmol of allyl-terminated poly(3-hexylthiophene), 0.025mmol of initiator, 0.040mmol of thiol, 45mL of THF were added. The vial was capped and stirred at specified wavelengths and temperatures for the specified amount of time (**Table 2**). The reaction mixture was then

precipitated into methanol and filtered through a cellulose thimble. Soxhelt extraction was performed using hexanes and chloroform.

Hydroxypropyl-Terminated Poly(3-hexylthiophene)[29] The literature procedure was followed except a borane-tetrahydrofuran complex (BH$_3$ in THF) was used instead of 9-BBN.

Attempted Azide-End-Functionalized Poly(3-hexylthiophene)[26]: To a 100 mL round bottom flask, 0.15 mmol of hydroxypropyl-terminated poly(3-hexylthiophene), 0.050mmol of *para*-toluenesulfonyl chloride, and 70mL of THF were added. The round bottom was capped and stirred under argon at r.t. overnight. 0.080mmol of sodium azide was then added, the mixture was heated to 50 degrees and left to react overnight. The reaction mixture was then precipitated into methanol and filtered through a cellulose thimble. Soxhelt extraction was performed using hexanes and chloroform.

Attempted Propargyl Propyl Ether End-Functionalized Poly(3-hexylthiophene)[26]: To a 50 mL round bottom flask, 0.20 mmol of hydroxypropyl-terminated poly(3-hexylthiophene) in 30mL of THF was cooled to 0ºC for 20 minutes prior to the addition of 0.35mmol of sodium hydride. The mixture was stirred for 3 hours between 0-5ºC. 0.45mmol of propargyl bromide was then added slowly via syringe while assuring the temperature did rise above 5ºC for the next 30mins. The reaction was then warmed to r.t. and reacted for 6 hours. The reaction mixture was then precipitated into methanol and filtered through a cellulose thimble. Soxhelt extraction was performed using hexanes and chloroform.

2.9 References

(1)   Jeffries-EL, M., Sauve, G., McCullough, R. *Advanced Materials* **2004**, *16*, 1017-1019.

(2)   Osaka, I., McCullough, R.D. *Accounts of Chemical Research* **2008**, *41*, 1202-1214.

(3)   Yokoyama, A., Miyakoshi, R., Yokozawa, T. *Macromolecules* **2004**, *37*, 1169.

(4)   Miyakoshi, R., Yokoyama, A., Yokozawa, T. *Journal of the American Chemical Society* **2005**, *127*, 17542.

(5)   Yokozawa, T., Shimura, H. *Journal of Polymer Science, Part A.* **1999**, *37*, 2607-2618.

(6)   Sheina, E. E., Liu, J., Iovu, M.C., Laird, D.W., McCullough, R.D. *Macromolecules* **2004**, *37*, 3526.

(7)   Iova, M. C., Sheina, E., Gil, R.R., Laird, D., McCullough, R.D. *Macromolecules* **2005**, *38*, 8649.

(8)   McCullough, R. D., Jeffries-EL, M.J. In *Handbook of Conducting Polymers*; 3 ed.; Skotheim, T. A. R., J. R., Ed.; CRC Press: Boca Raton, FL, 2007.

(9)   Andersson, M. R., Selse, D., Berggren, M., Jaerinen, H., Hjertberg, T., Inganaes, O., Wennerstroem, O., Oesterholm, J.E. *Macromolecules* **1994**, *27*, 6503-6506.

(10)   Jeffries-EL, M., Suave, G., McCullouch, R.D. *Advanced Materials* **2004**, *16*, 1017-1019.

(11)   Zhai, L., Pilston, R., Zaiger, K., Stokes, K., McCullough, R.D. *Macromolecules* **2003**, *36*, 61-64.

(12)   Langeveld-Voss, B. M. W., Janssen, R.A.J., Spiering, A.J.H, van Dongen, J.L.J., Vonk, E.C., Claessens, H.A. *Chemical Communications* **2000**, *1*, 81-82.

(13)   Jeffries-EL, M., Suave, G., McCullouch, R.D. *Macromolecules* **2005**, *38*, 103469-10352.

(14)   Cheng, Y. J., Yang, S.H, Hsu, C.S. *Chemical Reviews* **2009**, *ASAP*.

(15)   Liu, J., McCullough, R.D. *Macromolecules* **2002**, *38*, 9882.

(16)   Jeffries-EL, M., Sauve, G., McCullough, R. *Macromolecules* **2005**, *38*, 10346-10352.

(17)   Hanton, S. D. *Chemical Reviews* **2001**, *101*, 527.

(18)   Li, B., Santhanam, S., Schultz, L., Jeffries-EL, M., Iovu, M.C., Sauve, G., Cooper, J, Zhange, R., Revelli, J.C., Kusne, A.G., Snyder, J.L, Kowalewsi, T., Weiss, L.E., McCullough, R.D., Fedder, G.K., Lambeth, D.N. *Sensors and Actuators B. Chemical* **2007**, *123*, 651-660.

(19)   Byun, M., Laskowski, R., He, M., Qui, F., Jeffries-EL, M., Lin, Z. *Soft Matter* **2009**, *5*, 1583-1586.

(20)   Campos, L., Killops, K., Sakai, R., Paulusse, J., Damiron, D., Drockenmuller, E., Messmore, B., Hawker, C. *Macromolecules* **2008**, *41*, 7063-7070.

(21)   Choi, K. M., Rogers, J. *Journal of the American Chemical Society* **2003**, *125*, 4060.

(22)   Campos, L., Meinel, I., Guino, R., Schierhor, M., Gupta, M., Gupta, N., Stucky, G., Hawker, C. *Advanced Materials* **2008**, *20*, 3728-3733.

(23)   Harrisson, S. *Macromolecules* **2009**, *42*.

(24)   Killops, K., Campos, L., Hawker, C. *Journal of the American Chemical Society* **2008**, *130*, 5062-5064.

(25)   Lamps, J.-P., Catala, J-M. *Macromolecules* **2009**, *42*, 7282-7284.

(26)   Pardin, C., Roy, I., Lubell, W., Keillor, J., *Chemical Biology & Drug Design* **2008**, *72*, 189-196.

(27)   Munteanu, M., Choi, S., Ritter, H. *Macromolecules* **2009**, *42*, 3887-3891.

(28)   Loewe, R. S., Khersonsky, S.M., McCullough, R.D. *Advanced Materials* **1999**, *11*, 250-253.

(29)   Iovu, M., Craley, R., Jeffries-EL, M., Krankowski, A., Zhang, R.,

Kowalewski, T., McCullough, R. *Macromolecules* **2007**, *40*, 4733-4735.

CHAPTER 3:

Alkyne End-Functionalized Polythiophenes and "Click" Chemistry

3.1 Introduction: Background of "Click" Chemistry

One problem associated with the synthesis of end-group functionalized regioregular poly(3-alkylthiophene)s (P3ATs) is the difficulties associated of separating the polymers with functionalized end-groups from the unfunctionalized polymers. This hinders its use to form block copolymers. The use of high yielding reactions with minimal side products is beneficial. Given these specifications, "click" chemistry is seen as an ideal approach. "Click" chemistry is a chemical philosophy first introduced by Sharpless in 2001.[1] It was founded by naturally occurring processes that produce substances quickly and unfailingly by combining smaller units together. These "click" chemistry reactions must meet the several criteria. The reactions must proceed in high yields, tolerate a wide array of functional groups, present inoffensive by-products, be purified by non-chromatographic techniques, have simple reaction conditions that are not affected by water or oxygen, and the solvent used in the reaction must be easily removed.[1]

One reaction that has seen major resurgence since the idea of "click" reactions was founded is the Huisgen 1,3-dipolar cycloaddition between an alkyne and an azide to form a triazole.[2] Organic azides are a very selective, but highly energetic, functional group that will react with alkynes and quickly rose to be one of the top reactions fulfilling the "click" criteria.[3] Two isomers are possible with this cycloaddition—the 1,4 (**1**) and 1,5-regioisomers (**2**) (Scheme 1). A mixture of these isomers will form when the reactions are

conducted thermally. However, if copper is used as the catalyst, the 1,4 isomer will predominate, where as the 1,5 isomer is the major product when ruthenium is the catalyst. The discovery of the copper-catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) was accomplished simultaneously by Meldal[4] and Sharpless[1] in 2002 It was found to be one of the most reliable "click" reactions to produce covalent building of complex structures.
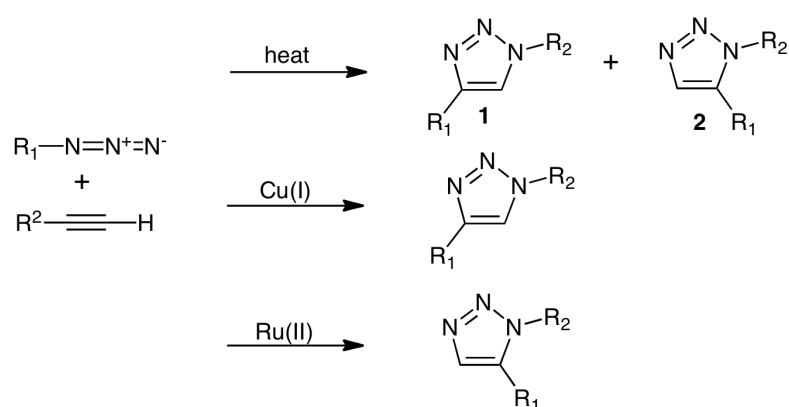
Scheme 1: 1,3-Dipolar cylcoadditions[5]

