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THIOPHENE AND DERIVATIVES FOR USE IN
PYRIDAZINES AND THIAPENTALENES

A Thesis
Presented to
The Faculty of the Department of Chemistry
Western Kentucky University
Bowling Green, Kentucky

In Partial Fulfillment
Of the Requirements for the Degree
Master of Chemistry

By
Benjamin Tyree Cannon

May 2015

THIOPHENE DERIVATIVES FOR USE IN
PYRIDAZINES AND THIAPENTALENES

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Dean, Graduate School Date

I dedicate this thesis to my parents, Ben and Denise Cannon who have loved and supported me during my academic career. Also, I would like to dedicate this work to my brother and best friend Shane. Finally, I would like to dedicate this work to all who have helped me here at Western Kentucky University.

ACKNOWLEDGEMENTS

First, I would like to thank my God and Savior Jesus Christ for His unending love, as well as for Him giving me the strength, wisdom, and determination to pursue my dreams. Next, I would like to thank Dr. Chad A. Snyder whom has taken me under his wing and served as my mentor in academia as well as in life. I would also like to thank Dr. Nathan Tice at Butler University for always responding rapidly to my emails and questions when I would reach a sticking point in my research. I also want to thank Mrs. Alicia Pesterfield and the stock room employees who always provided me with the chemicals I needed in a speedy fashion. I would also like to thank my committee members Dr. Yan and Dr. Zhang for their valuable insight.

I would also like to thank the Department of Chemistry faculty and staff for their support, as well as for providing me with a quality education that I have received during my graduate studies at Western Kentucky University.

Finally, I would like to thank my mom and dad, Denise and Ben Cannon for everything thing that they have taught me, and for always loving and supporting me no matter what. I would also like to thank my little brother Shane Cannon who helped me not take things too seriously; Shane, I am proud of the man you have become. I also want to thank my good friend and Masonic Brother Jeff Thompson and his family, you have done more for me than you can even imagine. I would also like to thank Dr. Amy Brausch whose counseling and guidance helped reshape my life. Lastly, I want to thank all of the members of New Roe Lodge #592 for their friendship and brotherly love.

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THIOPHENE AND DERIVATIVES FOR USE IN
PYRIDAZINE AND THIAPENTALENES

Benjamin Tyree Cannon

May 2015

70 pages

Directed by: Chad A. Snyder, Bangbo Yan, and Rui Zhang

Department of Chemistry

Western Kentucky University

This thesis introduces the idea of Band Theory and how it can be used to describe a solid-state materials ability to carry an electrical charge. Next, this thesis defines what makes a material a conductor, semiconductor, or insulator. Semiconductors are attracting interest in chemistry, as well as in the manufacturing of consumer electronics, because of their ability to carry a charge, without the risk of short-circuiting like traditional conductors.^{1,4} Organic semiconductors, which behave differently than traditional semiconductors, are of particular interest because they offer mechanical flexibility, low-cost, simplicity, and the ability to be manufactured at low temperatures.⁶ Nonorganic and organic semiconductors can be enhanced by a process called doping, which is further explained within this thesis. This thesis will focus on the unique properties and advantages that heterocycles, particularly thiophene and thiophene derivative complexes, and cyclopenta[*c*]thiophenes offer in the manufacturing of organic semiconductors. One area of thiophene research that has showed promise in leading to mass production of semiconductors derived from thiophene complexes is the use of thiophenes with electron withdrawing groups attached to the two and five position.²⁶⁻²⁷ In a recent publication in the *Journal of Sulfur Chemistry* a novel approach for developing thiophene derivatives was successfully investigated.²⁷⁻³¹ This novel approach will be explained, and a successful synthetic route using 2,5-dimethylthiophene as a starting material will be

provided. This thesis also explored using 2,5-dichlorothiophene and 2,5-dibromothiophene as novel starting materials in the previously successful route utilizing 2,5-dimethylthiophene. Unfortunately, however, this area of research was unsuccessful; therefore, research shifted towards the development of the lactone 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-c]oxepin-6-one, which is one of the many products needed for the newly proposed synthetic route of manufacturing cyclopenta[*c*]thiophenes utilizing a much shorter route than previously attempted. Even more importantly, the synthetic route that was attempted is filled with mostly fundamental bedrock organic chemistry that can be pulled straight from a textbook. Research stopped at the lactone due to time constraints; however, this creates an opportunity for ongoing research for future undergraduate and graduate students.

I. Chapter One

Band Theory

The ability of a material to carry an electrical charge in its solid-state can be explained using band theory.¹ “Band theory states that whenever atoms come together during the formation of a new compound, their atomic orbital energies mix to form molecular orbital energies” (Figure 1.1).¹⁻² As more and more atoms begin to mix and create new molecular orbitals many of the energy levels become extremely close to, or even completely degenerate in energy. These degenerate energy levels are said to have formed continuous bands of energy, which are then able to carry an electrical charge (Figure 1.2).³¹ These continuous bands of energy; however, are not uniform.

Instead, bands of different energy levels will form due to the differences that exist between the masses of the combining molecular orbitals.¹ The differences between the band energies are known as the band gap.¹ A band gap exists because electrons will either occupy the highest molecular orbital to form the valence band, while other electrons will occupy the lowest molecular orbital to form the conduction band; thus leading to a space between the valence band and conduction band where there are no electrons (Figure 1.3).³¹ The conduction band is made up of two different mobile charge carriers that are referred to as either positive or negative.¹

Negative mobile charge carriers are electrons that have enough energy to escape the valence band and jump to the conduction band.¹ Positive charge carriers are known as holes due to the lack of an electron being in the conduction band.¹ A hole is a place in the band where an electron can exist as a mobile charge carrier; however, it ceases to exist at that particular location.¹

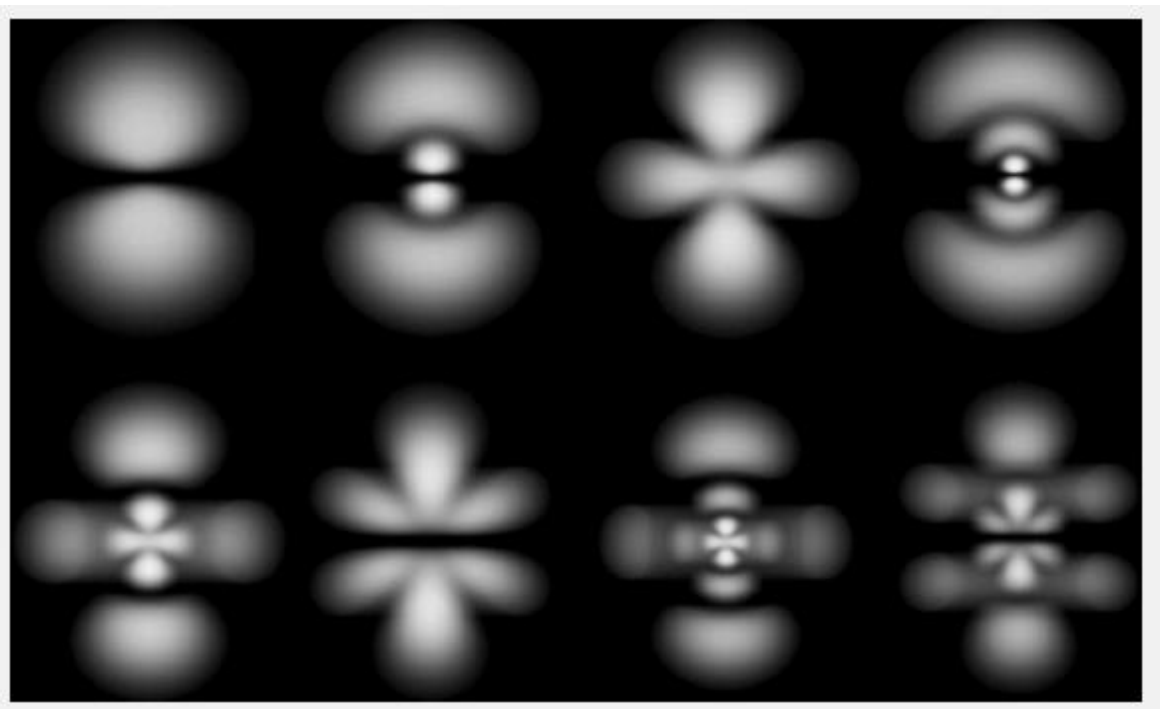


Figure 1.1: Cross section of atomic orbitals²

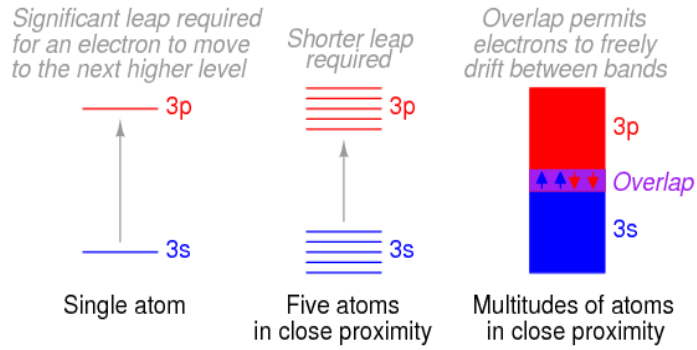


Figure 1.2: Diagram showing how molecular orbitals overlap to create continuous bands capable of conducting electrical charge.³

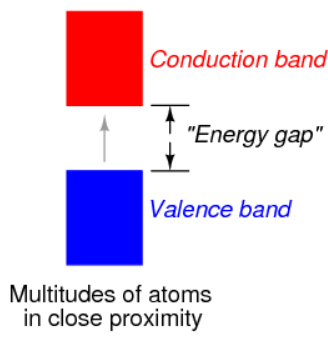


Figure 1.3: Diagram showing conduction band, valence band, and an “energy gap”³

How Conductors, Semiconductors, and Insulators Are Defined

All materials can be classified based on their ability to carry an electric charge. A conductor is a material that has a band gap that is nonexistent.¹ This allows thermally excited electrons to freely move from the valence band to the conduction band due to the molecular orbitals completely overlapping.¹ Some materials are not able to carry an electrical charge at all. These materials are known as insulators. An insulator is a material that has a band gap that is wide enough as to prevent the movement of electrons.¹

Some materials have properties of both conductors and insulators. These materials have a band gap, like an insulator; however, the band gap is not significant enough to block the flow of electrons from the valence band to the conduction band.¹ This then enables the material to carry an electrical charge, which intensity depends on the distance between the valence band and the conduction band.¹ These materials are classified as semiconductors, and they are attracting interest in chemistry as well as in the manufacturing of consumer electronics because of their ability to carry a charge, without the risk of short-circuiting like traditional conductors (Figure 1.4)^{4,1} Semiconductors are classified based upon whether it is a positive/p-type charge carrier, or a negative/n-type charge carrier (Figure 1.5)^{5,1}

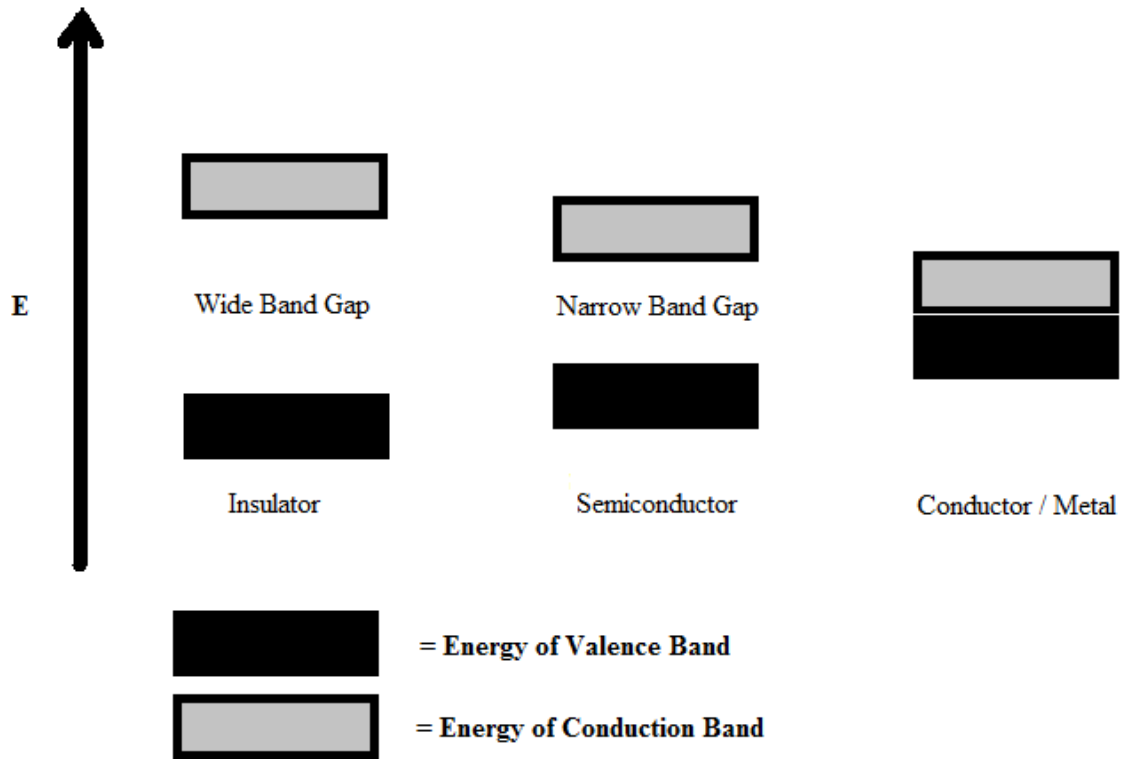


Figure 1.4: Molecular orbital diagram demonstrating the differences between an Insulator, Semiconductor, and a Conductor/ Metal.⁴

