Higher Kekulenes and Polymeric Helicenes

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by

Ruth L. Viboh

Dr. Benjamin T. King/Dissertation Advisor

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We recommend that the dissertation prepared under our supervision by

RUTH L. VIBOH

entitled

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Benjamin T. King, Ph.D., Advisor

Matio A. Alpuche, Ph.D., Committee Member

Kam K. Leang, Ph.D., Committee Member

Christopher M. Herald, Ph.D., Committee Member

Sean M. Casey, Ph.D., Graduate School Representative

Marsha H. Read, Ph. D., Associate Dean, Graduate School

May, 2011
Abstract

The main objective of this project was to synthesize, isolate and characterize polymeric helicenes. Because helicenes might have potential applications in the synthesis of ligands for asymmetric catalysis, molecular actuators, conductive and chiroptical materials, we are interested in developing them in polymeric form.

Ring closing metathesis (RCM) reaction was used to furnish the helicenes from a suitably designed polymer precursor, poly{4,6-di[(1E)-(2-$^3$H)-propenyl]}-$m$-phenylene. End group analysis revealed that the polymerization reaction resulted in the formation of both acyclic and cyclic polymers, precursors for helicenes and kekulenes respectively.

Large quantities of monomers were required to optimize both the polymerization and ring closing metathesis reactions. A key finding in the monomer synthesis was the use of the Wittig reaction to circumvent the low yield encountered in a dehydration route towards the synthesis of the target AB monomer for Suzuki polymerization. These reactions were optimized leading to the synthesis of 23 g of monomer in 12 weeks. The Suzuki polycondensation reaction was also optimized leading to the formation of acyclic polymers and macrocycles. RCM of the polymers afforded mixtures of polymeric helicenes and higher kekulenes.

A major finding in this project was the ability to monitor the RCM reaction by observing the disappearance on an IR spectrum of a C-$^3$D label that was incorporated
into the monomer. This allowed monitoring of the reaction, which in turn allowed the reaction conditions to be optimized.

Purification and chromatography using open column gel permeation chromatography afforded [7]kekulene, a mixture of higher kekulenes ([8] – [14]kekulenes) and mixtures of helicenes. The [7]kekulene and helicene mixture were partially characterized using NMR, MALDI-TOF, UV-vis and IR spectroscopic data. Enough material was not available for complete characterization of [7]kekulene. [n]Helicenes were isolated and characterized as a mixture.

We report in this dissertation the first synthesis of higher kekulenes by RCM. We have proof for the formation of polymeric helicenes. [7]Kekulene with a non-planar geometry, mixtures of higher kekulenes and mixtures of polymeric helicenes were synthesized and isolated. Having optimized the reactions for the synthesis of polymeric helicenes and higher kekulenes, these reactions can be carried out on a larger scale to obtain enough material for complete characterization of [7]kekulene and polymeric helicenes.
Dedication

To my parents Loh Michael (RIP) and Loh Mary, and my daughter Vizilanna

Wamucho.
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List of abbreviations

ATR: Attenuated total reflection
CD: Circular dichroism
D: Deuterium
ELSD: Evaporative light scattering detector
GCMS: Gas chromatography mass spectroscopy
GPC: Gel permeation chromatography
h: Hour
HOMO: Highest occupied molecular orbital
IR: Infrared
J: Coupling constant
LUMO: Lowest unoccupied molecular orbital
m: Multiplet
m/z: Mass to charge ratio
MALDI-TOF: Matrix-assisted laser desorption ionization
Min: minute
Mn: Number-average molecular weight
Mw: Weight-average molecular weight
PAH: Polycyclic aromatic hydrocarbon
RCM: Ring closing metathesis
s: Singlet
t : Triplet

t-Bu/"Bu : *tert*-Butyl

THF : Tetrahydrofuran

UV-Vis : Ultraviolet-Visible
Chapter 1: Introduction

Our research group focuses on the synthesis, characterization and determination of some physico-chemical properties of polycyclic aromatic hydrocarbons (PAHs). PAHs are compounds composed of fused benzene rings with all the carbon atoms being sp² hybridized.¹ They occur naturally in coal, tar and oil. Their occurrence in interstellar medium, meteorites and comets has also been documented.² ³ Some PAHs are generated as by-products of fuel combustion. Some are carcinogenic, mutagenic and teratogenic.⁴ ⁵ Carcinogenicity has been linked to the existence of bay regions in PAHs.¹ ⁶