3.1.2 Copper-Catalyzed Azide-Alkyne Cycloaddition

The elementary thermal reaction involving either a terminal or an internal alkyne has been known since the end of the 19th century.[6] Huisgen and co-workers comprehensively studied these reactions during the 1950s through the 1970s.[2] It was found that this addition has a high kinetic-energy barrier, but is strongly thermodynamically favored. Copper(I) catalysis accelerates the reaction significantly (10^7 times faster than an uncatalyzed reaction) and is unaffected by the steric and electronic properties of the groups bonded to alkyne and azide, nor is it affected by water and most inorganic and organic functional groups.[6] The 1,2,3-triazole containing product is highly

stable, exhibits a strong dipole moment, has an aromatic character, and is a sufficient hydrogen-bond acceptor.[2]

A wide number of copper catalysts have been used in this reaction. Copper(I) salts such as CuI or CuBr have been used extensively, but their solubility is limited in organic solvents. Coordination complexes such as $[Cu(CH_3CN)_4]PF_6$ and $[Cu(PPh_3)_3Br)$ have become widely used to overcome this problem.[6] Conversely, Cu(II) is commonly made in situ from oxidation of the thermally unstable Cu(I). Cu(II) can promote oxidative alkyne coupling reactions, known as Glasier couplings[7], deteriorating the probability of cycloaddition occurring. Various measures have been implemented in an attempt to minimize the copper-catalyzed coupling between the alkynes, such as trying to limit the amount of oxygen present in the system or place a sacrificial reducing agent into solution (such as copper(II) sulfate pentahydrate). Most commonly, the reaction is carried out with CuI in tetrahydrofuran, acetonitrile, dimethyl sulfoxide, or with a $CuSO_4$/ascorbate alcohol/water mixuture.[8]

Ligands are not mandatory for the Cu(I) catalyzed triazole formation to occur. However, the rate of reaction increases and the copper catalyst is further protected from oxidation in the presence of oxygen. Extensive studies have been completed to determine what effect specific ligands have on the rate of reaction.[5,9,10]

3.1.3 CuAAC Mechanism

The role of copper in the formation of triazole has been disputed since its discovery in cycloadditions. Quantum mechanical studies of non-copper catalyzed reactions have been completed recently and it was determined that the transition state is

mainly nonpolarized, with the alkyne remaining as a poor electrophile.[11,12] Azides can coordinate with Cu(I) in two different ways. Most commonly found is end-on coordination with a bond angle of 180°, while the other way of coordination has the carbon bonded nitrogen and needs another intramolecular partner to form a 120° angle between the N-N-Cu bond.[8] Various mechanisms have been proposed, but the exact mechanism has yet to be determined.[6]

3.1.4 Ruthenium-Catalyzed Azide-Alkyne Cycloaddition

Folkin, Jia, and co-workers first demonstrated the use of ruthenium(II) catalysts to form predominately the 1,5-regioisomer of 1,2,3-triazole in 2005.[13] Unlike the CuAAC reaction, either the internal or terminal alkynes can participate in the cycloaddition. Initial studies found that ruthenium complexes containing Cp or Cp* gave the highest percentage of conversion. Additionally, no base is required throughout this system, unlike copper-catalyzed reactions. It is hypothesized that the mechanism of this cycloaddition involves a six-membered ruthenacycle intermediate, which can undergo reductive elimination to produce the 1,5-regioisomer.[14,15] The attention given to the ruthenium-catalyzed reaction in our study is significantly less than that of the copper-catalyzed because the copper catalysts are easily accessible and purified, and are more cost-efficient.

3.1.5 Summary

Since the discovery of the CuAAC process, hundreds of papers have been published on the subject with 400 published between 2002-2007 alone.[16] "Click" chemistry has made a substantial impact in all areas of chemistry by fulfilling the need of chemically reliable, covalent bond-forming building blocks. Its range of uses is incredibly

diverse—this method is used in various syntheses in biological areas to further functionalizations of peptides, natural products, pharmaceuticals, DNA, nucleotides, and carbohydrates.[6] It also has been introduced in dendrimer and polymer chemistry and has become an efficient way for material scientists to synthesize various block, linear, graft, comb, star-shaped, gradient, random, and alternating copolymers.[5] However, there has not been any significant progress utilizing "click" chemistry with end-functionalized PTs.

3.2 Results and Discussion

As mentioned in Chapter 2, the "graft to" approach for synthesizing block copolymers is preferred because its control of the polydispersity of the polymer. The goal of this research is to use "click" chemistry to synthesize polythiophene containing rod-coil block copolymers using the "graft to" method. A schematic representation of this is shown in Figure 1. Thus to accomplish this, we needed to synthisize an alkyne terminated regioregular P3HT and an azide terminated coil block.
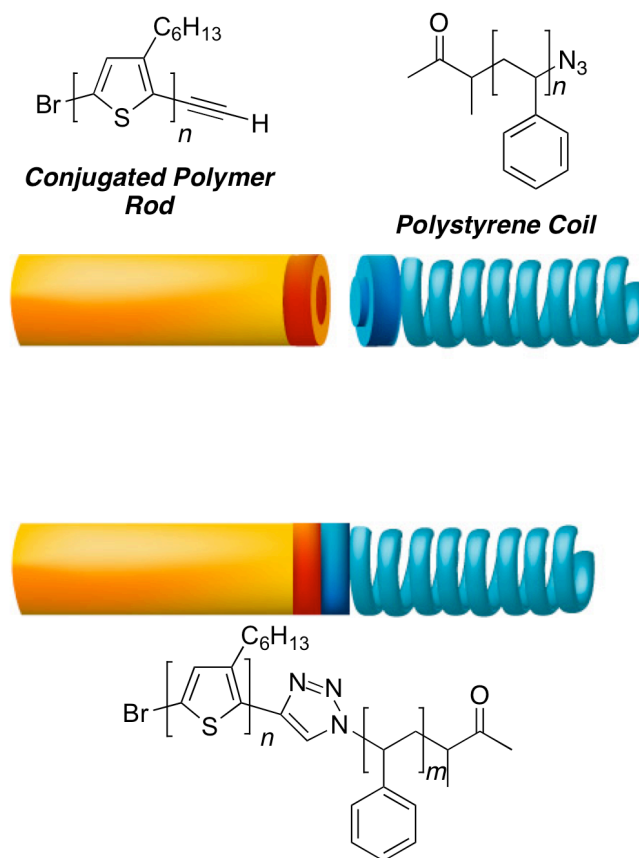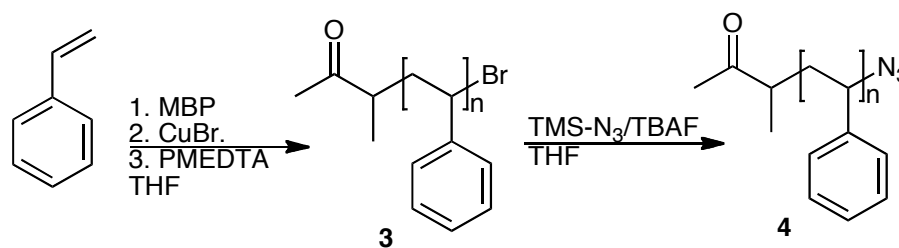
Figure 1: Rod-Coil Block Copolymer

Bulk synthesis of polystyrene via atom transfer radical polymerization (ATRP) was found

to work best (Scheme 2).

Scheme 2: Synthesis of Azide-Terminated Polystyrene[19]

The molecular weights could be targeted by using the following equation:

$$M_{nth} = M_{monomer} [M]_0 \text{ converstion} / [I]_0 \ , \qquad (1)$$

where $M_{monomer}$ is the molar mass of the monomer (molecular weight of styrene is 104.15 g/mol), $[M]_0$ is the initial monomer concentration, and $[I]_0$ is the initial initiator concentration.[18] Various molecular weight polystyrenes were synthesized, ranging from 3,000 to 10,000D with PDIs between 1.1-1.3 (**3**) Confirmation of the bromine terminal group via MALDI-TOF is difficult due to the lack of ionization. A sample was taken and reacted with tributyl phophine, to yield a tributyl phosphine terminated polystyrene, which is easily ionized via MALDI-TOF (Figure 2). The bromine-terminated polystyrene was then reacted with azido trimethylsilyl overnight to yield an azide-terminated polymer capable to be used in "click" reactions (Figure 3).[19]