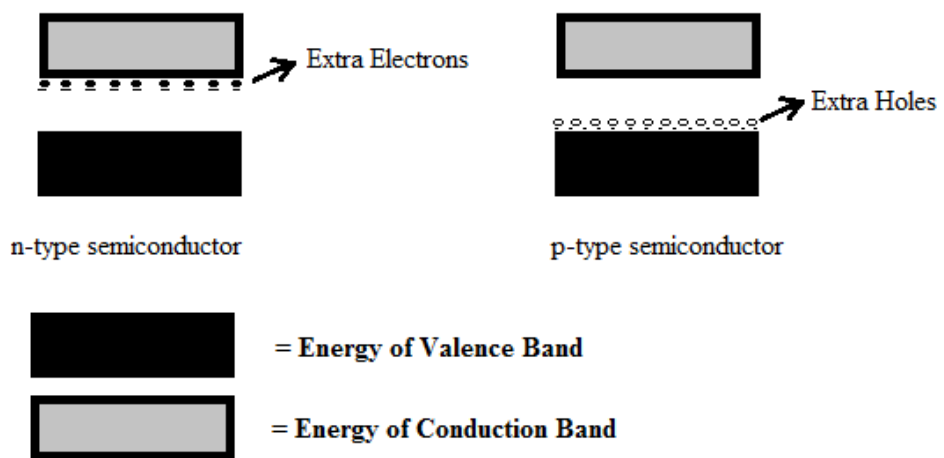
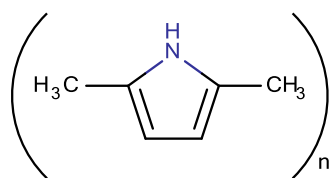


Figure 1.5: Molecular orbital diagram of n-type semiconductors and p-type semiconductors⁵

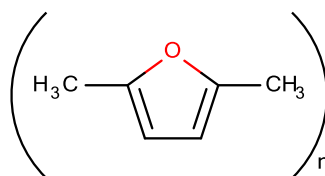
Organic semiconductors behave in a manner that is different from traditional semiconductors. Organic semiconductors require π -extended aromatic systems and/or highly conjugated systems, which offer up easy access to highly mobile electrons (Figure 1.6A).⁶ Other ways in which organic semiconductors differ from inorganic semiconductors are that heteroatoms (Figure 1.6B) are required for electron donating and withdrawing groups, performance is linked to pi-pi bonds, and charge carriers such as electrons or holes are required for conduction and are typically created via a process called doping.⁷



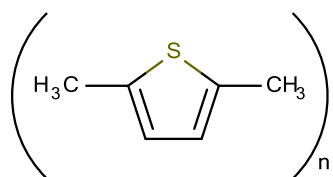
Figure 1.6 A: Example of a conjugated system (polyacetylene), and how highly mobile electrons (arrows) are able to freely flow thus enabling conduction to take place.



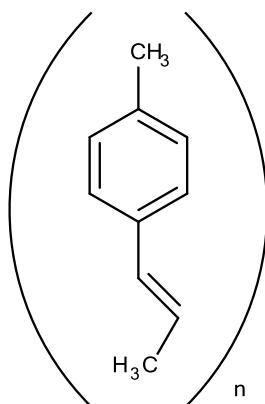
Polypyrrole



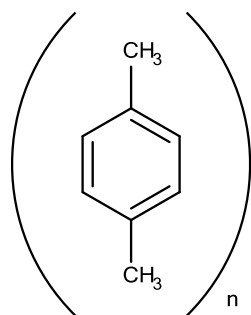
Polyfuran



Polythiophene



Polyphenylenevinylene



Polyphenylene

Figure 1.6B: Examples of various heteroatoms with different electron donating and withdrawing groups.

Doping

Doping is very important in the creation of organic semiconductors. Doping is a technique wherein different impurities are added to the starting material to help add additional energy levels (which act as steps) in between the conduction and valence band. Doping can also be carried out electrochemically by using anodes and cathodes to manipulate the conjugated π -bonds within the polymer to create holes (p-type semiconductors) by causing the material to oxidize or to create charge carriers (n-type semiconductors) by causing the material undergo a redox reaction.⁸ This has the effect of reducing the band gap, and improving the overall performance capabilities of the semiconductor.

P-type semiconductors can also be formed when materials such as cobalt complexes or other transition metals⁹, halogens, arsenates, antimonates or other similar salts and complexes are used to create holes via an acid-base reaction. N-type semiconductors present a special challenge because they are much more reactive than p-type semiconductors.⁸ The increased reactivity of n-type semiconductors often results in materials that rapidly lose their ability to conduct a charge, and therefore a lot of research is being conducted to create more stable n-type semiconductors.⁸ N-type semiconductors are created when materials such as sodium naphthalide, alkaline metal cations, R_4N^+ quaternary salts are used to add an additional positive charge to the conjugated system via acid-base chemistry under typical redox conditions.⁸ N-type organic semiconductors are needed because they help complete the circuit by forming a complementary circuit that can then be used in voltage gated channels to control the flow of electricity by acting as an on/off switch between the transistors.⁹

Due to these differences, organic semiconductors do not require partially filled or partially empty electron bands like electron band theory would suggest. Instead these conjugated systems behave in a manner similar to p-type semiconductors because current is caused by holes, which are areas inside of the conjugated ring that have the potential to hold the electrons but are currently empty.⁶ Organic n-type semiconductors are much rarer due to the complications that exist during manufacturing.⁶ Electrons can be injected into electron-deficient molecules and act as a transporter, or electron-withdrawing groups can be added to π -conjugated systems to prevent hole transporters from forming.⁶ This is difficult, however, due to the fact that most known n-type organic materials have charge carriers that are easily trapped by environmental oxidants at ambient conditions.⁶

What Makes Organic Semiconductors Appealing

Organic semiconducting materials are attractive alternatives to use in place of silicon-based semiconductors because of mechanical flexibility, low-cost, simplicity, and the ability to be manufactured at low temperatures.⁶ Traditional semiconductors are typically manufactured by harvesting the silicon that resides in the earth's crust. The silicon that is harvested is not pure silicon rather it is silicon dioxide (SiO_2). In order to derive pure silicon it is necessary to reduce the silicon dioxide to pure silicon via heating the silicon dioxide to extremely high temperatures with graphite.¹¹⁻¹³ This process causes the greenhouse gas carbon dioxide (CO_2) to be released into the atmosphere. As one can imagine the process is extremely labor intensive and requires meticulous care to avoid contamination from free-floating particles that exist within the environment. Therefore, the manufacturing process of traditional semiconductors takes place in what is termed a

“clean room” environment, wherein the room is sealed off from all outside air, and expensive filtration systems are used to keep the air pure and free from dust.

Alternative routes for the production of silicon that is pure enough to be used in electronic include reduction of the silica dioxide in the presence of halide gases. Another technique includes the Siemens process that grows high quality silicon crystallites are grown over a silicon rod by blowing gaseous trichlorosilane over the rods surface at extremely high temperatures causing chemical decomposition to occur.¹¹⁻¹³ The cost associated with these processes, as well as the environmental harm that comes from using the necessary fossil fuels needed to achieve the high temperatures required to reduce the silicon dioxide to pure silicon make organic semiconductors extremely attractive.

Organic semiconductors are more environmentally friendly due to the fact that they can typically be manufactured at ambient conditions in non-sterile environments.⁶ They are particularly appealing to use as organic thin film transistors (OTFTs) and organic field effect transistors (OFETs) which can then be used in solar cells, sensors, or various other electronic equipment.⁶ This is because of their unique ability to be manufactured in mass by ink-jet printing instead of complex sterile room manufacturing required in silicon based products.⁶

Problems with Organic Semiconductors

Organic semiconductors are not without their problems. Many OTFTs that are particularly attractive because of their electrical properties are not very stable when exposed to the atmosphere.⁶ Organic semiconductors typically do not offer the same performance characteristics as their silicon counterparts as well. One of two methods typically measures the performance capabilities of semiconductors either how well the

material conducts an electrical charge, or what its electrical resistivity is. A conductor has an electrical resistivity of $10^{-7} \Omega\text{m}$ to $10^{-8} \Omega\text{m}$, while an insulator has an electrical resistivity of $10^{10} \Omega\text{m}$ to $10^{14} \Omega\text{m}$.¹⁴ A semiconductor then is a material that falls within the middle of this gap with most semiconductors offering an electrical resistivity of $10^{-6} \Omega\text{m}$ to $10^7 \Omega\text{m}$.¹⁴ Electrical conductivity is directly related to the materials electrical resistivity in that the electrical conductivity (or ability to conduct a charge) is the reciprocal of the electrical resistivity.¹⁵

Table 1.1¹⁶⁻¹⁷ shows the conductivity of different metals, silicon semiconductors, and organic semiconductors. One should notice that even traditional semiconductors such as silicon or germanium do not display strong electrical conductivity in an undoped state; however, these materials are easily doped by a variety of materials that allows manufactures to establish how much the material acts as a conductor versus how much the material acts as an insulator. Silicon and germanium are also used because these materials demonstrate extreme durability as well as stability in atmospheric conditions. Notice that most organic semiconductors are normally half as efficient as semiconductors made of silicon or germanium, until doping takes place.

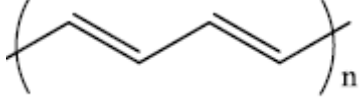
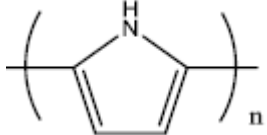
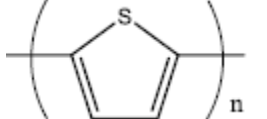


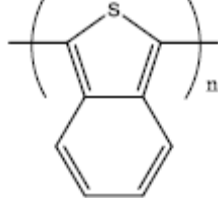
Material	Atomic Symbol or Structure	Approximate Conductivity (Siemens per cm)
Copper	Cu	5.8×10^5
Gold	Au	4.1×10^5
Iron	Fe	1.0×10^5
Pure Silicon	Si	4.3×10^{-6}
Pure Germanium	Ge	1.0×10^{-2}
Polyacetylene		1.0×10^5
Polypyrrole		$5.0 \times 10^2 - 7.5 \times 10^3$
Polythiophene		1.0×10^4
Polyphenylene		2.7×10^3
Polyfuran		1.0×10^2
Polysiothianaphthene		5.0×10^1

Table 1.1 Conductivity of various materials, and their atomic symbol or structure.¹⁶⁻¹⁷

Organic semiconductors are also plagued by problems that have been shown to arise during rapid mass production (such as that which takes place during ink-jet printing).⁶ One problem that occurs during ink-jet printing is dynamic disordering that occurs via nuclear motions while the material is being “printed” out.⁶ This dynamic disordering disrupts the charge carrier transporter by acting as a stop gap to the polarons that try to jump from one localized area to the next.⁶ Attempts to print materials that show supramolecular ordering often result in materials that are fragile, brittle, and difficult to process.⁶ Therefore, a happy medium needs to be achieved between the disordered state and the ordered state because the supramolecular order of the material directly correlates to how well the material performs.⁶

In order for organic semiconductors to operate at their peak proficiency the molecular orientation of the molecules must be aligned to not act as a stop gap for the electrons.¹⁵ Establishing and maintaining exact control over the molecular orientation of the molecules within the material is particularly hard to control because of the precision that is required to work on such a microscopic level.¹⁸ These problems are not as apparent in silicon semiconductors, and thus present another challenge for organic semiconductors. However, even with these difficulties organic semiconductors are still attractive alternatives to silicon semiconductors because of the aforementioned advantages.

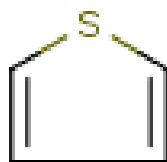
Heterocycles

Thiophenes (Figure 1.7A) and pyrroles (Figure 1.7B) as well corresponding compounds that have been synthesized from them are attracting interest in the organic chemistry world because of the unique properties that they possess. Their environmental stability, high processability, green chemistry (which reduces both toxic waste and

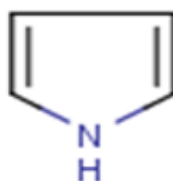
environmental harm), charge carrying abilities, and low production cost make them prime candidates to be used in a variety of advanced electronic devices.¹⁹⁻²² Fused thiophene and pyrrole compounds are an extremely attractive intermediate, due to the well-documented stability, and performance capabilities of the compounds made utilizing them.²³ These compounds have already found themselves being used in organic light emitting diodes (OLEDs), solar cell arrays, sensors for TNT and DNT detection, and in organic thin film transistors (a key component of plastic circuitry used in cell phones, laptops, and memory elements in credit card strips).^{19,24-25} The addition of a transition-metal component into synthesized thiophene and pyrrole complexes (doping) unlock additional unique properties, unlike those of common organic compounds, such as conductivity and optics.

Thiophene and polythiophene (Figure 1.7A-C) complexes are also attractive candidates due their unique nature of being highly soluble, which helps, in the manufacturing process.⁸ Interest in thiophene complexes also exist because they can easily form heterocyclic conjugated polymers by simple electrochemical or chemical oxidation reactions.⁸ When electrochemical methods are employed thiophene also

A.



B.



C.