PAHs comprise anywhere from two fused aromatic rings to enormous numbers of rings like in carbon nanotubes. We focus on the synthesis of small to large PAHs such as helicenes, coranulenes, kekulenes and circulenes in our group. In addition to their structural beauty, these compounds are the sub-units, or building blocks, for macromolecular PAH architectures like fullerenes and graphene. The synthesis and determination of the properties of these microstructures can serve as a gateway to understanding the higher analogs and can provide an insight to a better understanding of their adverse biological (carcinogenic) effects.

Our motive and that of other scientists like Harvey⁷ and Mussini⁸ for synthesizing these compounds is to study their structure, determine their properties and establish structure-activity relationships.
1.0 Aim/Relevance of study

My research project aims at the synthesis and characterization of extended polymeric n-helicenes and n-kekulenes.

![n-helicene](image1.png)  ![n-kekulene](image2.png)

**Figure 1-1:** Structure of n-helicene and n-kekulene (n = 0,1,2,3...)

Much success has been accomplished in the field of helicenes following the synthesis of the first helicene in 1903. This paved the way to the synthesis of the longest carbohelicene ([14]helicene) and the longest heterohelicene ([15]thiahelicene) in 1975 and 1981 respectively. It is worth mentioning here that although many reports have been made on the synthesis of various carbo- and heterohelicenes with interesting potential applications, no report has been made for the synthesis of polymeric helicenes. We report herein, the first attempt to synthesize and characterize extended polymeric helicenes and kekulenes. Shawn C. and co-workers demonstrated the effectiveness of the ring closing metathesis (RCM) reaction in the synthesis of helicenes. It is our intention to use this reaction to
form multiple bonds creating many rings from a suitably designed polymer precursor, and thus generate polymeric helicenes and kekulenes. This project is the continuation of work initiated by Margel M. Bonifacio of B. T. King group.

Scheme 1-1: Synthesis of n-helicene

While Bonifacio may have prepared polymeric helicenes, he lacked definitive prove of structure. We seek to overcome this challenge by synthesizing and proving the structure of not only the polymeric helicene, but also n-kekulenes, which happen to be a by-product of our ring closing metathesis reaction (RCM).
In order to obtain sufficient quantities of the monomer, much effort was invested in optimizing certain key reactions in the project like the isomerization reaction of a mixture of 1,5-dibromo-2,4-bis[(2-^2^H)propenylbenzene to afford predominantly the E,E isomer (3), base-catalyzed polymerization reaction leading to the formation of the polymer (5) and the ring closing metathesis (RCM) reaction to generate the product (6) plus [n]kekulenes.

This chapter provides the context for our work in this area.

1.1 Overview of monomer synthesis

Our reaction route for the synthesis of the monomer is the same as that established by Bonifacio (refer to scheme 1.1) with two major differences. The first difference with our current synthesis is the introduction of a deuterium label (in our current synthesis) on the monomer to be used later in monitoring the progress of the RCM reaction. The second difference lies in the reaction used to generate the divinyl monomer (3 and 13). We used Wittig reaction followed by isomerization while Bonifacio used Grignard reaction followed by dehydration.

The reactions below were optimized leading to high product yields (70-98%). The isomerization reaction was both thermally and photochemically catalysed. The photochemical reaction using unstabilized tetrahydrofuran required shorter reaction times and afforded higher yields of product. This isomerization step was an improvement on the dehydration reaction used by Bonifacio. The monomer (14) was obtained in good yield (70 – 80%) and the reaction was reliable and reproducible. We were able to synthesize > 20 g of monomer to be used in the
polymerization. Bonifacio optimized the synthesis leading to the generation of the dialdehyde. The reaction scheme from the dialdehyde to the monomer (14) is illustrated below.