Figure 2: MALDI-TOF spectrum of tributylphosphine-terminated polystyrene[20]
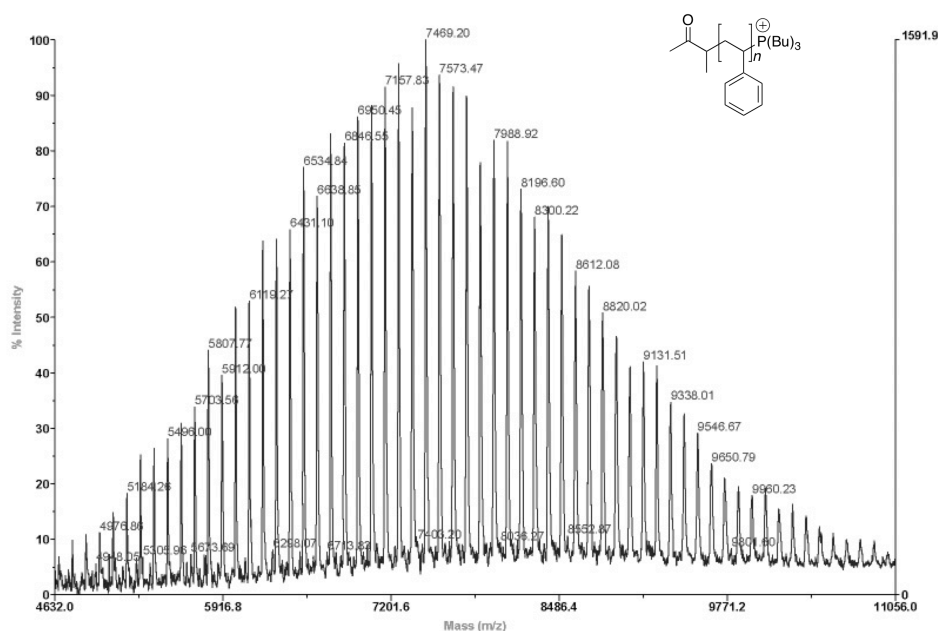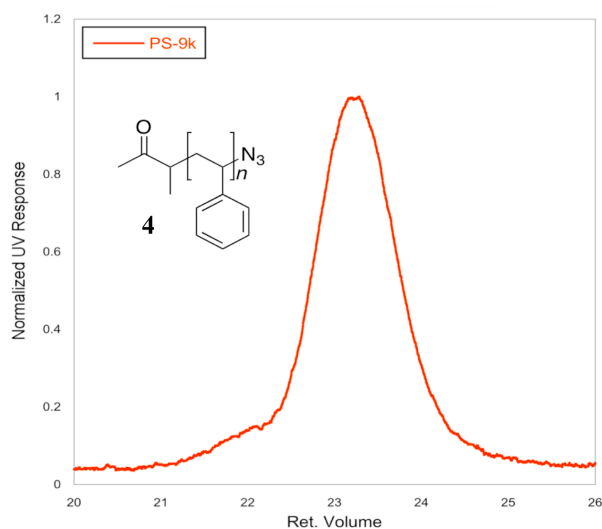
Figure 3: GPC of **4**

The protocols for the synthesis of alkyne terminated rr-P3AT bearing groups was reported previously by Mitchell et. al. [17] and is shown in Scheme 3. The procedure easily yielded the ethynyl (**5**) and propargyl-terminated P3HTs (**6**) target polymers and their structures were verified via ^{1}H-NMR and MALDI-TOF. First the "click" reaction between ethynyl P3HT and benzyl azide was performed by using CuBr(PPh$_3$)$_3$ as the catalyst and diisopropylethylamine, DIPEA, as the base (Scheme 4).
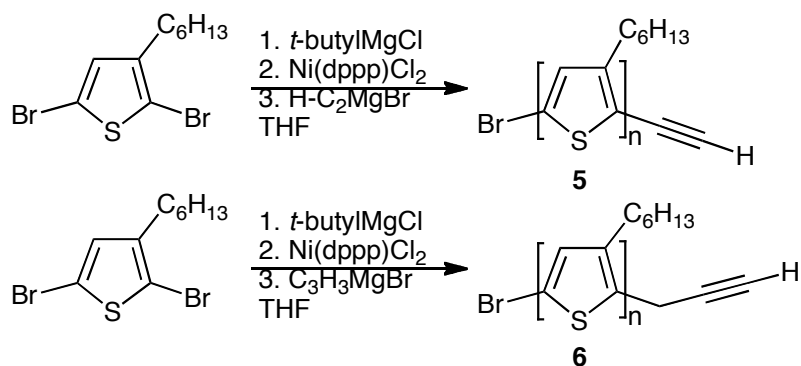
Scheme 3: Ethynyl and Propargyl-Terminated P3HT[17]
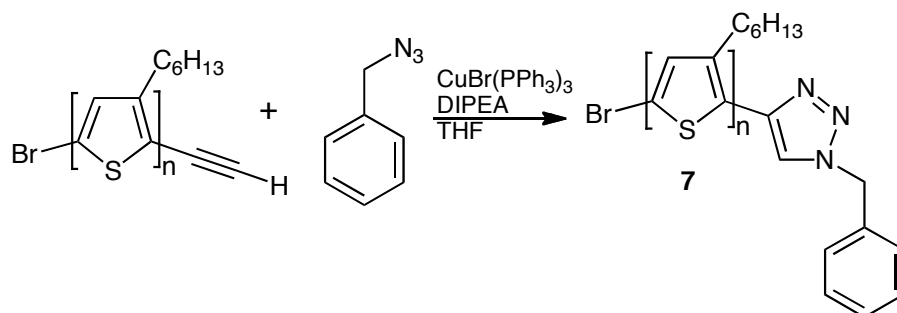
Scheme 4: Click Model Reaction[17]

"Click" reactions between the ethynyl-terminated P3HT and the azide-terminated polystyrene were carried out using CuBr and N,N,N',N",N'-pentamethylethylenetriamine, (PMDETA) as the base (Scheme 5). The reactions were monitored via GPC at 456 nm to monitor the molecular weight change of the P3HT (Figure 4).
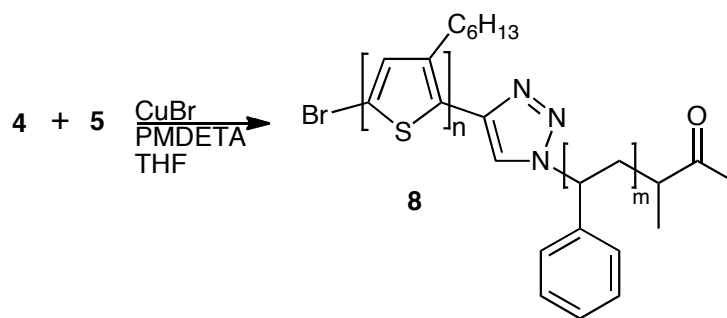
Scheme 5: "Click" reaction between P3HT and Polystyrene

As Figure 4 shows, the GPCs of the reaction taken at various time points almost appear bimodal in nature. Given the starting molecular weights of the polystyrene (10,500) and the P3HT (12,700) used, and comparing the peaks observed on the GPC, it was believed that the "click" reaction (24,000) were not progressing towards completion, resulting in a mixture of unreacted ethynyl-terminated P3HT and "clicked" diblock copolymer.
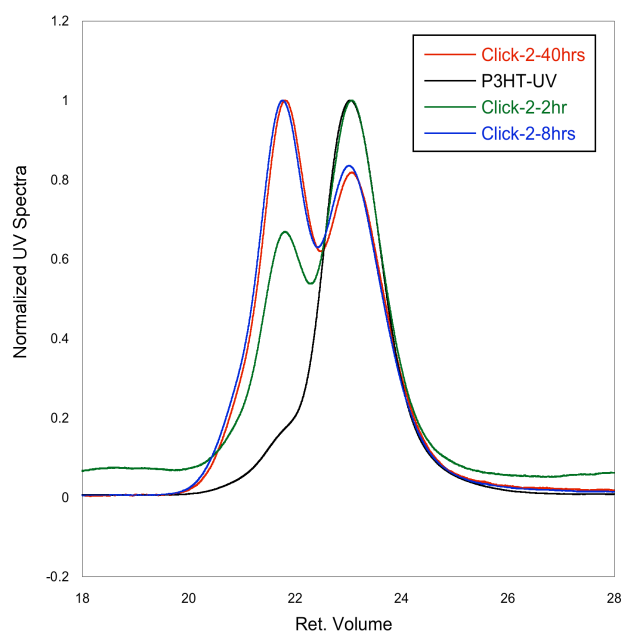
Figure 4: GPC data of ethynyl P3HT and azide terminated polystyrene "Click" Reactions

Numerous papers utilizing alternative "click" conditions have been published since 2008.[6] Therefore, it was determined that a ligand study using various bases that were successfully used with other polymeric systems would be beneficial to determine the best ligand to use for our systems (Figure 5). The conditions of the study are shown below in Table 1, with the reactions monitored again via GPC (Figures 6-8).
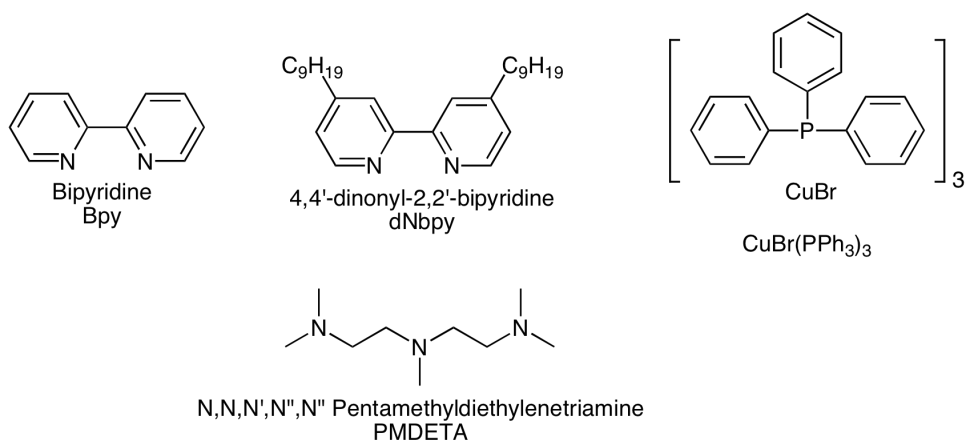
Figure 5: Ligands and additional catalyst used in the ligand investigation