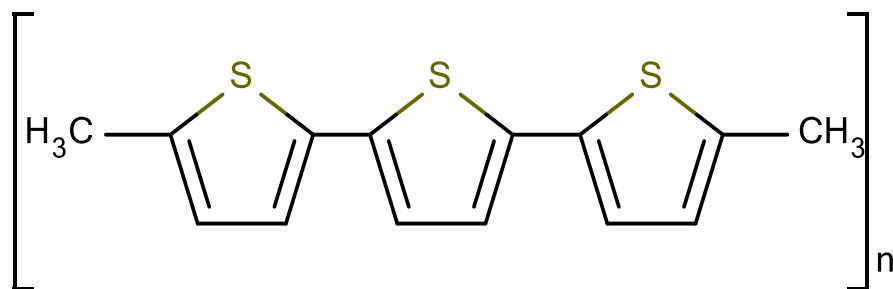
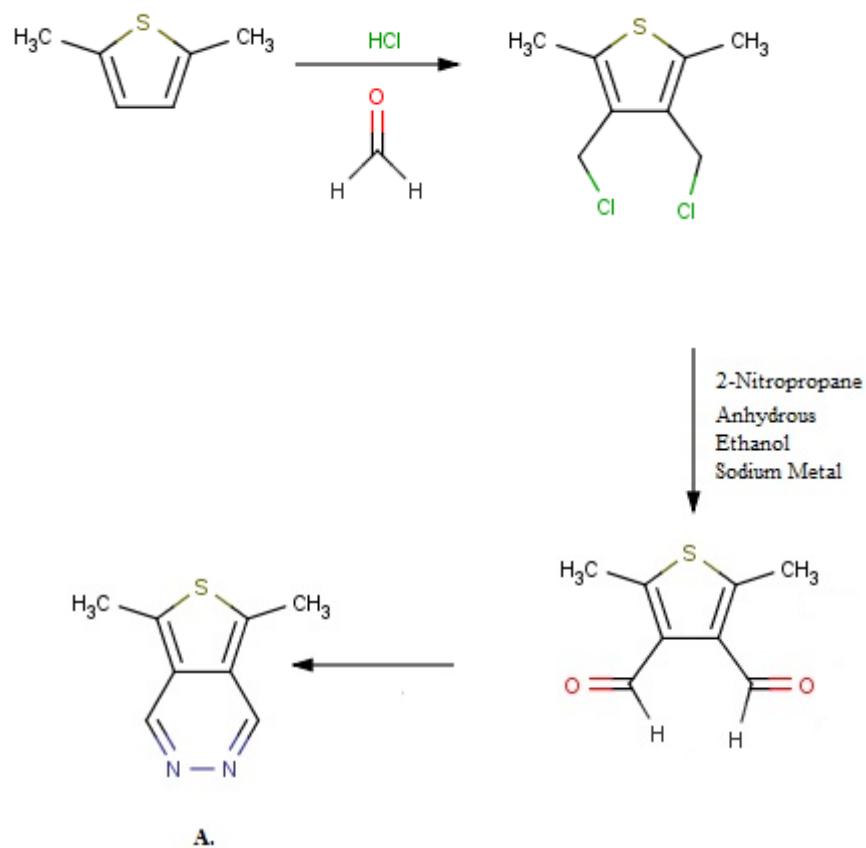


Figure 1.7: Structures of A. Thiophene, B. Pyrrole, and C. Polythiophene

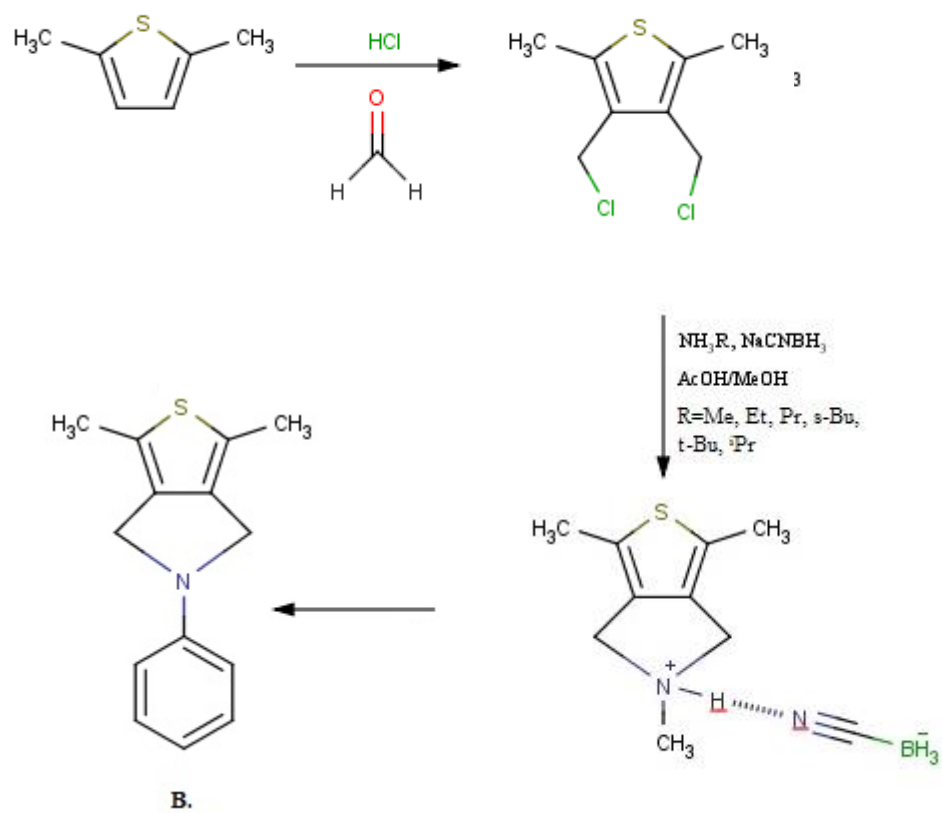
offers the distinct advantage of being easily removed from the electrode after the organic film has formed.⁸ Thiophenes are also excellent candidates for use as organic semiconductors because while they are being fused into a polymer the oxidation reaction typically results in the formation of a film that is already slightly doped.⁸ The method that this happens by is currently debated, but it does help explain why thiophene complexes show such stronger performance characteristics in a “non-doped state” than other organic semiconductors.⁸

One area of thiophene research that has showed promise in leading to mass production of semiconductors derived from thiophene complexes is the use of thiophenes with electron withdrawing groups attached to the two and five position.²⁶⁻²⁷ These complexes offer increased stability, and offer an easy jumping off point for the creation of various polymers.²⁷ In a recent publication in the *Journal of Sulfur Chemistry* a novel approach for developing thiophene derivatives was successfully investigated.²⁷⁻³¹ These fully aromatic systems (also known as pyrroles) would act as building blocks for organic and organometallic semiconductors (Scheme 1.1A and 1.1B).²⁷ These complexes make ideal candidates due to their favorable electrical properties, as well as their demonstrated readiness to form polymers via electrochemical polymerization.²⁷

This research is needed because one of the more common ways of manufacturing pyrroles and/or polythiophenes via the Paal-Knorr synthesis leaves the two and five position blocked so that oxidation cannot take place in the monomer thus blocking the formation of the polymer.^{27,32} The method that is being described in this thesis and within the *Journal of Sulfur Chemistry* instead depends upon the reductive



Scheme 1.1A Reaction Scheme Outline by Tice and Snyder.²⁷



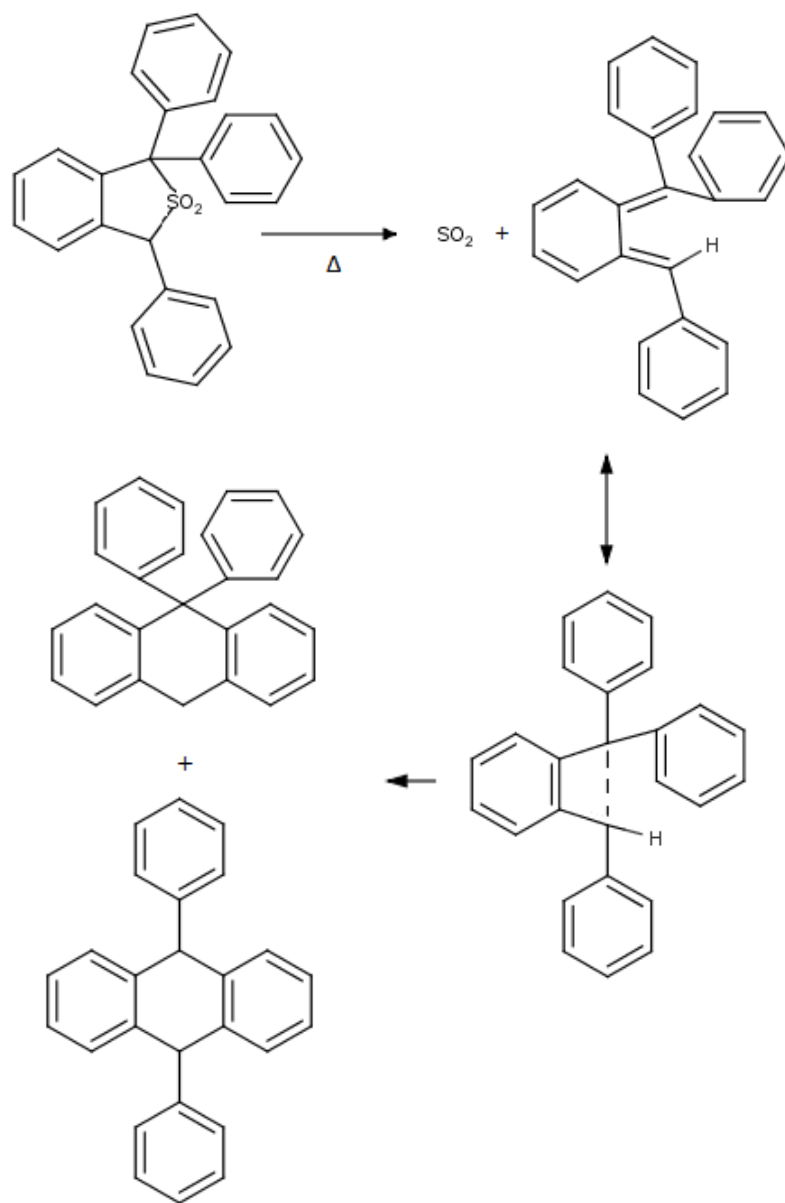
Scheme 1.1B Reaction Scheme Outline by Tice and Snyder.²⁷

amination of diformyl precursors as described by Boit and coworkers.^{27, 33-34} This method has already been found to be successful even in bimolecular systems under mild conditions, and therefore, offers promise for even easier manufacturing using primary amines in an intermolecular fashion.^{27,33-34} These thieno and cyclopenta[*c*]pyrroles have already demonstrated improved electronic and solid-state properties and offer significant promise for future use in organic and organometallic semiconductors or light emitting diodes .^{27,35-38}

Cyclopenta[*c*]thiophenes

H. Staudinger and F. Pfenninger first described cyclopenta[*c*]thiophenes and similarly related compounds via a thermal decomposition study in 1916.³⁹ Not much was known about these compounds, and they faded into relative obscurity until another H. Kloosterziel and H.J. Backer rediscovered these products as a derivative of 1,1,3-triphenyl-1,3-dihydrothianaphthene-2,2-dioxide (Scheme 1.2)⁴⁰ after heating to 150°C yielding a very low yield (less than 20%) of these compounds.⁴⁰ In 1959 M.P. Cava and A.A. Deana were attempting to discover a new route to synthesize various benzocyclobutene ring systems to study the effect of ring-strain as reported by Mills-Nixon in 1930.⁴¹ Cava and Deana's study afforded very low yields of the desired product (4-16%); however, their method produced a much purer product than any other previous method (80% pure).⁴¹

The chemical techniques involved in obtaining the product at such a low yield were very strenuous, and labor intensive. In addition, the chemistry being described was not directed at cyclopenta[*c*]thiophenes and their derivatives instead; they were just an interesting by-product. It was not until 1964 when Hans



Scheme 1.2: Synthesis of 1,1,3-tri-phenyl-1,3-dihydrothiananthrene-2,2-dioxide and its derivatives.⁴⁰

Wynberg and D. J. Zwaneburg decided to study five-membered heteroaromatic systems with fused five-membered rings that research into cyclopenta[*c*]thiophenes began in earnest.⁴² Wynberg and Zwaneburg were interested in determining how bond order influenced the formation of the bond connecting both rings in the heterocyclic compound.⁴²

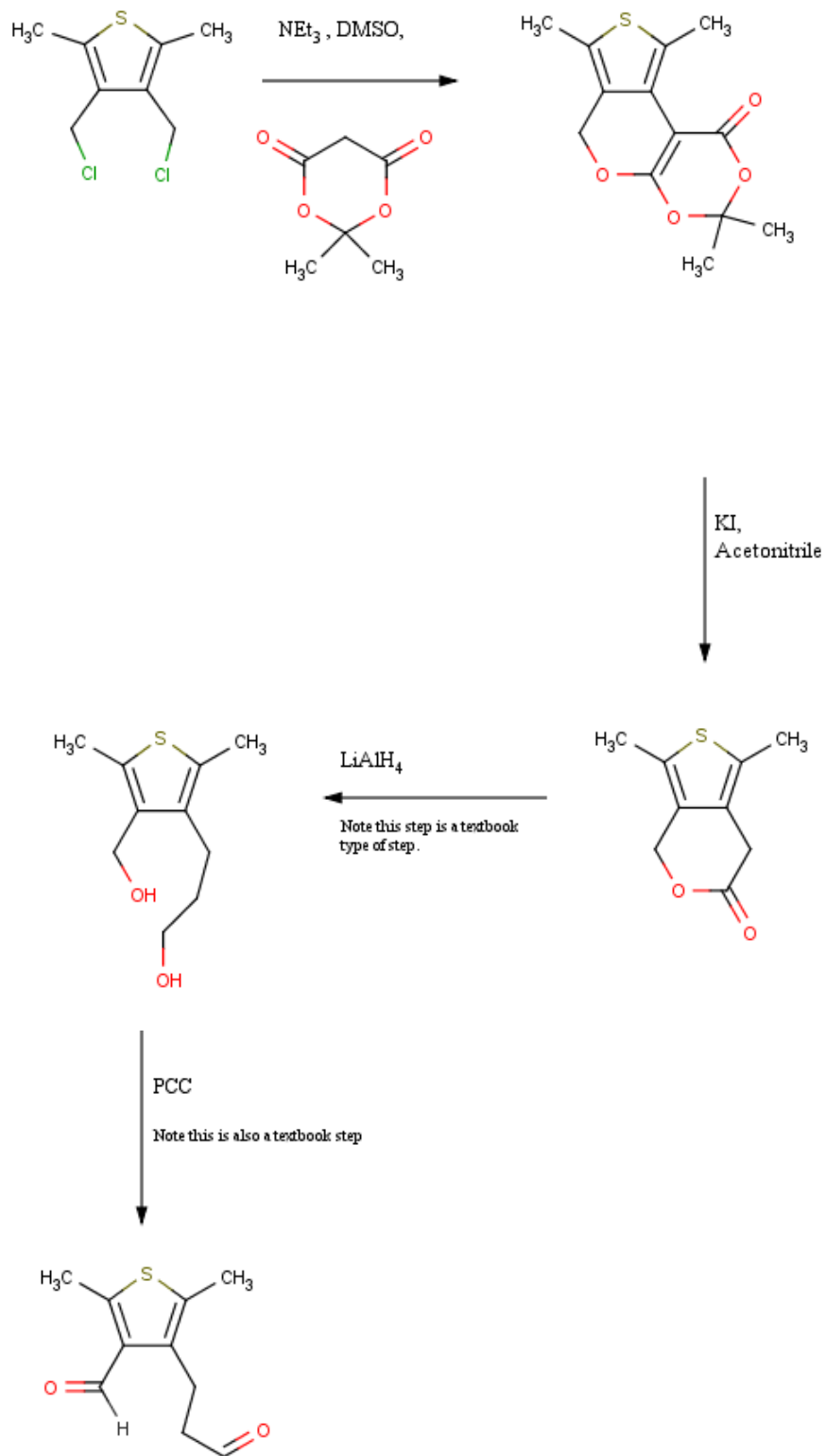
Once again, the techniques described by Wynberg and Zwaneburg were very meticulous and labor intensive, and afforded similarly low yields. Their methods depended upon various temperature changes, time sensitive additions of multiple reactants, reactions carried out in reflux conditions, and purification techniques involving CO₂(s) as well as suspension filtration and recrystallizations steps.⁴² However, Wynberg and Zwaneburg were able to show a mechanism of how the system forms. Their mechanism suggested that an S_N2 transition state causes the thienopyrrole ring system to form.⁴³ This is important because it showed that the tetrachloride atom during the closure of the ring with ethylamine causes substantial steric hindrance and makes it crucial that the entire ring closing system must occur in the plane of the aromatic ring to be successful.⁴³ This discovery was significant because it was the first explanation of why the synthesis of these compounds was so difficult.

Due to the difficulties in manufacturing these compounds research into the cyclopenta[*c*]thiophenes once again took a back seat to materials, which afforded higher yields and better return on investments. However, in 1987 Jean Roncali and coworkers once again decided to pick up where Wynberg and Zwaneburg left off. Research had already shown that poly(thiophene) derivatives make excellent organic conducting polymers due to their excellent chemical stability and relative ease of manufacturing via

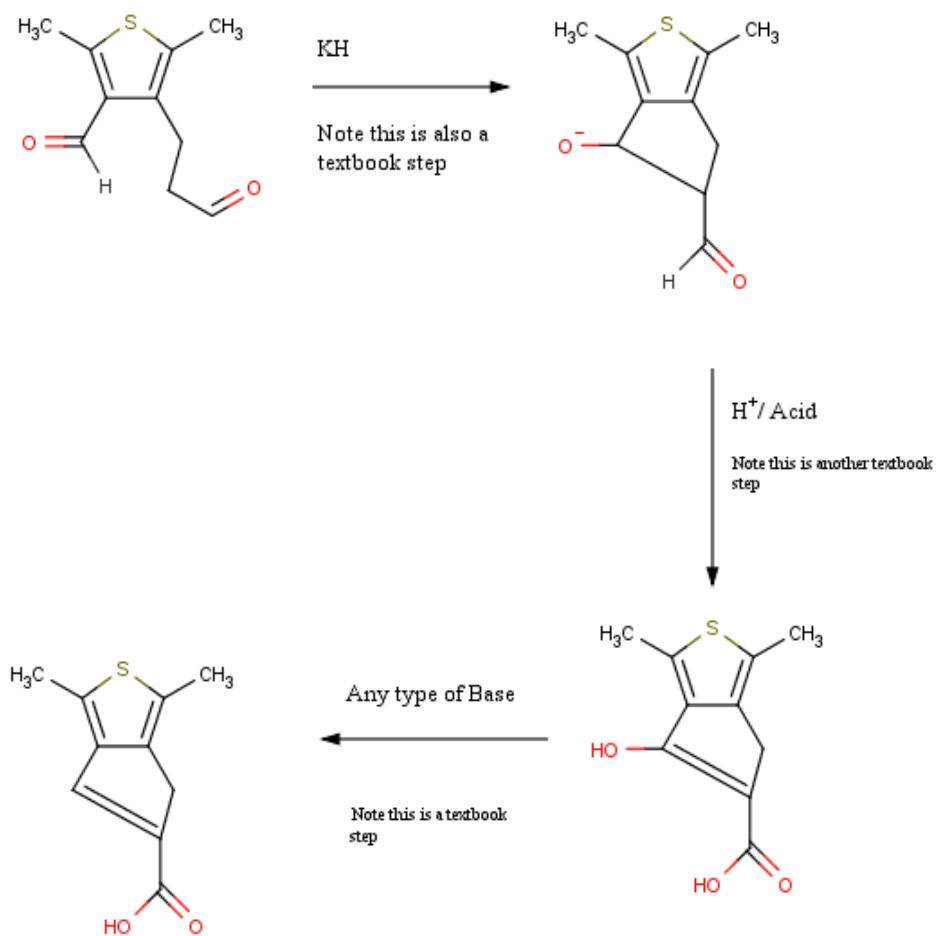
electrochemical synthesis.⁴⁴ Roncali and coworkers believed that 3,4-disubstituted poly(thiophenes) offered the best chance at manufacturing cyclopenta[*c*]thiophene polymers and various derivatives because the atoms at the third and fourth position reduced the number of parasitic 2-4' couplings that act as a road block to polymerization occurring.⁴⁴ In addition, methyl groups and other various atoms also have an inductive effect that acts to lower the oxidation potential of the monomer.⁴⁴ This is important during the final electropolymerization step because it leads to the formation of fewer highly reactive radical cations that can destroy the polymer.⁴⁴ Roncali and coworkers attempted to modify Wynberg and Zwaneburg's original procedures described in a theoretical study by Bredas *et al* who suggested taking the polymer to the quinoid form to provide extra stabilization.⁴⁴ Their attempts relied on two different sets of electropolymerization conditions; however, their research did not prove successful.⁴⁴ Since, that time various others have looked into manufacturing cyclopenta[*c*]thiophenes and their derivatives by utilizing various modifications and novel approaches, and yet they too experienced similar results to Wynberg, Zwaneburg, and Roncali.⁴⁵⁻⁴⁹

Where the research that is being proposed in this thesis differs from all of the aforementioned techniques is that the synthetic route (Scheme 1.3A and Scheme 1.3B) being proposed is actually a much shorter route than previously attempted. Even more importantly, the synthetic route that is being attempted is filled with mostly fundamental bedrock organic chemistry that can be pulled straight from a textbook. Unfortunately, the research described in this thesis only reaches the lactone step due to time constraints. However, ongoing research is still being conducted in the Snyder lab to see this synthesis reach completion with the desired result of cyclopenta[*c*]thiophene anions (Figure 1.8A)

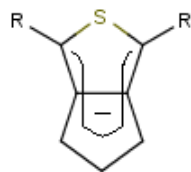
formed to create conductive polymers (Figure 1.8B), or cyclopenta[*c*]thienyl manganese complexes (Figure 1.8C) and similar organometallic compounds to create various diodes.



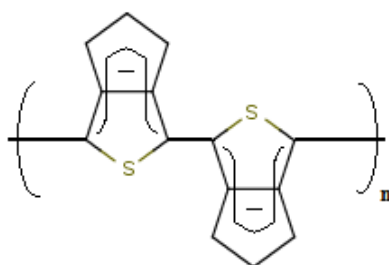
Scheme 1.3A: Proposed synthetic route for synthesis of cyclopenta[*c*]thiophenes



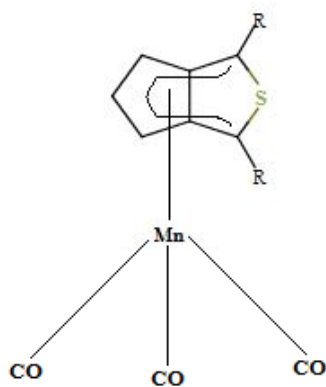
Scheme 1.3B: Continuation of proposed route for synthesis of cyclopenta[*c*]thiophenes



A.



B.



C.

Figure 1.8: A. cyclopenta[*c*]thiophene anion, B. cyclopenta[*c*]thiophene polymer, C. cyclopenta[*c*]manganese complex.

II. Chapter Two

Reactions took place utilizing standard organic synthetic techniques under air unless otherwise noted, CDCl_3 (Sigma-Aldrich Chemistry,) aqueous formaldehyde (Sigma-Aldrich Chemistry), triethylamine (Sigma-Aldrich Chemistry), dimethyl sulfoxide (Sigma-Aldrich Chemistry), and MgSO_4 (Sigma-Aldrich Chemistry) were used without any further purification. **(1A)** 3,4-Bis(chloromethyl)-2,5-dimethylthiophene, **(1B)** 3,4-Bis(chloromethyl)-2,5-dimethylthiophene **(2)** 3,4-diformyl-2,5-dimethylthiophene, **(3)** 3,4-Bischloromethyl-2,5-dichlorothiophene, **(4)** 3,4-Bis(chloromethyl)-2,5-dibromothiophene, **(5)** 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one, and **(6)** 1,3-Dimethyl-7,8-dihydro-4H-thiene[3,4-c]oxepin-6-one were prepared according to methods listed in the literature with modifications being reported.

^1H and ^{13}C NMR spectra were recorded on a JEOL-500MHz spectrometer at ca. 22 °C and were referenced to residual solvent peaks. Infrared spectra were recorded on a PerkinElmer Spectrum One FT-IR spectrometer. Elemental Analysis was recorded via a LECO *TruSpec Micro CHN* analyzer. X-ray crystallographic data was obtained using a Bruker AXS Kappa APEX II single crystal x-ray diffraction instrument. Melting points were taken on a standard MEL-TEMP II apparatus.

Preparation of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene, $(\text{Me})_2\text{C}_4\text{S}(\text{CH}_2\text{Cl})_2$.

(1A)

3,4-Bis(chloromethyl)-2,5-dimethylthiophene was previously by Wallace and Selegue.²⁶ Details of a modification of their procedure are reported here. 2,5-Dimethylthiophene (Sigma-Aldrich Chemistry) (5.00 g, 44.6 mmol, 5.08 mL) was added to a solution of concentrated 12M HCl (100 mL) and 36.8% aqueous formaldehyde

solution (4.02 g, 134 mmol, 3.72 mL) in a 250 mL round bottom flask. The solution, which stirred overnight at room temperature, turned an amber brown-mustard yellow color with a similarly colored precipitate forming. Dichloromethane (200 mL) was added to dissolve the precipitate. Using a separatory funnel the organic layer was separated from the aqueous layer. After separation of the organic layer from the aqueous layer, the aqueous layer was further extracted with an additional 100 mL of dichloromethane. The combined organic layers were then dried using (MgSO_4). The volatiles were removed using rotary evaporation, which resulted in a tar like product being formed. Thin-layer chromatography was then performed using a mixture of 50/50 chloroform and pentane. Thin-layer chromatography showed multiple bands, some of which corresponded with 2,5-dimethylthiophene indicating that reaction did not reach completion. The reaction scheme was then characterized as unsuccessful with suspected products being Chloromethyl-2,5-dimethylthiophene and 3,4-Bis(chloromethyl)-2,5-dimethylthiophene with unreacted 2,5-Dimethylthiophene also remaining.

Preparation of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene, $(\text{Me})_2\text{C}_4\text{S}(\text{CH}_2\text{Cl})_2$.

(1B)

3,4-Bis(chloromethyl)-2,5-dimethylthiophene was prepared by using the same reaction scheme listed in (1A) with additional modifications of the procedure taking place as reported here. 2,5-Dimethylthiophene (Sigma-Aldrich Chemistry) (5.00 g, 44.6 mmol, 5.08 mL) was added to a solution of concentrated 12M HCl (100 mL) and 36.8% aqueous formaldehyde solution (8.66 g, 289 mmol, 8.00 mL) in a 250 mL round bottom flask. Upon addition of the 2,5-dimethylthiophene the solution turned a vibrant royal blue color. The solution was then allowed to stir overnight at room temperature, after

which period the solution became a deep blue-green color with a royal blue and teal solid precipitating out. Dichloromethane (200 mL) was added to dissolve the precipitate. Using a separatory funnel the organic layer was separated from the aqueous layer. After separation of the organic layer from the aqueous layer, the aqueous layer was further extracted with an additional 100 mL of dichloromethane. The combined organic layers were then dried using (MgSO_4). The volatiles were removed using rotary evaporation, which resulted in a straw yellow solution remaining. Thin-layer chromatography was then performed using a mixture of 50:50 chloroform and pentane. Thin-layer chromatography showed a single distinct band that differed from the initial reactants indicating the reaction had reached completion. The organic solution was then eluted through a silica plug using 50:50 chloroform/pentane to give a clear solution with a very faint golden yellow tint. The solution was then dried using (MgSO_4). The volatiles were removed using rotary evaporation resulting in a solution that was off-white/cream yellow with a consistency of honey. Trituration was then performed using chilled pentane resulting in an off-white solution. Volatiles were then removed using a Schlenk line (vacuum gas manifold) until an off-white powder formed (8.43 g, 40.31 mmol, 90.5%). Crystals were then grown using by taking the unpurified 3,4-Bis(chloromethyl)-2,5-dimethylthiophene solution and then pushing it through a silica plug with 50/50 mixture of hexane and dichloromethane. The resulting liquid was then collected into a clean beaker. The crystal was then grown by spontaneous evaporation in open air inside a 100 mL beaker and a 50 mL beaker. A large dark black crystal was harvested from aforementioned beaker and then cut to size with a scalpel under a stereographic microscope-using plane polarized light. A clear light blue plate-like crystal with the

dimensions of 0.160 mm x 0.300 mm x 0.400 mm was selected and mounted on the goniometer. The Bruker AXS Kappa APEX II collected data for a period of 19.33 hours with data being collected at a temperature of 120 Kelvins. The data was collected along six different axes with 2320 frames being collected over an interval of every 30 seconds. The unit cell dimensions were: $\underline{a} = 7.2287(10) \text{ \AA}$, $\underline{b} = 7.9642(11) \text{ \AA}$, $\underline{c} = 8.9013(16) \text{ \AA}$, $\alpha = 83.807(7)^\circ$, $\beta = 89.913(7)^\circ$, $\gamma = 69.860(5)^\circ$, with a volume = $477.96(13) \text{ \AA}^3$. These values were based upon the refinement of the XYZ-centroids of 5595 reflections above 2θ with $5.484^\circ < 2\theta < 56.59^\circ$. **¹H NMR (¹H (500 MHz, CDCl₃, ppm) $\delta(2.38 (\text{CH}_3), 4.60 (\text{CH}_2)$. Melting point range 48.5-51°C.**

Preparation of 3,4-Diformyl-2,5-dimethylthiophene, (Me)₂C₄S(CHO)₂. (2)