Table 1: Initial "Click" Ligand Study

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
1	CuBr	Bpy	polystyrene	ethynyl	THF	r.t
2	CuBr	dNbpy	polystyrene	ethynyl	THF	r.t
3	CuBr	PMDETA	polystyrene	ethynyl	THF	r.t
4	CuBr(PPh₃)₃	Bpy	polystyrene	ethynyl	THF	r.t
5	CuBr(PPh₃)₃	dNbpy	polystyrene	ethynyl	THF	r.t
6	CuBr(PPh₃)₃	PMDETA	polystyrene	ethynyl	THF	r.t
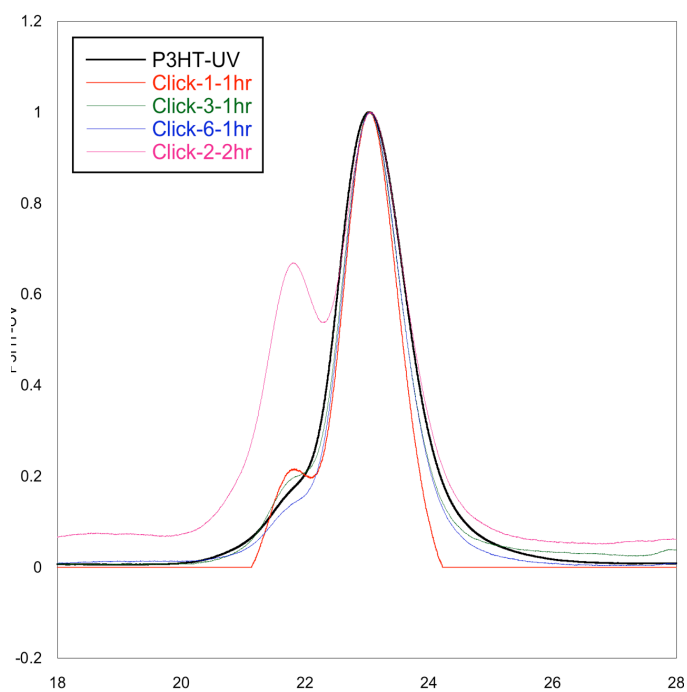
Figure 6: GPC of model reactions after 1 hour at r.t.
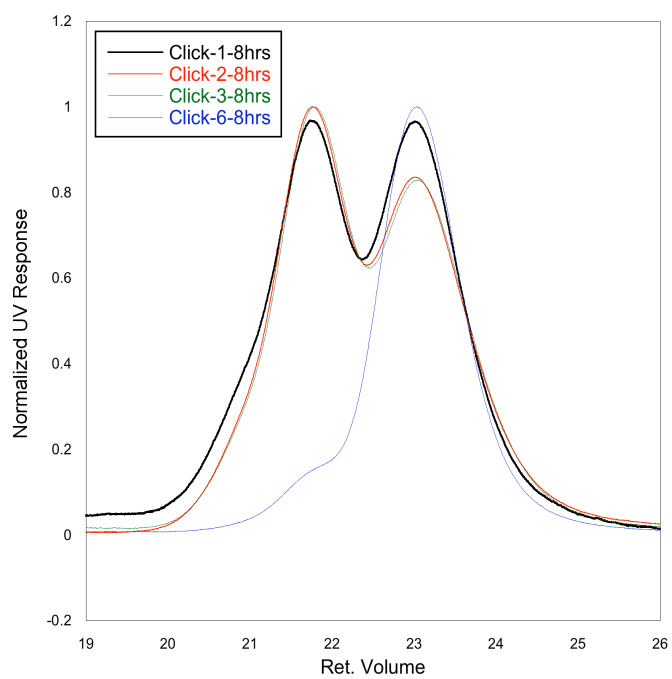
Figure 7: GPC of model reactions after 8 hours at r.t
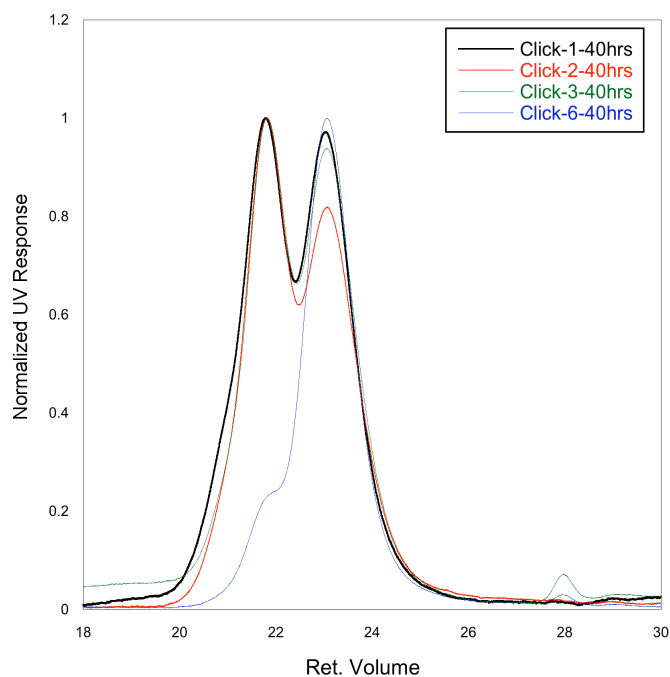
Figure 8: GPC of model reactions after 40 hours at r.t.

Comparing the progress of all reactions shown in Figures 6-8 to those of the initial reaction in Figure 4, it was once again believed the "click" reactions were hindered from completion by an unknown source.

Concurrent work published by Dubois cited that block copolymers were synthesized using the combination of ATRP and "click" chemistry.[21] 2-(2-Azidoethoxy)ethylbromoisobutyrate (**9**) was synthesized to be used two ways—a macroinitiator (MI) to synthesize an azide-terminated polystyrene in one step prior to a "click" reaction or conversely, a "click" reaction prior to utilizing ATRP to synthesize the other block. This versatile compound was deemed logical to develop to continue this project (Scheme 6).
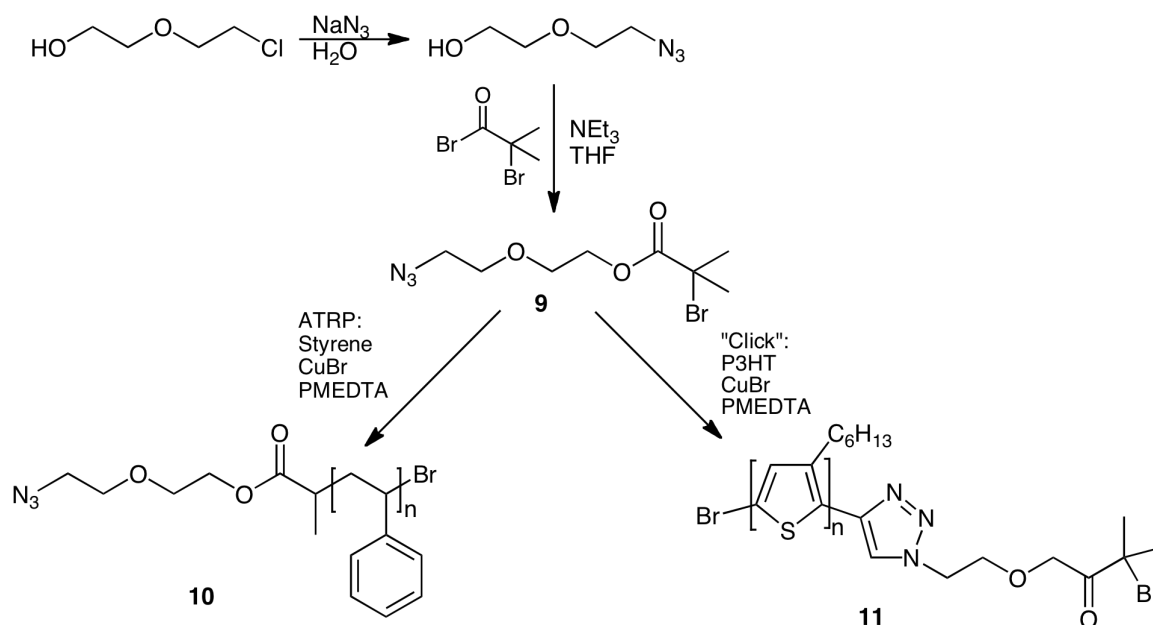
Scheme 6: Incorporation of the MI to synthesize diblock copolymers[21]

The MI was synthesized via published procedures[21] and a "click" reaction was attempted. Upon analysis by GPC, an expected result was obtained. As shown in Figure 9, the GPC of the attempted reaction was astonishingly similar to those obtained from the previous "click" reactions. Given the molecular weight of the MI is only 188.02 g/mol, the molecular weight of the "clicked" polymer should not shift to be double of the starting ethynyl-terminated P3HT because the difference in molecular weight would be negligible.
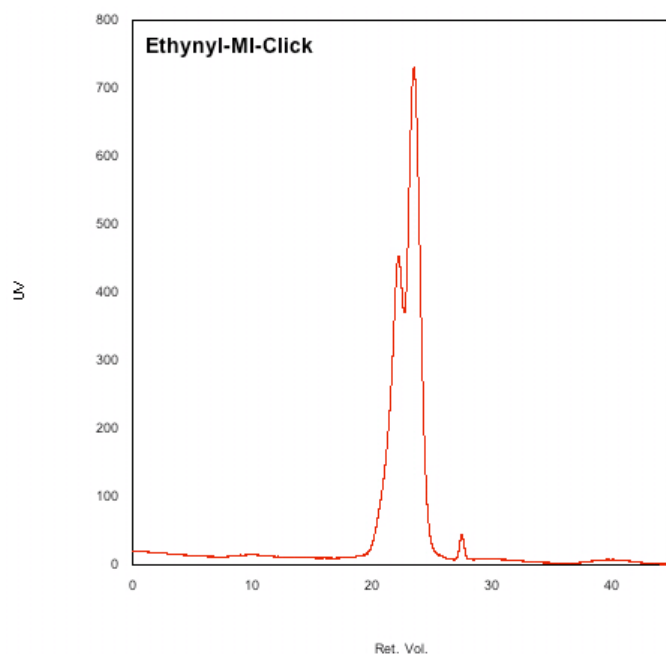
Figure 9: GPC of attempted reaction to make **11**