3,4-Diformyl-2,5-dimethylthiophene was previously prepared by Brown, Carruthers, and Pellatt.⁵⁰ The product was prepared exactly as described in the literature with the following modifications taking place. In a clean, oven dried 250 mL three-neck flask 1.16 grams of sodium metal was dissolved into a mixture of 6.1 grams 2-nitropropane and 100 cm³ of anhydrous ethanol at room temperature in an inert N₂ gas environment. After 2 hours 4.4 grams of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was added and allowed to stir overnight at room temperature in an inert N₂ gas environment. The product yielded was a brownish yellow color. The purification method was followed exactly as described in the literature with the following change occurring. During rotary vacuum evaporation, the product was dislodged from the equipment and fell into distilled water that was contained in the water bath. Care was taken using a large separatory funnel to carefully collect the entire organic product, which appeared as an oily yellow film floating on top of the water. Diethyl ether was used to separate the

product from the water, and then the product was dried multiple times with (MgSO₄). The product was then carefully run through a silica plug with a 50:50 mixture of Diethyl ether and Hexane. This afforded a light yellow liquid product. That was then dried using (MgSO₄). This product was then placed directly on a Schlenk line to remove all volatiles. This yielded a mustard yellow crystalline product. Trituration using chilled pentane was then performed to remove additional hydrocarbon impurities and then placed on the Schlenk line to remove the added pentane. This afforded a light yellow crystalline product. The product was then run through two additional silica plugs, trituration, and Schlenk line cycles using the aforementioned procedure yielding a final product that was a pale yellow crystal (0.76 g, 18.2%). **¹H NMR (¹H (500 MHz, CDCl₃, ppm) δ (2.69 (CH₃), 10.52 (C=O)). ¹³C NMR (¹³C (125 MHz, CDCl₃): δ (14.5 (CH₃), 135.3, 149.6 (C=C), 186.9 (C=O)). IR (C₆H₁₂): 1652 (C=C), 1683 (C=O), 2659 (CHO). EA: 58.2% C, 6.94% H, 0.07715% N. Melting point range 80.5-92.0°C.**

Attempted preparation of 3,4-Bis(chloromethyl)-2,5-dichlorothiophene, Cl₂C₄S(CH₂Cl)₂. (3)

Method A: In a clean 250 mL round bottom flask 2,5-Dichlorothiophene (Sigma-Aldrich Chemistry) (5.00 g, 32.67 mmol, 3.47 mL) was added to a mixture of concentrated 12M HCl (100 mL) and 36.8% aqueous formaldehyde solution (6.80g, 213.36 mmol, 6.28 mL). This was allowed to stir overnight at room temperature. This yielded an opalescent clear liquid to which 200 mL of dichloromethane was added to separate the organic layer via separatory funnel. An additional rinse with 100 mL of dichloromethane was then performed on the inorganic layer; afterwards the organic layers were collected and dried via (MgSO₄). The volatiles when the removed using

rotary evaporation, yielding a viscous pearlescent liquid. This was then pushed through a silica plug using a 50:50 mixture of dichloromethane and hexane, affording a clear liquid product. Volatiles were removed using rotary evaporation and ^1H NMR was performed. There was no trace of the desired product, and Thin layer chromatography using pentane was performed which indicated that the reaction did not go to completion.

Method B: In a 250 mL round bottom flask 2,5-Dichlorothiophene (5.00 g, 32.67 mmol, 3.47 mL) was combined with concentrated 12 M HCl (100 mL), 36.8% aqueous formaldehyde solution 6.80 g, 212.36 mmol, 6.28 mL), and Aliquat 336 (5.00 mL) and allowed to stir at 30.0-40.0°C for 24 hours. This yielded an opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by 10°C and allowed to stir for additional 24 hours. This yielded an opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by 15°C so that overall temperature was 75°C and allowed to stir for additional 24 hours. This yielded a dark brown-yellow liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by 15°C so that overall temperature was 90°C and allowed to stir for additional 72 hours. This yielded a dark brown-yellow liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature of the reaction was then increased to 110°C and allowed to stir for 120 hours. Two TLC plates were performed each day, yet reaction did not reach completion. After 120 hours, the product was a dark burnt brown color with an oil slick like appearance. TLC plates indicated that reaction

had not reached completion and had actively decomposed. Reaction was deemed unsuccessful.

Method C: In a 250 mL round bottom flask 2,5-Dichlorothiophene (5.00 g, 32.67 mmol, 3.47 mL) was combined with concentrated 12 M HCl (100 mL), 36.8% aqueous formaldehyde solution 6.80 g, 212.36 mmol, 6.28 mL), and Aliquat 336 (5.00 mL) and allowed to stir at 30.0-40.0°C for 24 hours. This yielded an opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by 5°C and allowed to stir for additional 24 hours. This yielded an opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by and 5°C so that overall temperature was 50°C and allowed to stir for additional 24 hours. This yielded a opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature was then increased by 5°C so that overall temperature was 55°C and allowed to stir for additional 72 hours. This yielded a opalescent clear liquid. Thin layer chromatography using pentane was performed, which indicated the reaction did not reach completion. The temperature of the reaction was then increased to 60-65°C and allowed to stir for 120 hours. Two TLC plates were performed each day, yet reaction did not reach completion. After 120 hours, the product was a dark brown-yellowish color with an oil slick like appearance. TLC plates indicated that reaction had not reached completion and had actively decomposed. Reaction was deemed unsuccessful.

Method D: The following synthesis is a modification of synthetic route first described by W.D. Liu and coworkers.⁵¹ The reactants were first allowed to chill

overnight in a refrigerator. A 250 mL clean round bottom flask was placed in a large plastic tub on top of a magnetic stirrer. A magnetic stir bar was then placed inside of the round bottom flask. To the large plastic tub ice, salt, and water were added to create an ice bath. The round bottom flask was chilled to 0°C. To the chilled round bottom flask the chilled concentrated 12 M HCl (100 mL) and 36.8% aqueous formaldehyde solution (6.80 g, 212.36 mmol, 6.28 mL) and allowed to stir for three minutes. Next, 2,5-Dichlorothiophene (5.00 g, 32.67 mmol, 3.47 mL) was added in a drop wise fashion over a period of seven minutes. Next, Aliquat 336 (2.50 mL) was slowly added. The reaction was carried out over a 32-hour period, with ice, salt, and water being added to the ice bath as need; while every one to two hours a TLC plate was run to track the progress of the reaction to see when it reached completion. After the 32-hour period, the TLC plates indicated that no reaction had taken place. The product remained an opalescent clear liquid. The reaction was then removed from the ice bath and allowed to reach room temperature. After 38 hours had passed the TLC plate showed three spots indicating the reaction had begun. The product was allowed to stir at room temperature for an additional 336 hours, after which TLC was performed that indicated that the reaction did not reach completion. This reaction was then deemed unsuccessful.

Attempted preparation of 3,4-Bis(chloromethyl)-2,5-dibromothiophene, $\text{Cl}_2\text{C}_4\text{S}(\text{CH}_2\text{Br})_2$. (4)

In a clean 250 mL round bottom flask 2,5-Dibromothiophene (3.00 g, 12.40 mmol, 1.40 mL) was added to a solution of concentrated 12 M HCl (100 mL), 36.8% aqueous formaldehyde (2.58 g, 80.6 mmol, 2.38 mL), and Aliquat 336 (2.00 mL) and allowed to stir overnight at room temperature. The solution remained clear, and thin layer

chromatography was performed indicating that no reaction had taken place. The reaction was then allowed to stir for 72 hours at room temperature. Thin layer chromatography showed three different spots, one of which corresponded with the reactants and the other two did not. During the 72-hour period, the solution went from a clear liquid to an opalescent yellow color. The reaction was then allowed to stir an additional 72 hours at room temperature. There was no change in color, and TLC continued to show three different spots. The reaction was then heated to 30.0-40.0 °C and allowed to stir for 24 hours. There was no changes indicated; therefore, reaction was allowed to stir an additional 120 hours at room temperature. After the 120-hour period, there was no change in appearance and TLC continued to show three different spots. The reaction was then deemed unsuccessful.

Preparation of 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one, C₁₄H₁₆O₄S. (5)

1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one was previously prepared by Snyder, Selegue, Dosunmu, Tice, and Parkin.⁴⁹ The product was prepared exactly as described in the literature with the following modifications taking place. To a solution of Dimethyl sulfoxide (33.0 g, 423 mmol, 40.1 mL) 2,2-dimethyl-1,3-dioxane-4,6-dione (3.85 g, 26.74 mmol) was dissolved. To this solution, triethylamine (5.55 g, 54.82 mmol, 7.70 mL) was added. The resulting mixture was placed in a clean 250 mL round bottom flask and allowed to stir for 30 minutes at room temperature. Next, 3,4-Bis(chloromethyl)-2,5-dimethylthiophene (3.00 g, 26.74 mmol) was added to the solution and allowed to stir 24 hours at room temperature. A yellow liquid formed overnight. The mixture was then purified using the exact methods indicated

in the literature; however, a sludge-like yellow product formed instead of large colorless crystals. The product was then run through a silica plug using a 50:50 mixture of ethyl ether and hexane. The resulting yellow product was then placed on a rotary evaporator to remove all volatiles. Next trituration was performed using chilled pentane while chilling the 250 mL round bottom flask over liquid nitrogen. Product was then placed on a Schlenk line, yielding a yellow needle-like product. **¹H NMR (¹H (500 MHz, CDCl₃, ppm) δ 1.57 (2, 6H), 2.23, 2.38 (s, CH₃), 3.89, 4.56 (s, CH₂)).**

Preparation of 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-c]oxepin-6-one, C₁₀H₁₂O₂S.
(6)

1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-c]oxepin-6-one, was previously prepared by Snyder, Selegue, Dosunmu, Tice, and Parkin.⁴⁹ The product was prepared exactly as described in the literature with the following modifications taking place. 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one (0.14 g, 0.499 mmol) was dissolved into a 100 mL round bottom flask that contained acetonitrile (10 mL) and KI (1 crystal). This mixture was allowed to stir for 24 hours at room temperature under reflux conditions. A yellow sludge like residue was formed. The solvent was extracted via rotary evaporation. The yellow residue was then flushed through a silica plug with 50:50 dichloromethane and ethyl acetate yielding a blue-greenish liquid. This liquid was then dried using (MgSO₄), and then placed on a rotary vacuum to remove all volatiles. The blue-green sludge like product was then placed on a Schlenk line for 30 minutes yielding a forest green solid residue (0.07 g). **¹H NMR (¹H (500 MHz, CDCl₃, ppm): δ 1.75, 2.30, 2.98, 3.78, 5.29). ¹³C NMR (¹³C (500 MHz, CDCl₃, ppm): δ 76.8, 77.1, 77.4). IR (C₆H₁₂): 1612 , 1713, 1737 (C=O).**

III. Chapter Three

Synthesis and Analysis of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

The first attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dimethylthiophene used a ratio of three times the mmol of reaction grade formaldehyde for every one mmol of reaction grade 2,5-dimethylthiophene. To this mixture, concentrated 12 *M* HCl was added. The reaction took on an oily like appearance; however, there was no notable color change. This reaction was carried out in a clean 250 mL round bottom flask that contained a magnetic stir bar, and was situated over a magnetic stir while being exposed to atmospheric conditions. After twenty-four hours of stirring a burnt yellow, tar like product was formed. This product was then purified using the materials and methods described in the experimental section. Thin layer chromatography showed three bands, one of which was consistent with the starting reactant and the other two that were separate. No further characterization techniques such as ¹H NMR, ¹³C NMR, or IR Spectroscopy were performed.

The success of the reaction was called into question because of the color and consistency that the product took on. According to the literature, the product was expected to take on a bright blue-green color twenty-four hours after stirring. Furthermore, the product was expected to have dark green solid precipitate that had formed in the bottom of the flask. This was clearly not the case, as the product did not have the right consistency or color. This in turn led to thin layer chromatography being performed to check if reaction had indeed reached completion. Multiple bands on a TLC plate indicate that something did not go right with the experiment. Additionally, with one of the TLC plate's band corresponding to the reactant, this showed that the reaction did

not reach completion. It is speculated that the monochlorinated product, as well as the bis/dichlorinated product formed. This conclusion is gathered from the fact that the two other bands on the TLC plate did not correspond to the reaction, and each showed different affinities for the TLC plate.

The second attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dimethylthiophene used a ratio of six times the mmol of reaction grade formaldehyde for every one mmol of reaction grade 2,5-dimethylthiophene. To this mixture, concentrated 12 *M* HCl was added. One key observation was that upon the addition of the respective reactants the mixture became a vivid blue/green color with a texture that appeared rather viscous. This reaction was carried out under identical conditions as the first attempt; however, the results obtained were significantly different. After twenty-four hours, the product was a deep blue-green color with royal blue and teal precipitate forming having formed in the flask. The product was then purified using the same methodology employed during the first attempt. Afterwards, the success of the reaction was tested by performing thin layer chromatography on the product. The results of the thin layer chromatography plate showed the formation of one unique band that was separate from the reactants band. The product was then further purified until an off-white powder remained. The synthetic route performed afforded a high yield of 90.5%.

The second attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was much more successful than the first attempt. The reaction proceeded as expected, with color changes mirroring those previously observed in the literature. The success of this reaction can also be noted from the one unique band that formed on the TLC plate, instead of the three bands previously observed. A benefit of this synthetic route was the

relative ease, and simplicity of synthesizing the desired product. The simplicity of this reaction can be seen in the number of reactants required to yield the desired product, as well as the fact that the reaction did not require any special atmospheric and/or heating/cooling steps.

In order to confirm that the product yielded from the synthesis described above was indeed 3,4-Bis(chloromethyl)-2,5-dimethylthiophene additional analytical techniques were performed in conjunction with thin layer chromatography. The first analytical technique performed was the determination of the melting temperature, which can help confirm the purity of the product. The product had a melting temperature of 48.5-51.0 °C, indicating a relatively pure substance.

In order to determine the structure of the product a ^1H NMR was obtained. The ^1H NMR spectra showed two major singlets (Figure 4.0). The first singlet occurred at $\sim\delta 2.38$ (CH_3) while the second singlet appeared at $\sim\delta 4.60$ (CH_2). The singlet observed at 2.38 ppm corresponds to a methyl (CH_3) chemical shift, and directly matched the reported value that Wallace and Selegue obtained for their first singlet.²⁶ Additionally, the singlet observed at 4.60 ppm corresponds to a methylene (CH_2) chemical shift, and is almost the exact same value that Wallace and Selegue obtained of 4.59 ppm²⁶. The ^1H NMR spectra also showed that there were trace amounts of contaminants that were not removed during the purification steps. This can be seen by noting the small singlet that appeared at 1.56 ppm. Nevertheless, the results of the ^1H NMR spectra provide strong evidence that the product is indeed 3,4-Bis(chloromethyl)-2,5-dimethylthiophene.