After work up of this attempted "click" reaction, the P3HT used was isolated and analysis via MALDI-TOF was completed (Figure 10). The spectrum provided insight to why the previously attempted "click" reactions did not work as expected. It was found that instead of performing a "click" reaction, the ethynyl-terminated P3HT was homocoupling to itself via Glaser couplings[22] to obtain a diacetylene. This gave valuable insight to the doubling of molecular weights observed in the previous figures (Figures 6-8), as well as the pronounced starting polymer peak. Recent publications also provided reasonable explanations of this occurrence. It was found that the Huisgen-type "click" reactions and Glaser-type couplings occur under very similar conditions.[7,10] It is believed that the conjugation of the ethynyl group on the polythiophene system led to deactivation of the alkyne, severely limiting the cycloaddition pathway and ultimately giving way to

homocoupling.[23] To circumvent this problem, it is believed that using a propargyl-terminated P3HT, a less conjugated system, or a protected alkyne-terminated P3HT will limit the potential homocoupling that was previously observed.
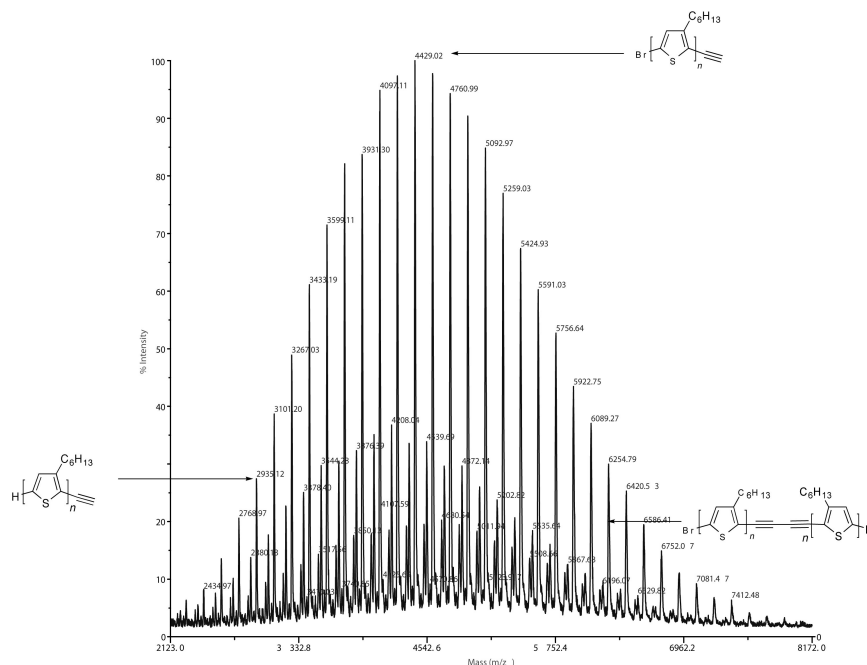
Figure 10: MALDI-TOF of ethynyl-P3HT post attempted "click" reactions

After examining commercially available starting materials, a protected propargyl system was proposed, as shown in Scheme 7. Activated Rieke magnesium (Mg*), prepared by reducing anhydrous magnesium chloride using lithium and naphthalene[24], was used instead of the conventional Grignard magnesium because it does not contain trace impurities that could potentially decrease the yields of the end-capping reactions. Polymerization was completed using the 3-magnesium-bromo-1-trimethylsilyl-1-propyne

(**12**) as the Grignard reagent added to end-cap the P3HT. This approach was successful in preparing predominately Br/propargyl-TMS terminated P3HT. This produced a much cleaner alkyne-terminated P3HT, as measured by the GPC in Figure 11.
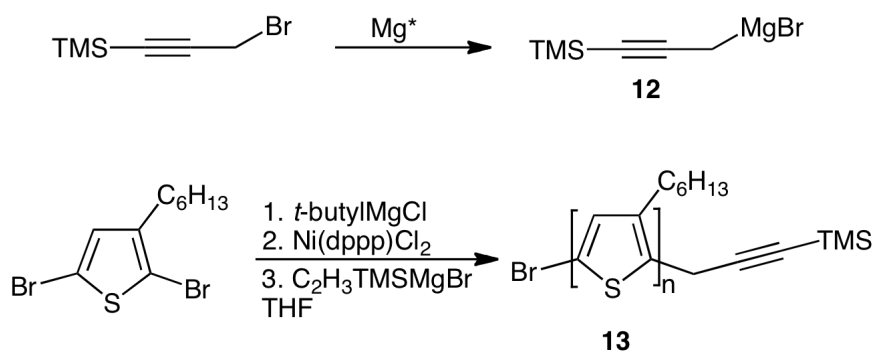
Scheme 7: Synthesis of TMS-propargyl P3HT
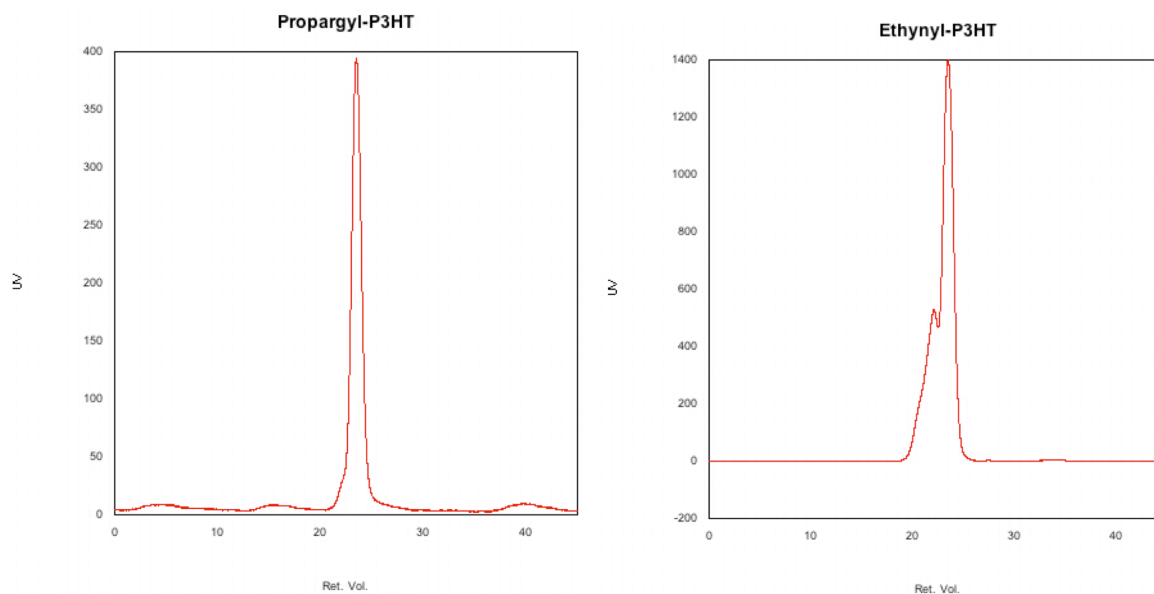
Figure 11: Propargyl vs. Ethynyl Terminated P3HT GPCs

After deprotection of the TMS-propargyl P3HT by using *tert*-butylammonium fluoride (TBAF), another series of "click" reactions were attempted with the azide-terminated MI and the azide terminated polystyrene using the CuBr/PMEDTA system again. None of these reactions produced any triazole products, however, no Glaser-type homocouplings were observed in the reaction.

Some difficulties were encountered during the reproduction of a successful end-capping reaction with both the propargyl- and ethynyl-terminated P3HT using Rieke Mg*. The reaction using the same conditions continually gave different results without clear rationale. It was hypothesized that water may have been a contaminant, thus lowering the reactivity of the $MgCl_2$. However, transferring newly purchased $MgCl_2$ to a reaction vial in a glove box, and attempting to make the Grignard reagent using Rieke Mg* still gave sporadic end-fuctionalization of the polymer. Subsequently, Mg* was purchased from Rieke Metals, Inc. (Lincoln, NE) to try to eliminate any possible contaminants. This method worked better than synthesizing the Mg*, but only slightly. Finally, we obtained a custom synthesized 3-magnesium-bromo-1-trimethylsilyl-1-propyne (**9**) from Novel Chemical Solutions, INC. (Crete, NE), which greatly improved the results of the polymerizations. Br/progargyl-TMS terminated P3HT was made very cleanly with good molecular weights (4-7K) and low PDIs (1.1-1.25) and was easily deprotected using *tert*-butylammonium fluoride (Figure 12).
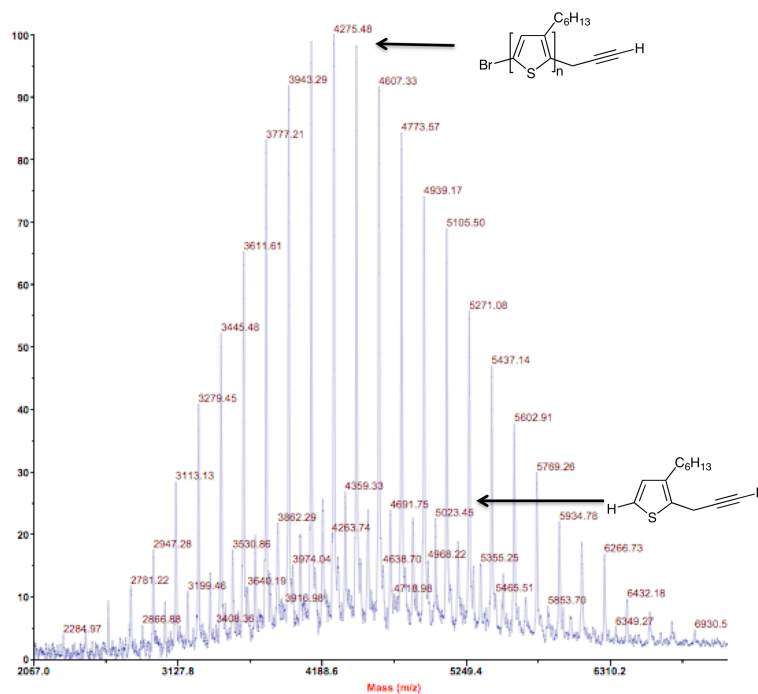
Figure 12: MALDI-TOF of a Propargyl-Terminated P3HT