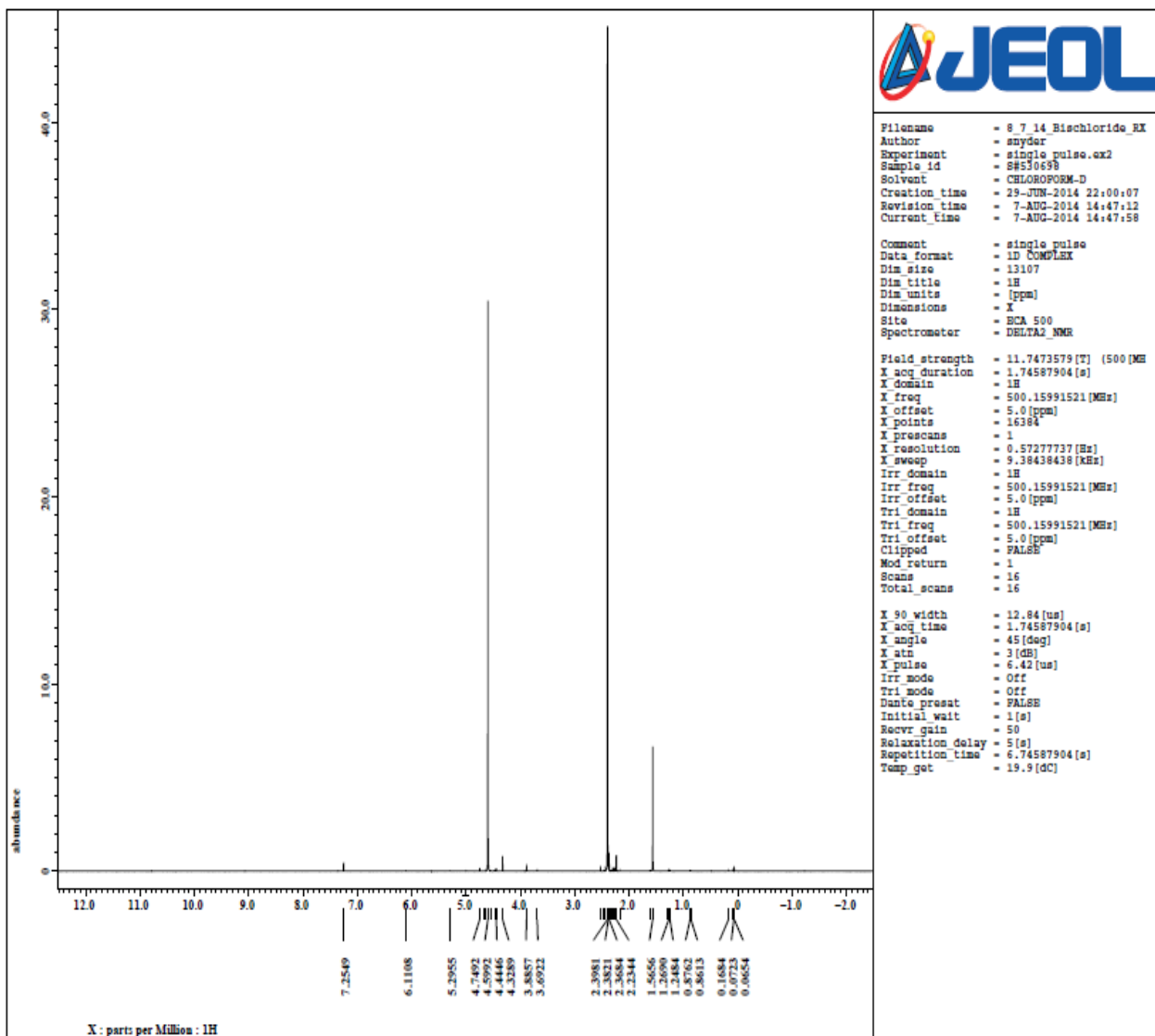


Figure 4.0: ^1H NMR Spectra of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

An x-ray crystallographic study was also performed on the product to further confirm its identity as 3,4-Bis(chloromethyl)-2,5-dimethylthiophene and to determine the final structure. Crystals were grown using the unpurified 3,4-Bis(chloromethyl)-2,5-dimethylthiophene solution and then pushing it through a silica plug with 50/50 mixture of hexane and dichloromethane. The resulting liquid was then collected into a clean beaker. Crystals were then grown by spontaneous evaporation in open air inside a 100 mL beaker and a 50 mL beaker. Recrystallization was highly successful. On multiple occasions with differing atmospheric and environmental conditions, the product readily started to crystallize even before completing the purification process.

A clear light blue plate-like crystal with the dimensions of 0.160 mm x 0.300 mm x 0.400 mm was harvested from the beaker and then mounted inside of the goniometer. The Bruker AXS Kappa APEX II collected data for a period of 19.33 hours with data being collected at a temperature of 120 Kelvin. The data was collected along six different axes with 2320 frames being collected over an interval of every 30 seconds. The structure of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene can be seen in Figure 4.1, and the crystal data collection and structure refinement parameters can be seen in Table 4.1 and 4.2 respectively. The bond angles and bond lengths of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene can be seen in Table 4.3 and Table 4.4 respectively.

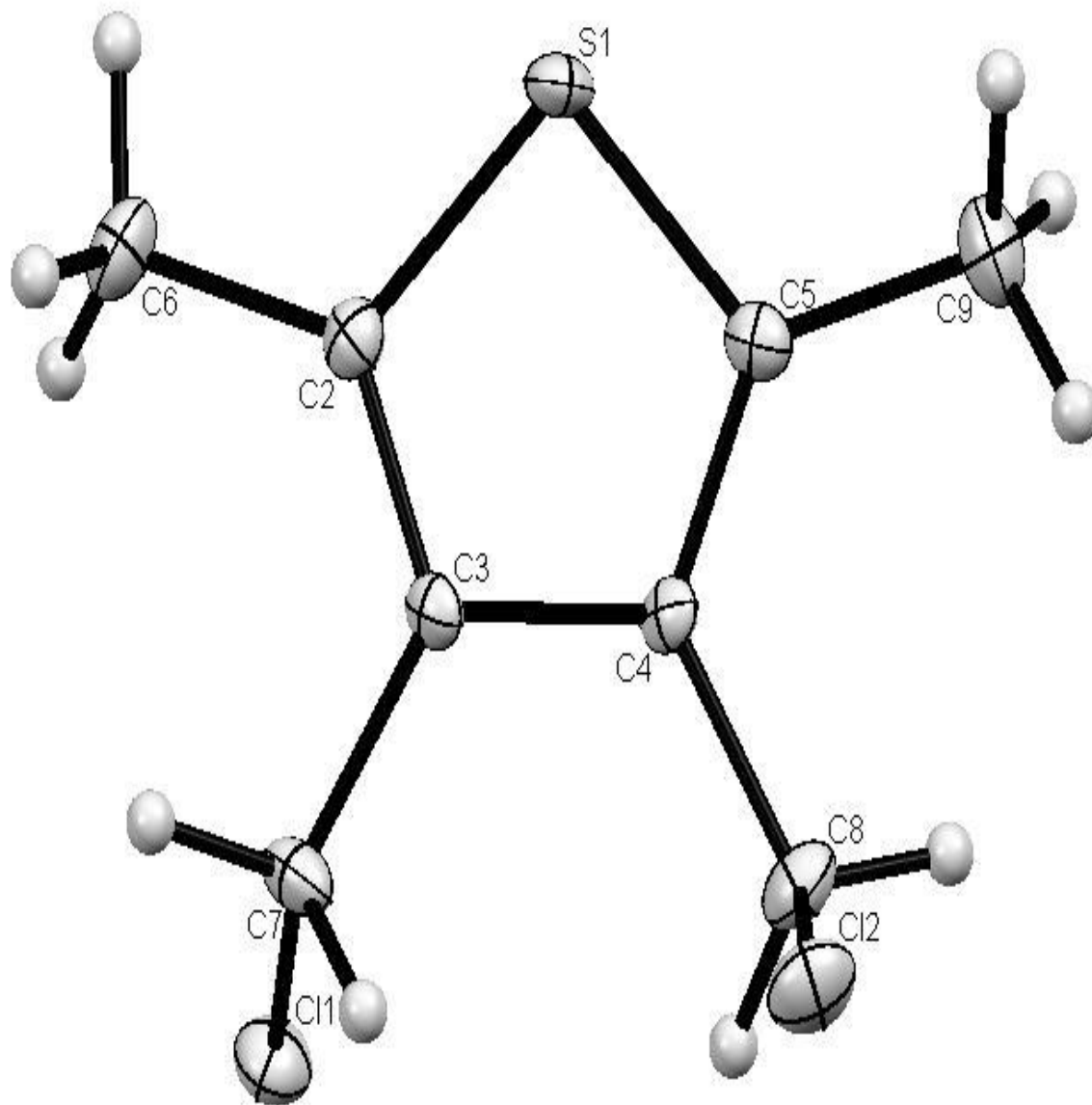


Figure 4.1: Crystal structure of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

Table 4.1: Crystal Data Collection for 3,4-Bis(chloromethyl)-2,5-dimethylthiophene.

Identification code	BisChloroS	
Chemical formula	C ₈ H ₁₀ Cl ₂ S	
Formula weight	209.12 g/mol	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal size	0.160 x 0.300 x 0.400 mm	
Crystal habit	clear light blue plate	
Crystal system	Triclinic	
Space group	P $\bar{1}$	
Unit cell dimensions	a = 7.2287(10) Å	$\alpha = 83.807(7)^\circ$
	b = 7.9642(11) Å	$\beta = 89.913(7)^\circ$
	c = 8.9013(16) Å	$\gamma = 69.860(5)^\circ$
Volume	477.96(13) Å ³	
Z	2	
Density (calculated)	1.453 g/cm ³	
Absorption coefficient	0.831 mm ⁻¹	
F(000)	216	

Table 4.2: Structure Refinement Parameters for Crystallographic Determination of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

Theta range for data collection	2.30 to 27.50°
Index ranges	-9<=h<=9, -10<=k<=10, -11<=l<=7
Reflections collected	6152
Independent reflections	2134 [R(int) = 0.0291]
Coverage of independent reflections	96.8%
Absorption correction	multi-scan
Max. and min. transmission	0.8790 and 0.7320
Refinement method	Full-matrix least-squares on F ²
Refinement program	SHELXL-2014/6 (Sheldrick, 2014)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	2134 / 0 / 102
Goodness-of-fit on F²	1.120
Δ/σ_{\max}	0.059
Final R indices	1987 data; I>2 σ (I) R1 = 0.0866, wR2 = 0.2309
	all data R1 = 0.0890, wR2 = 0.2321
Weighting scheme	w=1/[$\sigma^2(F_o^2)+(0.1199P)^2+3.3317P$] where P=(F _o ² +2F _c ²)/3
Largest diff. peak and hole	3.134 and -0.756 eÅ ⁻³
R.M.S. deviation from mean	0.202 eÅ ⁻³

Table 4.3: Bond Angles of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

C5-S1-C2	93.4(2)	C3-C2-C6	128.4(4)
C3-C2-S1	110.9(3)	C6-C2-S1	120.7(4)
C2-C3-C4	112.9(4)	C2-C3-C7	124.1(4)
C4-C3-C7	123.0(4)	C5-C4-C3	112.3(4)
C5-C4-C8	123.8(4)	C3-C4-C8	123.9(4)
C4-C5-C9	128.9(4)	C4-C5-S1	110.6(3)
C9-C5-S1	120.5(3)	C3-C7-C11	112.0(3)
C4-C8-C12	111.6(3)		

Table 4.4: Bond Lengths of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene

S1-C5	1.720(5)	S1-C2	1.713(5)
C11-C7	1.813(5)	Cl2-C8	1.815(5)
C2-C3	1.364(6)	C2-C6	1.504(6)
C3-C4	1.447(6)	C3-C7	1.482(6)
C4-C5	1.373(6)	C4-C8	1.489(6)
C5-C9	1.497(6)		

The X-ray crystallographic confirms the product to be 3,4-Bis(chloromethyl)-2,5-dimethylthiophene. This can be concluded by observing the bond angles, bond lengths, and reported density of the crystal. The 3,4-Bis(chloromethyl)-2,5-dimethylthiophene product is expected to have two double bonds within the thiophene system. These two double bonds are expected to be between the second (C2) and third (C3) carbon as well as between the fourth (C4) and fifth (C5) carbon when examining Figure 4.1. A carbon carbon double bond has an average bond length of 1.34 Angstroms and an average bond angle of 120 degrees if sp^2 hybridized which is the case for the aforementioned carbons. If one were to examine the experimental values obtained from the x-ray crystallographic study with these values one would see that the experimental values closely correlate to the values reported in the literature. Case in point the C2-C3 bond has a reported bond length of 1.365 Angstroms. The percent difference between the experimental values and the reported values for the C2-C3 bond length is only 1.87% different, and for C4-C5 the difference is only 2.54%. This is well within reason, as the values can fluctuate slightly due to the dynamic interactions that are occurring within the molecule.

Synthesis and Analysis of 3,4-Diformyl-2,5-dimethylthiophene

The next reaction scheme that was attempted was the synthesis of 3,4-Diformyl-2,5-dimethylthiophene. The use of sodium metal dissolved in 2-nitropropane and anhydrous ethanol created the very strong based of sodium ethoxide. When the 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was added to the mixture and allowed to stir overnight in an inert N_2 gas environment a brownish yellow liquid product was obtained. During purification steps, the round bottom flask that contained the product became dislodged from the rotary vacuum evaporator and fell into the water bath. This caused

water to rush into the flask, pushing some of the desired product into the water bath and contaminating the remaining product in the flask. Due to the inherently high cost of the experiment, care had to be salvage as much of the organic product as possible. Therefore, the intense purification methods described in the experimental section were put in place. After the purification steps were completed, a solid yellow crystalline product was obtained with an 18.2% yield.