By completing this synthesis of the propargyl-terminated P3HT, it was believed the complications of the previous "click" reactions would be circumvented. The "click" reaction shown in Scheme 5 was attempted once again. Unfortunately, analysis by MALDI-TOF proved that no reaction occurred once again. We also attempted to use a CuI/DIPEA catalytic system, which has been shown useful to obtain the 1,4-isomer when attempting "click" reactions in organic solvents, in recent literature.[5] This catalytic system was used again to try the "click" reactions between the azide-terminated polystrene, benzyl azide, and the propargyl-P3HT. However, this more favorable system did not result in a "click" reaction. Finally, we attemped a series of model reactions with various azides and using both copper and ruthenium catalysts would be advantageous (Table 2).

Table 2: "Click" Model Reactions

Run	Catalyst	Ligand	N$_3$	P3HT	Solvent	Temp. (°C)
1.1	CuI	DIPEA	azidoethanol	propargyl	THF	r.t.
1.2	CuI	BiPy	azidoethanol	propargyl	THF	r.t.
1.3	CuI	DIPEA	methylbenzyl azide	propargyl	THF	r.t.
1.4	CuI	BiPy	methylbenzyl azide	propargyl	THF	r.t.
1.5	RuCp(PPh$_3$)Cl	none	azidoethanol	TMS-propargyl	THF	r.t.
1.6	RuCp*(PPh$_3$)Cl	none	azidoethanol	TMS-propargyl	THF	r.t.
1.7	RuCp(PPh$_3$)Cl	none	methylbenzyl azide	TMS-propargyl	THF	r.t.
1.8	RuCp*(PPh$_3$)Cl	none	methylbenzyl azide	TMS-propargyl	THF	r.t.

MALDI-TOF spectrum of these reactions showed no evidence of a "click" reaction occurring. Hawker and co-workers published a paper stating the use of various copper and ruthenium catalysts used in "click" reactions to make vinyl monomers containing 1,2,3-triazoles.[25] One of the catalysts reported was a homogeneous copper on carbon (Cu/C) catalyst that is bench stable, can be used an a wide array of solvents, is recyclable, and is easily isolated.[26] This catalyst was synthesized via the literature procedure[26], and another series of model reactions was completed (Table 3). A mixture of solvents was also used to try and increase the solubility of the materials. In this series of reactions, the "click" reaction that Mitchell[17] reported was repeated (Run 2.1, Table 3).[17] Similar to all previous runs, no conclusive evidence was obtained that a "click" reaction occurred.

Table 3

Run	Catalyst	Ligand	N$_3$	P3HT	Solvent	Temp. (°C)
2.1	CuBr(PPh$_3$)$_3$	DIPEA	benzyl azide	propargyl	THF	40
2.2	Cu/C	NEt$_3$	benzyl azide	propargyl	THF/1,4 dioxane	40
2.3	Cu/C	DIPEA	benzyl azide	propargyl	THF/1,4 dioxane	40
2.4	Cu/C	PMDETA	benzyl azide	propargyl	THF/1,4 dioxane	40
2.5	CuI	PMDETA	benzyl azide	propargyl	THF/1,4 dioxane	40
2.6	CuSO$_4$	Na Asc.	benzyl azide	propargyl	THF/H$_2$O	40
2.7	RuCp(PPh$_3$)Cl	none	benzyl azide	TMS-propargyl	THF	40
2.8	RuCp*(PPh$_3$)Cl	none	benzyl azide	TMS-propargyl	THF	40
2.9	CuI	PMDETA	sodium azide	propargyl	THF/H$_2$O	40

Given the lack of success using the TMS-propargyl-terminated P3HT, a propynyl terminated (Scheme 8) was then used to determine if the TMS- group was too sterically hindering for synthesis the 1,5-isomer catalyzed by ruthenium catalysts. At this time the reactions were then attempted in mixtures of THF and DMF, DMF and chloroform (CHCl$_3$), and CHCl$_3$ alone. Also, the reaction was run at an elevated temperature to determine if any thermal cycloadditions would occur (Table 4). MALDI-TOF spectrum of these reactions again provided no evidence of a "click" reaction occurring.
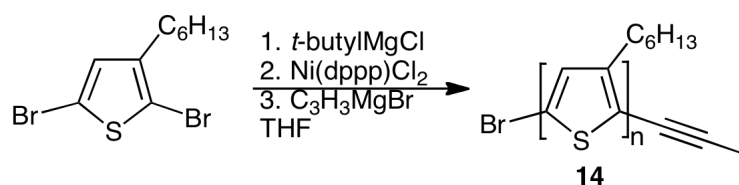
Scheme 8: Synthesis of propynyl-terminated P3HT

Meldal and Tornoe completed an intensive review of a wide array of "click" reaction conditions.[6] Analysis of what reaction conditions would be favorable with this system was completed and a wide array of catalysts were selected and used, as seen in Tables 5 and 6.

Table 4

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
3.1	CuI	DIPEA	TMS-azide	propargyl	THF/DMF	60
3.2	CuBr	PMDETA	TMS-azide	propargyl	THF/DMF	60
3.3	CuBr	Bpy	TMS-azide	propargyl	THF/DMF	60
3.4	RuCp(PPh$_3$)Cl	none	benzyl azide	propynyl	THF/DMF	60
3.5	RuCp(PPh$_3$)Cl	none	TMS-azide	propynyl	THF/DMF	60
3.6	RuCp*(PPh$_3$)Cl	none	TMS-azide	propynyl	THF/DMF	60
3.7	CuI	DIPEA	benzyl azide	propargyl	THF/DMF	60
3.8	CuI	Bpy	benzyl azide	propargyl	THF/DMF	60
3.9	RuCp*(PPh$_3$)Cl	none	benzyl azide	propynyl	THF/DMF	60
3.10	CuBr, Cu/C	NEt$_3$	benzyl azide	propargyl	THF/DMF	60
3.11	CuI	dNbpy	benzyl azide	propargyl	THF/DMF	60
3.12	CuI	DIPEA	benzyl azide	propargyl	CHCl$_3$/DMF	60
3.13	CuI	NEt$_3$	benzyl azide	propargyl	CHCl$_3$/DMF	60
3.14	CuI/CuBr	PMDETA	benzyl azide	propargyl	CHCl$_3$/DMF	60
3.15	RuCp(PPh$_3$)Cl	none	benzyl azide	propynyl	CHCl$_3$	60
3.16	RuCp(PPh$_3$)Cl	none	benzyl azide	propynyl	CHCl$_3$/DMF	60

Table 5

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
4.1	CuI	DIPEA	sodium azide	propargyl	THF	r.t.
4.2	CuSO$_4$	Na Asc.	sodium azide	propargyl	THF	r.t.
4.3	CuCl	DIPEA	sodium azide	propargyl	THF	r.t.
4.4	CuBr	dNbpy	sodium azide	propargyl	THF	r.t.
4.5	CuBr	dNbpy	TMS-azide	propargyl	THF	r.t.
4.6	CuI	DIPEA	TMS-azide	propargyl	THF	r.t.

Table 6

Run	Catalyst	Ligand	N$_3$	P3HT	Solvent	Temp. (°C)
5.1	CuI	DIPEA	benzyl azide	propargyl	THF	60
5.2	CuSO$_4$	Na Asc.	benzyl azide	propargyl	THF/H$_2$O	60
5.3	CuCl	DIPEA	benzyl azide	propargyl	THF	60
5.4	CuBr/Cu(OAc)$_2$	dNbpy	benzyl azide	propargyl	THF	60
5.5	CuBr/Cu(OAc)$_2$	dNbpy	TMS-azide	propargyl	THF	60
5.6	CuI	DIPEA	TMS-azide	propargyl	THF	60

Once again, work up of these reactions and their resulting MALDI-TOF spectra proved that no "click" reactions were observed. Benzyl azide was synthesized again and distilled via Kugelrhor to insure its purity. Reactions shown in Tables 7 and 8 were then attempted. Run 7.1 was completed near neat conditions, adding only enough solvent to dissolve the P3HT.