One of the biggest negatives associated with this synthetic route is the fact that anhydrous ethanol must be used, which in turn greatly increase the overall cost of carrying out the reaction. The alternative method of obtaining anhydrous ethanol would require traditional distillation as well as fractional distillation. These two processes are extremely time consuming, and can be difficult to accomplish. The reason why anhydrous ethanol had to be used is that this reaction is extremely hydrophilic during its initial stages. Therefore, any water that is within the reagents or the environment can hijack the reaction and cause the formation of undesired products. This in turn increased the difficulty of the reaction, and meant that special procedure such as setting up an inert N₂ gas environment. Extreme caution also had to be exercised because of the high reactivity that sodium metal displays. Unfortunately, due to equipment malfunctioning the overall yield and purity was quite low. Therefore, it is hard to say that the reaction was a success or a failure.

To characterize the product and confirm its identity as 3,4-Diformyl-2,5-dimethylthiophene the first characterization technique employed was determining a melting point range. The product had a melting point of 80.5-92.0 °C, a quality that could be attributed to the thermal instability of the product. Next, an elemental analysis was

performed on a small sample of the product. The results of the elemental analysis showed that 58.2% of the product was made of carbon, while 6.94% of the product was hydrogen. The experimental values indicate that carbon should make up 57.1% of the product while hydrogen should make up 4.76% of the overall product. The increased amount of carbon and hydrogen in the product likely corresponds to trace hydrocarbon impurities that were not removed during the purification stage. There was a trace amount of nitrogen (0.07715%) that appeared in the report; however, this small amount is not significant and can likely be attributed to minute contamination of the equipment used to conduct the elemental analysis.

To determine the structure of the product ^1H NMR, ^{13}C NMR, and IR spectroscopy were performed. The ^1H NMR spectra showed two major singlets. The first singlet appeared at $\sim\delta 2.69$ (CH_3) while the second singlet appeared at $\sim\delta 10.52$ ($\text{C}=\text{O}$). The first major singlet that appeared at ~ 2.69 ppm corresponds to a methyl chemical shift, while the second singlet that occurs further downfield at ~ 10.52 ppm corresponds to a carbon-oxygen double bond. It was very encouraging to see the second singlet because a singlet that appears between 9.5 ppm to 10.75 ppm generally relates directly to an aromatic aldehyde, of which the desired product should contain.

The ^1H NMR did show that there was minor contamination from benzene and various other hydrocarbons as is evident by the multiple small signals that appear before $\delta 2.69$ ppm.

The ^{13}C NMR spectra showed four major singlets. The first signal relates to a carbon in a CH_3 environment. This singlet appeared at $\sim\delta 14.5$ (CH_3). The next two signals relate to a carbon that has a double bond to another carbon atom, that is to say a

carbon that is in a C=C environment. These singlets appeared at $\sim \delta 135.3$ (C=C) and $\sim \delta 149.6$ (C=C) respectively. The signal that was farthest downfield corresponds to a carbon that has a bond to an oxygen atom. That is to say that that particular carbon is in a C=O type of environment. This singlet appeared at $\sim \delta 186.9$ (C=O) and is particularly important in providing evidence that the diformyl aldehyde was created. One important item to note is that the signals that appear in the range of $\sim \delta 76.0-77.8$ are due to hydrocarbon impurities that were not successfully removed during the purification stage.

The final structural analysis technique employed to determine the 3,4-Diformyl-2,5-dimethylthiophene's structure was an IR spectroscopy. Infrared spectroscopy is helpful in regards to determining a product's structure because it helps reveal which structural groups are present within the analyzed product. The IR spectra obtained from analyzing the suspected diformyl product showed three key peaks. The key peaks seen were (C₆H₁₂): 1652 cm^{-1} (C=C), 1683 cm^{-1} (C=O), 2659 cm^{-1} (CHO). The signal seen at 1683 cm^{-1} corresponds directly to an α,β -unsaturated aldehyde, while the signal seen at 2659 cm^{-1} corresponds directly to an aldehyde that has a sp^2 hybridized carbon that is double bonded to oxygen and has a single bond to hydrogen. These two signals provide the final piece of evidence to help definitively state that the diformyl aldehyde was formed.

Results and Analysis of the Attempted Syntheses of 3,4-Bis(chloromethyl)-2,5-dichlorothiophene.

The next attempted synthesis was the synthesis of 3,4-Bis(chloromethyl)-2,5-dichlorothiophene. Multiple attempts were made to synthesize the desired product; however, each synthesis failed to have the desired results. The method used during the

first attempt was based on the previously successful synthesis of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene. The exact same ratios of 6 mmol of reaction grade formaldehyde for every 1 mmol of reaction grade 2,5-Dichlorothiophene were used along with concentrated twelve molality hydrochloric acid. This mixture of reactants caused an opalescent clear liquid with an oil slick appearance to form, especially when stirred for twenty-four hours at room temperature. Afterwards, the product was purified using the previously mentioned methods, and an attempt to characterize the product took place.

The first attempt at synthesizing the product was believed to be successful, and would have been an exciting result due to the simplicity and straightforwardness of obtaining the product. Since there is little detail on how to synthesize this particular compound in the literature, the results of this experiment if successful may have well presented an opportunity for publication. Nevertheless, this was not the case as evident by the first analysis of the product and the subsequent attempts to synthesize the desired product.

The first analytical technique employed was a ^1H NMR of the product. The NMR showed three major peaks instead of one major peak that would have corresponded to the methylene (CH_2) group that was bound to the chlorine atom at either the third or the fourth carbon. The three peaks that were observed were seen as singlets at $\sim\delta 1.57$, $\sim\delta 2.38$, and $\sim\delta 4.60$. The only signal that should have been observed was the signal at ~ 2.38 ppm. One of the main ways that three signals could be observed is if the product was not dichlorinated, but rather monochlorinated. This result would mean that the ^1H NMR was not examining a symmetrical product (as expected), but rather an unsymmetrical product. Due to the unexpected results seen in the ^1H NMR, thin layer

chromatography was used to determine if the reaction had reached completion. The thin layer chromatography plate showed three different bands, one of which corresponded directly with the 2,5-dichlorothiophene and two others that had traveled further on the plate. This indicated that the reaction did not reach completion, and that there was unreacted reactant and monochloromethylated byproduct within the desired product. This too could have caused the multiple singlets to appear in the ^1H NMR report.

The next attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dichlorothiophene began using the same methods employed during the first synthesis attempt; however, a phase transfer catalysis (Aliquat 336) was added to help lower the activation energy and push the reaction towards completion. In addition to the phase transfer catalysis, being added a heat was added so that the mixture reached a temperature of 30-40 °C. After twenty-four hours of stirring under a gentle, heat the product had the same opalescent clear appearance as before, but it did not have the oil slick like appearance. Instead of performing an ^1H NMR first, thin layer chromatography was used to check if the product had reached completion. The results of performing TLC were the same as the previous trial. Multiple heating and stirring cycles were then used in an attempt to drive the reaction to completion. An interesting observation occurred after increasing the heat to 75 °C and that was that the liquid inside the round bottom flask turned a dark brown-yellow color. Thin layer chromatography; however, still showed that the reaction had not reached completion. In a last ditch, effort to drive the reaction to completion the mixture was heated to 110 °C and allowed to stir for one hundred twenty hours. Each day two different TLC analysis were performed; however, the TLC plates showed that unreacted reactant remained. After 120 hours, the product took on a dark burnt brown color with an

oil slick appearance. Thin layer chromatography showed multiple bands indicating that the reaction had not reached completion, and instead started to decompose.

The next attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dichlorothiophene tried to hone in on the exact temperature that caused the liquid product to change from the opalescent clear color to the dark brown-yellow color. It was believed that the reaction might be highly sensitive, and therefore a narrow temperature range existed where the reaction would reach completion while not decomposing.

To test this hypothesis the reaction was slowly heated up from 30 °C to 50 °C over a period of three days. Each day the thin layer chromatography showed multiple bands. Next, the temperature was increased to 55 °C and the mixture was allowed to stir for seventy-two hours, after which time TLC was performed. Once again, TLC showed that the reaction had not reached completion. Furthermore, the mixture had yet to change colors to the dark brown-yellow color previously observed. In one last attempt to drive the reaction to completion, the temperature was increased to 60-65 °C and allowed to stir for 120 hours. Multiple TLC plates were taken over that period, yet the results were the same as the previous results. The only thing of note was that at the end of 120 hours the product took on the same dark brown-yellow color with the oil slick like appearance. The synthesis was then deemed unsuccessful.

The next attempt at synthesizing 3,4-Bis(chloromethyl)-2,5-dichlorothiophene utilized a different approach and was based on a modified version a synthetic route suggested by W.D. Liu and coworkers. Utilizing chilled reactants and an ice bath, the aforementioned reactants were combined in 250 mL round bottom flask and allowed to stir at 0 °C for 32 hours. Each hour TLC was performed, and with the results showing

unreacted reactant, and two product bands. The mixture itself stayed the opalescent clear color and no noticeable changes were observed. After 38 hours, the reaction was allowed to heat from 0 °C to room temperature. After which time it was allowed to stir for an additional 336 hours, after which TLC was performed that indicated that the reaction did not reach completion. The reaction was then deemed unsuccessful.

The overall attempts to synthesize 3,4-Bis(chloromethyl)-2,5-dichlorothiophene were exhaustive, and labor intrusive. The failure to find the perfect conditions necessary to cause the reaction to go to completion currently presents an interesting aside that could use further exploration. One technique that may help drive the reaction to completion is the use of a more concentrated form of formaldehyde to help overcome the strong electronegative nature of the chlorine atoms initially attached to the thiophene derivative. The reason why this is suspected is that the suspected mechanism that this reaction undergoes to reach completion takes place by electrophilic aromatic substitution using a Lewis acid. When chlorine atoms are added to an aromatic ring, they typically deactivate the ring by removing some of the available electron density. This in turn leads to slow reaction rates, incomplete reactions, and complex mixtures forming. This describes the results that were observed during the multiple attempted syntheses perfectly.

Another way to possibly force the reaction to reach completion would be to use a much stronger Lewis acid instead of the more protic hydrochloric acid; however, this is undesirable due to the added risk that comes from working with strong acids. A literature search relived that a successful method of synthesizing the desired product had been rediscovered in 2001 by Wen-Dar Liu *et. al.*, who used a modified procedure discovered by Wynberg *et. al* in 1964. There suggested prep; however, used tin tetrachloride which

is a very strong and dangerous Lewis acid that reacts aggressively, was extremely complicated, and only afforded a low yield of 48%.⁵¹

Results and Analysis of Attempted Synthesis of 3,4-Bis(chloromethyl)-2,5-dibromothiophene

Due to the complications associated with the synthesis of 3,4-Bis(chloromethyl)-2,5-dichlorothiophene a different synthesis utilizing 3,4-Bis(chloromethyl)-2,5-dibromothiophene was attempted. The compound 2,5-dibromothiophene was selected as the starting reagent because it is much less electronegative than chlorine; therefore, it was suspected that using it would circumvent the problems seen during the 2,5-dichloromethane experiment. This synthesis was carried out exactly like the successful 3,4-Bis(chloromethyl)-2,5-dimethylthiophene reaction, except that the phase transfer catalyst (Aliquat 336) was added to the mixture. However, after twenty-four hours of stirring at room temperature the TLC plate indicated that the reaction had not reached completion.

The reaction was then allowed to stir for an additional seventy-two hours at room temperature. Nevertheless, the increase in amount of time stirring did not cause the reaction to reach completion as indicated by TLC. One promising change that was observed, however, was the mixture changed from a clear liquid to an opalescent light yellow color. Therefore, the reaction was allowed to stir for an additional seventy-two hours. Yet again, the results of the TLC plate remained the same and there was no further color change observed.

In the hope to facilitate the reaction of the 2,5-dibromothiophene with the formaldehyde and hydrochloric acid the reaction was heated to 30.0- 40.0 °C and allowed

to stir for one hundred twenty hours. Yet, after this additional increase in temperature and time allowed react the TLC plates continued to show that the reaction would not reach completion. Furthermore, there was no visible change in color or appearance of the reaction mixture, which lead to the synthesis being deemed unsuccessful. Additional trials were not completed due to previous failures during the attempted synthesis of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene.

Synthesis and Analysis of 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one.

After the multiple failed attempts to synthesis either 3,4-Bis(chloromethyl)-2,5-dichlorothiophene or 3-4-Bis(chloromethyl)-2,5-dibromothiophene a new synthetic route was taken utilizing Meldrum's acid to form a lactone from 3,4-Bis(chloromethyl)-2,5-dimethylthiophene. Utilizing a successful reaction scheme described by Snyder *et. al*⁴⁹ the synthesis of 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one was attempted. The reaction was carried out and purified via the steps outlined in the experimental section, and as described in the literature.

One interesting observation was that the product formed appeared as a yellow needle-like material instead of large colorless crystals as described in the literature. Attempts to recrystallize the product were unsuccessful; therefore, trituration using liquid nitrogen was performed to purify the product. One possible reason to explain the difference in color of the product as well as its failure to crystallize could be due to the fact that many of the reactants were old, and of suspect quality. If the reactants were not to their upmost potency then they would not behave as expected. This could cause the

reaction to either take longer, or could result in additional impurities being seen in the final “purified” product.

To analyze the structure and nature of the product formed a ^1H NMR was performed. The ^1H NMR showed five major singlets. The five singlets were seen at $\sim\delta 1.57$, $\sim\delta 2.23$, $\sim\delta 2.38$, $\sim\delta 3.89$, and $\sim\delta 4.56$. Upon initial examination of the suspected product’s structure (Figure 4.2) one would think that a ^1H NMR spectrum would show six major signals instead of five. However, this is not the case because the hydrogens on two of the methyl groups are close enough that the ^1H NMR instrument sees them as one set of six hydrogens instead of two sets of three hydrogens. This signal can be seen as a singlet at ~ 1.57 ppm (2, 6H). The singlets observed at ~ 2.23 ppm and ~ 2.38 ppm are due to methyl chemical shifts. The final two singlets seen at ~ 3.89 ppm and ~ 4.56 ppm are caused by a methylene chemical shift. Even though the ^1H NMR values observed were different than the values reported in the literature, which reported singlets at $\delta 1.63$ (2, 6H), $\delta 2.31$ (s, 3H), $\delta 2.37$ (s, 3H), $\delta 3.57$ (s, 2H), and $\delta 5.09$ (s, 2H); the results are similar enough as to render any difference between the values as insignificant.⁴⁹ The values reported in the literature were obtained using an instrument that was capable of 200 MHz; however, the values seen in ^1H NMR report were obtained using an instrument that was capable of 500 MHz, which could help explain the slight difference in values observed. In addition, there were notable signs of contamination as evident by the vast amount of small signals observed throughout the spectrum.

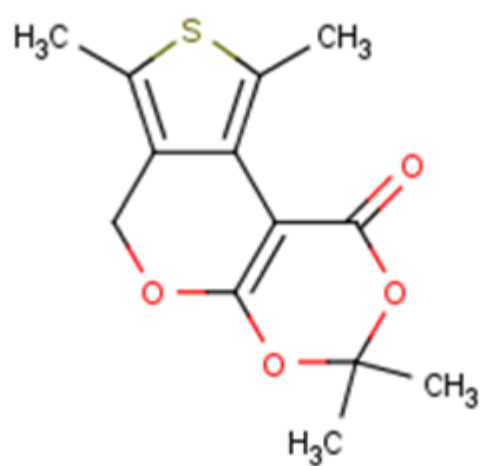


Figure 4.7: Structure of 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one.

Synthesis and Analysis of 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-c]oxepin-6-one

The final product created utilized 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[f]azulen-5-one, which was then dissolved into a 100 mL round bottom flask that contained acetonitrile and KI. The KI served as a catalysis, which helped to lower the activation energy of the reaction. This mixture then stirred for 24 hours at room temperature under reflux conditions. A yellow sludge like residue formed. The solvent was extracted via rotary evaporation. The yellow residue was then flushed through a silica plug that left behind blue-greenish liquid. This liquid was then dried using (MgSO₄), and then placed on a rotary vacuum to remove all volatiles. The final product obtained after the synthesis and purification steps were complete was a forest green solid. This was a notable observation that differed from the results reported by Snyder *et. al*, which reported a product that was white and solid.⁴⁹

Overall, this reaction was straightforward and proceeded with very few problems. In an attempt to duplicate, the results reported in the literature this experiment was performed on a very small scale, which did make it slightly difficult to measure out the necessary reactants. Another problem with carrying the reaction out on a small scale is the little amount of product that it yields. This, therefore, made analytical techniques difficult due to the limited sample size. It should also be noted that the smaller the scale one works on the larger and more drastic mistakes and/or impurities show up. This could explain why the product was a completely different color than the reported product, and it could explain the high degree of impurities seen in the final product. Due to time constraints, and a lack of available pure starting reactants; however, this reaction was

regrettably not attempted on a larger scale. This, in turn, presents an area of research that could be continued by future graduate students.

To help characterize the product, and determine the structure the following analytical techniques were utilized: ^1H NMR, ^{13}C NMR, and IR spectroscopy. The ^1H NMR showed a very busy spectrum that was difficult to interpret. This indicates that there are significant amounts of contaminants within the product. The key “singlets” observed occur at $\sim\delta 1.75$, $\sim\delta 2.30$, $\sim\delta 2.98$, $\sim\delta 3.78$, and $\sim\delta 5.29$. These values roughly correlate to the values observed in the literature.⁴⁹ Nevertheless; it is hard to definitively state which signals are significant, or even state that the signals observed are singlets in the first place.

The ^{13}C NMR showed three singlets that occurred at $\sim\delta 76.8$, $\sim\delta 77.1$, and $\sim\delta 77.4$. This is significantly different from the expected results, which suggest that ten different singlets should be observed in the spectrum. Furthermore, the three signals that are observed do not directly correlate with any values reported in the literature.⁴⁹ One should note how thick the spectrum is compared to previous spectra, indicating contaminants within the product. These impurities may be overwhelming the ^{13}C NMR machine, and thus hiding the actual signals behind noise within the instrument. Due to the nature the ^{13}C NMR, it is also hard to define which carbons correlate to the signals observed. This greatly increased the difficulty, as well as the reliability of stating that this product is indeed the expected product.

The final analytical technique used was IR spectroscopy. The IR spectrum can be seen in Figure 4.3 Some notable bands include the band at $\sim 1612\text{ cm}^{-1}$, as well as the bands at $\sim 1713\text{ cm}^{-1}$ and $\sim 1737\text{ cm}^{-1}$. The signals observed at $\sim 1713\text{ cm}^{-1}$ and $\sim 1737\text{ cm}^{-1}$

indicate a (C=O) bond. One interesting signal not reported in the literature, which could be related to the contaminate within the product is seen at $\sim 2851\text{ cm}^{-1}$ and $\sim 2921\text{ cm}^{-1}$ this signals are a result of (CH₂ asymmetric stretching which is not expected in this product.

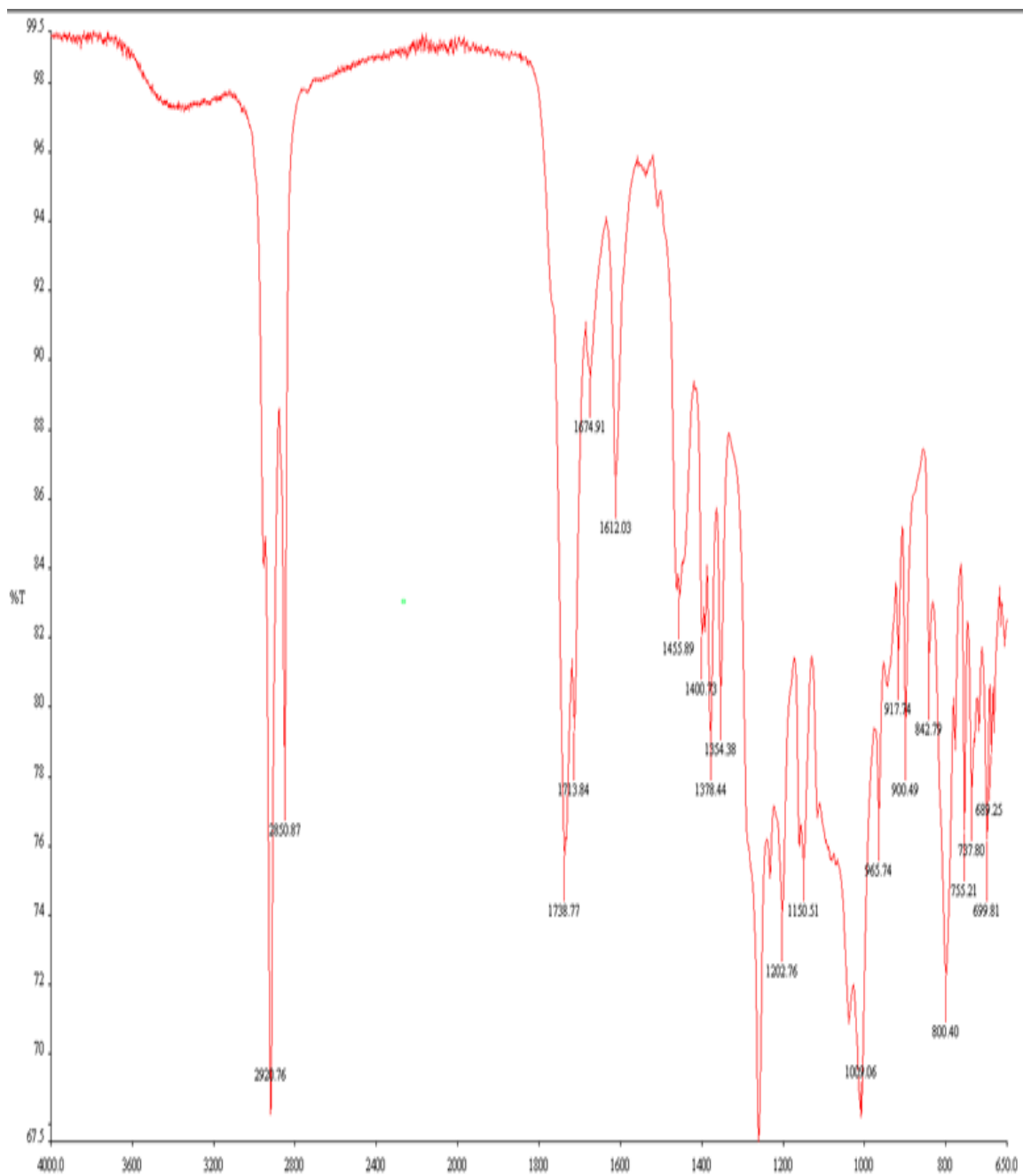


Figure 4.3: IR Spectroscopy of suspected 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-c]oxepin-6-one.

IV. Chapter Four

The formation of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was accomplished using concentrated 12 *M HCl* and reaction grade formaldehyde. This reaction afforded a high yield (90.5%), and was very successful overall. Next, 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was used to create the dialdehyde analog 3,4-Diformyl-2,5-dimethylthiophene. This reaction was carried out using sodium metal and 2-nitropropane. Due to equipment failure, the overall percent yield was very low (18.2%); however, enough product was made so that full characterization and analysis could be performed. The next attempted reactions focused on synthesizing 3,4-Bis(chloromethyl)-2,5-dichlorothiophene from reaction grade 2,5-dichlorothiophene, concentrated 12 *M HCl*, and formaldehyde. Multiple attempts to synthesize the desired product; however, were unsuccessful even after varying the reaction conditions. This series of failed reactions are believed to have occurred due to the strong electronegative nature of the chlorine atoms initially attached to the thiophene derivative. The suspected mechanism that this reaction undergoes to reach completion takes place by electrophilic aromatic substitution using a Lewis acid. When chlorine atoms are added to an aromatic ring, they typically deactivate the ring by removing some of the available electron density. This in turn leads to slow reaction rates, incomplete reactions, and complex mixtures forming. The next attempted reaction was the synthesis of 3,4-Bis(chloromethyl)-2,5-dibromothiophene from reaction grade 2,5-dibromothiophene, concentrated 12 *M HCl*, and formaldehyde. This reaction was chosen because bromine is less electronegative than chlorine, and thus 2,5-dibromothiophene might be able to undergo electrophilic aromatic substitution easier than the 2,5-dichlorothiophene analog. This reaction; however, was also unsuccessful as

it failed to reach completion as well.

Due to multiple failed reactions using either 2,5-dichlorothiophene or 2,5-dibromothiophene it was decided that a different direction in terms of research needed to be taken. Therefore, research shifted into the formation of a lactone from 3,4-Bis(chloromethyl)-2,5-dimethylthiophene with the overall goal of forming cyclopenta[*c*]thiophene anions used to create conductive polymers, or cyclopenta[*c*]thienyl manganese complexes and similar organometallic compounds to create various diodes. Currently, the synthetic route to obtain such complexes is very meticulous due to the complex and exotic chemical techniques that end up yielding a very small amount of product. Where this research hopes to differ is that the synthetic route used in this research will rely on mostly fundamental bedrock organic chemistry that can be pulled straight from a textbook. The first reaction in the new synthetic route was the formation of 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[*f*]azulen-5-one from 3,4-Bis(chloromethyl)-2,5-dimethylthiophene, dimethyl sulfoxide, 2,2-dimethyl-1,3-dioxane-4,6-dione, and triethylamine using the exact procedure established by Snyder *et al.*⁴⁶ This reaction was successful overall, but may have been improved if fresher reactants were used. The next reaction attempted was the synthesis of 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-*c*]oxepin-6-one using 1,3,7,7-Tetramethyl-4H,10H-6,8,9-trioxa-2-thiabenz[*f*]azulen-5-one, acetonitrile, and KI via the procedure outline by Snyder *et al.*⁴⁶ Comparison of the synthesized product's ¹H NMR to that of the literature⁴⁶ offer promising evidence that 1,3-Dimethyl-7,8-dihydro-4H-thieno[3,4-*c*]oxepin-6-one was indeed synthesized. Further evidence comes from the IR spectroscopy, which shows bands at 1612 cm⁻¹, as well as the bands at ~1713 cm⁻¹ and ~1737 cm⁻¹. The signals

observed at $\sim 1713\text{ cm}^{-1}$ and $\sim 1737\text{ cm}^{-1}$ indicate a (C=O) bond. These signals also correlate to the values reported in the literature.⁴⁶ However, one area of concern is that the ^{13}C NMR only shows three singlets that appear at $\sim\delta 76.8$, $\sim\delta 77.1$, and $\sim\delta 77.4$. These values do not match anything in the literature; furthermore, the desired product was suspected to have at least ten unique signals instead of three.⁴⁶ Additionally, there appears to be a lot of contamination within the product. Due to time constraints, research was stopped at this step; however, if there were ample time it is highly recommended that this reaction be carried out again using higher quality reactants.

V. Chapter Five

Due to time constraints, research into the formation of the cyclopenta[*c*]thiophene anions used to create conductive polymers, or cyclopenta[*c*]thienyl manganese complexes did not reach completion, and instead stopped at the formation of the lactone. This, therefore, presents an exciting area of research that can be continued on by future graduate students and undergraduate students alike. If the proposed reaction scheme (Scheme 1.3A and Scheme 1.3B) is successful it would significantly increase the ease of manufacturing cyclopenta[*c*]thiophene complex, thus opening up a new avenue for the creation of organic semiconductors that offer excellent chemical stability and performance characteristics. Furthermore, if this research is successfully pursued it offers graduate and undergraduate students alike an opportunity to be published in a peer reviewed journal. If no significant problems occur, and if higher quality reactants can be obtained it is speculated that this research could be completed within a two-year period maximum.

An additional area of research that could be continued by future graduate and undergraduate students alike would be that of successfully synthesizing either the 3,4-Bis(chloromethyl)-2,5-dichlorothiophene or 3,4-Bis(chloromethyl)-2,5-dibromothiophene. These compounds are relatively novel, and offer the added benefit of being able to be used in multiple different ways much like that of 3,4-Bis(chloromethyl)-2,5-dimethylthiophene was used. These compounds could be made into cyclopenta[*c*]thiophene analogues, pyridazines, pyrroles, or other heterocyclic complexes. This research would also offer the opportunity to be published in a peer review journal, and is speculated that it could be completed within a two-year period.

VI. References

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