Table 7

Run	Catalyst	Ligand	N$_3$	P3HT	Solvent	Temp. (°C)
6.1	CuBr(PPh$_3$)$_3$	DIPEA	benzyl azide	propargyl	THF	50
6.2	Cu/C	NEt$_3$	benzyl azide	propargyl	THF/1,4-dioxane	50
6.3	Cu/C	DIPEA	benzyl azide	propargyl	THF/1,4-dioxane	50
6.4	Cu/C	PMDETA	benzyl azide	propargyl	THF/1,4-dioxane	50
6.5	CuI	PMDETA	benzyl azide	propargyl	THF/1,4-dioxane	50
6.6	CuSO$_4$	Na. Asc.	benzyl azide	propargyl	THF/H$_2$O	50
6.7	CuI	PMDETA	sodium azide	propargyl	THF/H$_2$O	50
6.8	RuCp(PPh$_3$)Cl	none	benzyl azide	TMS-propargyl	THF	50
6.9	RuCp*(PPh$_3$)Cl	none	benzyl azide	TMS-propargyl	THF	50

After these reactions failed again, a more thorough search of the literature was completed. Mechanistic studies completed previously found that the reaction rates of "click" reactions using polyvalent structures as ligand were unusually high. However, it was found that 1,2,3-triazoles had not been utilized in any ligand. Sharpless developed a

trivalent ligand, tris[1-benzyl-1H-1,2,3-triazole-4-yl)methyl]amine (TBTA) (**15**), which is a strong stabilizing ligand for copper (I) , as it protects it from both oxidation and disproportionation, while increasing its catalytic activity.[27] The synthesis of TBTA utilizes tetrakis(acetonitrile)copper(I) hexafluorophosphate, $Cu(MeCN)_4PF_6$ as the copper catalyst. Additional sets of reactions were set up—one using previous combinations of catalyst and ligand, and the second using TBTA. However, this time these reactions were set up in duplicate, using both the propargyl and the ethynyl-terminated P3HT to verify that the "click" reactions that failed previously with the propargyl system were also consistently not working with the ethynyl system. Also, the solvent was changed from THF to 1,4-dioxane ensure that evaporation would not be an issue while running the reaction at elevated temperatures (Table 9). The reactions summarized in Tables 9 and 10 using the TBTA ligand produced no successful "click" reactions.
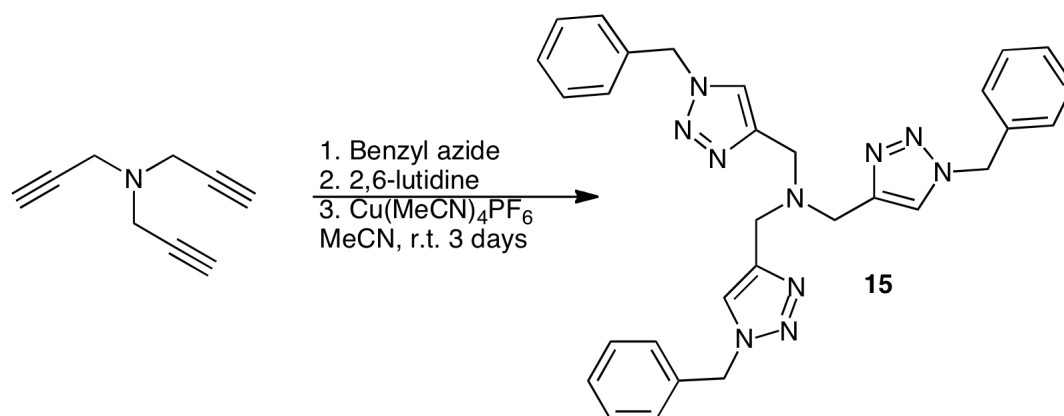
Scheme 9: Synthesis of TBTA[27]

Table 8

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
7.1	CuI	PMDETA	benzyl azide	propargyl	THF[a]	50
7.2	CuI	PMDETA	benzyl azide	propargyl	DMF	50
7.3	$CuSO_4$/CuI	Na. Asc.	benzyl azide	propargyl	DMF/H_2O	50
7.4	$Cu(OAc)_2$	PMEDTA	benzyl azide	propargyl	THF	50
[a]: minimal amount of solvent was used to dissolve P3HT (~2mL)						

Table 9

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
8.1	CuI	DIPEA	benzyl azide	propargyl	1,4-dioxane	70
8.2	CuI	DIPEA	benzyl azide	ethynyl	1,4-dioxane	70
8.3	CuBr	PMDETA	benzyl azide	propargyl	1,4-dioxane	70
8.4	CuBr	PMDETA	benzyl azide	ethynyl	1,4-dioxane	70
8.5	Cu/C	DIPEA	benzyl azide	propargyl	1,4-dioxane	70
8.6	Cu/C	DIPEA	benzyl azide	ethynyl	1,4-dioxane	70
8.7	$Cu(MeCN)_4PF_6$	PMDETA	benzyl azide	propargyl	1,4-dioxane	70
8.8	$Cu(MeCN)_4PF_6$	PMDETA	benzyl azide	ethynyl	1,4-dioxane	70

Table 10

Run	Catalyst	Ligand	N_3	P3HT	Solvent	Temp. (°C)
9.1	CuI	TBTA/DIPEA	benzyl azide	propargyl	1,4-dioxane	60
9.2	CuI	TBTA/DIPEA	benzyl azide	ethynyl	1,4-dioxane	60
9.3	CuBr	TBTA/DIPEA	benzyl azide	propargyl	1,4-dioxane	60
9.4	CuBr	TBTA/DIPEA	benzyl azide	ethynyl	1,4-dioxane	60
9.5	Cu/C	TBTA/DIPEA	benzyl azide	propargyl	1,4-dioxane	60
9.6	Cu/C	TBTA/DIPEA	benzyl azide	ethynyl	1,4-dioxane	60
9.7	$Cu(MeCN)_4PF_6$	TBTA/DIPEA	benzyl azide	propargyl	1,4-dioxane	60
9.8	$Cu(MeCN)_4PF_6$	TBTA/DIPEA	benzyl azide	ethynyl	1,4-dioxane	60
9.9	$CuSO_4$	TBTA/DIPEA	benzyl azide	propargyl	1,4-dioxane	60
9.10	$CuSO_4$	TBTA/DIPEA	benzyl azide	ethynyl	1,4-dioxane	60

Table 11: Microwave Assisted "Click" Reactions

Run	Catalyst	Ligand	N₃	P3HT	Solvent	Temp. (°C)	Watts
MW1	CuI	DIPEA	benzyl azide	propargyl	THF	50	130
MW2	CuBr	PMDETA	benzyl azide	propargyl	THF	50	130
MW3	Cu/C	DIPEA	benzyl azide	propargyl	1,4-dioxane	70	130
MW4	Cu(MeCN)$_4$PF$_6$	DIPEA	benzyl azide	propargyl	1,4-dioxane	80	140
MW5	RuCp*(PPh$_3$)Cl	none	benzyl azide	propargyl	1,4-dioxane	100	140

Microwave assisted "click" reactions were then attempted as multiple sources described the reaction as going to completion in a matter of minutes (Table 11).[6] While initial results appeared promising, further work-up of the polymers resulted in nothing more than starting materials as seen by MALDI-TOF.

3.3 Conclusion

"Click" chemistry was viewed to be the ideal way to synthesize a rod-coil diblock copolymer containing polythiophene and polystyrene because of its versatile uses in other organic, biological, and materials syntheses. Initial synthesis of a polythiophene-*b*-polystyrene diblock copolymer proved to be problematic because of the occurrence of the Glaser homocoupling between the ethynyl-terminated P3HTs. Changing the alkyne from an ethynyl group to a propargyl was hypothesized to reduce the effects of conjugation on the system and also reduce the probability of Glaser coupling from occurring. Through exhaustive studies using a wide array of catalysts (both copper and ruthenium), bases, solvents, temperatures, and reaction times, there was no 1,2,3-triazole formation from any of the attempted cycloadditions of an alkyne-terminated P3HT and an azide. Current work has now shifted to synthesizing a 2-alkyne-3-hexylthiophene as another model compound to determine if a "click" reaction is possible on a non-polymeric thiophene system.

3.4 Experimental Methods

All reactions, when specified, were performed under purified nitrogen or argon, using oven-dried glassware. Tetrahydrofuran (THF) was dried using an Innovative Technologies (Pleasant Valley, MO) purification system. Anhydrous magnesium chloride, lithium wire, napththalene, Ni(dppp)Cl$_2$, tert-butylmagnesium chloride, ethynyl magnesium bromide, *N,N,N′,N″,N″*-Pentamethyldiethylenetriamine, N,N-diisopropylethylamine, triethylamine, 2,2′-dipyridyl, 4,4'-dinonyl-2,2'-bipyridine, sodium ascorbate, copper (I) bromide, copper (I) iodide, copper (I) chlroride, CuSO$_4$, CuBr(PPh$_3$)$_3$, Cu(OAc$_2$), RuCp(PPh$_3$)Cl, 2,6-lutidine, trimethylsilyl azide were purchased from Sigma-Aldrich and used without further purification. Cu(MeCN)$_4$PF$_6$ and RuCp*(PPh$_3$)Cl were purchased from STREM Chemical Co. and used without further purification. 3-Bromo-1-trimethylsilyl-1-propyne, and tripropargylamine were purchased from GFS Chemicals and used without further purification. Styrene was purchased from Sigma-Aldrich and purified by running through basic alumina to remove an inhibitor. 2,5-dibromo-3-hexylthiophene was synthesized according to the literature procedures from 3-hexylthiophene.[28] Bromine-terminated polystyrene[18], tributylphosphine-terminated polystyrene[20], azide-terminated polystyrene[29], 2-(2-azidoethoxy)ethylbromoisobutyrate[19], benzyl azide[30], azido ethanol[31], methylbenzyl azide[30,32], Cu/C catalyst[26] and TBTA[27] were all prepared according to literature procedures.

Instrumentation.

^{1}H NMR spectra were recorded using a Varian 400 MHz instrument. A MALDI-TOF MS (Voyager-DE STR BioSpectrometry) workstation by Biosystems, Inc. was used to record spectra in the linear mode, where 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 30 °C using THF as the eluent and the flow rate was 1.0μL/min. Calibration was based on polystyrene standards obtained from Viscotek. Microwave-assisted "click" reactions were carried out in a CEM Corporation Discover Manual Single Mode Microwave System.

Synthesis of 3-magnesium-bromo-1-trimethylsilyl-1-propyne: To a 25 mL Schlenk flask, 0.005 mol MgCl$_2$, 0.00103 mol naphthalene, 6 mL of THF and 0.0105 mol Li wire were added. The reaction mixture was stirred vigorously for 24 hours at room temperature. After 24 hours the Grignard was taken up in a syringe and added dropwise to the polymerization reaction as described for the general method.

Typical End-Capping Reaction[28]. In a three neck round bottom flask, 5 mmol 2,5-dibromo-3-hexylthiophene was dissolved in 10mL THF and stirred under argon. 5 mmol *tert*-Butylmagnesium chloride 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. 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 a cellulose 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); GPC: M_n: 8333 , PDI: 1.15 m/z: 5936.30 [M+] (calcd: 5937.01, DP of 44, propargyl/Br end groups); GPC: M_n: 8722, PDI: 1.09   m/z: 6010.63 [M+] (calcd: 6006.95, DP of 44, TMS-propargyl/Br end groups); GPC: M_n: 6860, PDI: 1.2 m/z: 4611.07 [M+] (calc: 4607.11, DP of 35, propynyl/Br end groups)

Synthesis of Low Molecular Weight Bromine Terminated Polystyrene [6][18]: To a 25 mL Schlenk flask, 0.087 mol of purified styrene and 0.00087 mol of CuBr were added. Argon was bubbled through the mixture for 25 min. 0.435 mmol PMDETA was added and stirred for 15 min at room temperature. A solution of 0.698mmol methyl 2-bromopropionate in 0.020mol purified styrene was added via syringe and the mixture was heated at 110 °C and stirred for 8 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 200 mL of methanol to give a white solid. The polymer was filtered into a cellulose thimble and then washed by Soxhlet extraction with methanol, and THF. The polymer was isolated from the THF extraction. GPC: M_n = 3200, PDI = 1.25

Synthesis of High Molecular Weight Bromine Terminated Polystyrene [6][18]: To a 100 mL Schlenk flask, 0.437 mol of purified styrene and 0.00219 mol of CuBr was added. Argon was bubbled through the mixture for 25 min. 0.00219 mol PMDETA was added and stirred for 15 min at room temperature. A solution of 2.094 mmol methyl 2-

bromopropionate in 0.040mol purified styrene was added via syringe and mixture was heated at 110 °C and stirred for 8 hours. The solution became viscous and eventually solidified. The Schlenk flask was then opened to air and 45 mL of THF was added. The organics were then passed through a neutral alumina column and precipitated into 500 mL of methanol. The polymer was filtered into a cellulose thimble and then washed by Soxhlet extraction with methanol, and THF. The polymer was isolated from the THF extraction. GPC: M_n = 10500, PDI = 1.1

Synthesis of Azide Terminated Polystyrene [7][19]: In a 50mL Schlenk flask, a solution of 0.44 mmol bromine terminated polystyrene in 10mL THF, 3.86 mmol azidotrimethylsilane and 4 mmol TBAF were added. The reaction mixture was stirred overnight at room temperatrue in an argon atmosphere. The resulting polymer was precipitated in 200 mL of methanol and was was filtered into a cellulose thimble and then washed by Soxhlet extraction with methanol, and THF. The polymer was isolated from the THF extraction. GPC: M_n=10250, PDI 1.21

Attempts at Alkyne Terminated P3HT Clicked with Various Azides: To a 20 mL scintillation vial, 0.10 mmol of alkyne-terminated poly(3-hexylthiophene), 0.025 mmol catalyst, 0.040 mmol of base, 10 mL of solvent and 0.25 mmol of azide were added. The vial was capped and stirred at specified temperatures for 5 days. The reaction mixture was then diluted with THF and run through a mini-alumina column to filter out the catalyst and the polymer was isolated.

MALDI-MS: m/z: 4429.02 [M+] (calcd: 4426.20, DP of 26, ethynyl/Br end groups); m/z: 5936.30 [M+] (calcd: 5937.01, DP of 44, propargyl/Br end groups); m/z: 6010.63

[M+] (calcd: 6006.95, DP of 44, TMS-propargyl/Br end groups); m/z 4611.07 [M+]

(calc: 4607.11, DP of 35, propynyl/Br end groups)

3.5 References

(1)   Rostovtsev, V. V., Green, L.G., Fokin, V.V., Sharpless, K.B. *Angewandte Chemie International Edition* **2002**, *41*, 2596-2599.

(2)   Huisgen, R. *Pure and Applied Chemistry* **1989**, *61*, 613-628.

(3)   Nandivada, H., Jiang, X., Lahann, J. *Advanced Materials* **2007**, *19*, 2197-2208.

(4)   Tornoe, C. W., Christensen, C., Meldal, M. *Journal of Organic Chemistry* **2002**, *67*, 3057-3064.

(5)   Fournier, D., Hoogenboom, R., Schuber, U.S. *Chemical Society Reviews* **2007**, *36*, 1369-1380.

(6)   Meldel, M., Tornoe, C.W. *Chemical Reviews* **2008**, *108*.

(7)   Duxbury, C., Cummins, D., Heise, A. *Journal of Polymer Science: Part A: Polymer Chemistry* **2009**, *47*, 3795-3802.

(8)   Meldel, M., Tornoe, C.W. *Chemical Reviews* **208**, *108*.

(9)   Tang, W., Matyjaszewski, K. *Macromolecules* **2006**, *39*, 4953-4959.

(10)   Adimurthy, S., Malakar, C.C., Beifuss, U. *Journal of Organic Chemistry* **2009**, *74*, 5648-5651.

(11)   Jones, G. O., Ess, D.H, Houk, K.N. *Helvetica Chimica Acta* **2005**, *88*, 1702.

(12)   Perez, P., Domingo, L.R., Aurell, M.J., Contreras, R. *Tetrahedron* **2005**, *59*, 3117.

(13)   Zhang, L., Chen, X., Xue, Peng, Sun, H., Williams, I., Sharpless, K.B., Fokin, V.V., Jia, Guochen, J. *Journal of the American Chemical Society* **2005**, *127*, 15998-15999.

(14)   Gil, M. V., Arevalo, M.J., Lopez, O. *Synthesis* **2007**, *11*.

(15)   Boren, B., Narayan, S., Rasmussen, L., Zhang, L., Zhao, H., Lin, Z., Jia, G., Fokin, V.V *Journal of the American Chemical Society* **2008**, *130*, 8923-8930.

(16)   Hawker, C. J., Fokin, V.V., Sharpless, K.B. *Australian Journal of Chemistry* **2007**, *60*, 381-383.

(17)   Mitchell, M., Iowa State University, 2007.

(18)   Lutz, J. F., Matyjaszewski, K. *Journal of Polymer Science: Part A: Polymer Chemistry* **2005**, *43*, 897-910.

(19)   Lutz, J. F., Borner, H., Weichenhan, K. *Macromolecular Rapid Communications* **2005**, *26*, 514-518.

(20)   Byrd, M. H. C., Bencherif, S, Bauer, B., Beers, K, Burns, Y., Lin-Gibson, S., Sari, N. *Macromolecules* **2005**, *38*, 1564.

(21)   Mespouille, L., Vachaudez, M., Suriano, F., Gerbaux, P., Coulembier, O., Degee, P., Flammang, R., Dubois, P. *Macromolecular Rapid Communications* **2007**, *28*, 2151-2158.

(22)   Siemsen, P., Livingston, R.C., Diederich, F. *Angewandte Chemie International Edition* **2000**, *39*.

(23)   Urien, M., Erothu, H., Cloutet, E., Hiorns, R., Vignau, L., Cramail, H. *Macromolecules* **2008**, *41*, 7033-7040.

(24)   Rieke, R. D. *Accounts of Chemical Research* **1977**, *10*, 301-306.

(25)   Nulwala, H., Takizawa, K., Odukale, A., Khan, A., Thibault, R., Taft, B.R., Lipshutz, B.H., Hawker, C.J. *Macromolecules* **2009**, *42*, 6068-6074.

(26)   Lipshutz, B. H., Taft, B.R. *Angewandte Chemie International Edition* **2006**, *45*, 8235-8238.

(27)   Chan, T. R., Hilgraf, R., Sharpless, K.B., Fokin, V.V. *Organic Letters* **2004**, *6*, 2853-2855.

(28)   Jeffries-EL, M., Suave, G., McCullouch, R.D. *Macromolecules* **2005**, *38*, 10349-10352.

(29)   Dirks, A. J., van Berkel, S., Hatzakis, N., Opsteen, J., van Delft, F., Cornelissen, J., Rowan, A. van Hest, J., Rutjes, F., Nolte, R. *Chemical Communications* **2005**, 4172-4174.

(30)   Pardin, C., Roy, I., Lubell, W., Keillor, J., *Chemical Biology & Drug Design* **2008**, *72*, 189-196.

(31)   del Barriot, J., Oriol, L., Alcala, R. Sanchez, C. *Macromolecules* **2009**, *42*, 5752-5760.

(32)   Nishiyama, K., Karigomi, H. *Chemistry Letters* **1982**, *9*, 1477-1478.