**Scheme 1- 2: Synthesis of labeled monomer (14)**

1.2 Overview of Suzuki polymerization reaction

Our interest in Suzuki coupling reaction stems from our search for an effective reaction to transform our target borylated monomer (14) to our desired poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene (15), the precursor of our RCM reaction.
**Scheme 1-3**: Polymerization reaction with Pd(PPh₃)₄ catalyst.

Initially, we used commercially prepared Pd(PPh₃)₄. This catalyst furnished clean polymerization products from ¹H NMR analysis. Extra peaks were observed in the aromatic region when the same reaction was carried out under similar conditions with aged catalyst. We attributed this to an isomerization product caused by the oxidation of the palladium species in the catalyst to Pd(II). This problem was circumvented by using a freshly prepared palladium catalyst, Pd[(p-tol)₃P]₃.

The polymer generated from these different reactions were characterized using ¹H NMR, ¹³C NMR, matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectroscopy, and gel permeation chromatography (GPC). The Pd[(p-tol)₃P]₃-catalyzed reaction generated polymers with higher molecular weights compared to the Pd(PPh₃)₄-catalyzed reactions. End group analysis performed on data generated from MALDI-TOF revealed the absence of any functional groups at the end of the polymer chains. Calculations and analysis of the
polymer structure revealed the presence of cycles. Some of the polymers had formed macrocycles during the polymerization process. Efficient ring closing metathesis reaction on these cycles furnishes the [n]kekulenes.

1.3 Overview of Ring Closing Metathesis (RCM) reaction

We were able to optimize the preceding polymerization reaction for the synthesis of poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene, resulting in about 1.5 g of our desired product from a single batch. The ring closing metathesis reaction was conducted using a variety of catalysts under different conditions. Grubbs 2nd generation catalyst proved to be the most effective catalyst and 1,2,4-trichlorobenzene was the solvent of choice because it was the only available solvent in which the product was soluble. Details of the reaction conditions leading to the optimization will be discussed in chapter 4. Scheme 1-10 is a generalized equation for the optimized RCM reaction.

Bonifacio utilized 1HNMR data to monitor the progression of his RCM reaction. This did not work well because the product was not fully soluble in any deuterated solvents used. In my project, we used infrared spectroscopy on solid samples using attenuated total reflection (ATR) technique to circumvent this dilemma. We were able to monitor the consumption of the polymer as the reaction progressed and avoided the solubility issues. This method was a lot cheaper and more convenient compared to the 1HNMR method.
Scheme 1-4: RCM reactions

The RCM reaction yielded a mixture of products, [n]helicenes and [n]kekulenes that was separated by chromatography on a polymer-based resin, Biorad s-x1 column eluting with 1,2,4-trichlorobenzene. Kekulenes were isolated from the earlier fractions by virtue of their relatively smaller molecular weight compared to the corresponding helicenes. These compounds were by-products of the RCM reaction resulting from a fully cyclized polymers as illustrated in scheme 1-10. The products were characterized by MALDI-TOF, nuclear magnetic resonance (NMR), Infrared (IR) and ultraviolet (UV) spectroscopies.
1.4 Helicenes

Helicenes, defined as ortho-fused, condensed polycyclic aromatic rings with helical shapes resulting from angularly annulated aromatic rings, represent a class of polycyclic compounds with unique properties and intriguing potential applications. Helicenes came to the limelight in the early 1900s following the synthesis of the first racemic diaza(5)helicene (3,4-diazadibenzo[c,g] phenanthrene (7)) by Meisenheimer and Witte in 1903. This pioneering report served as the basis and springboard for spectacular and innovative research in the history of helicenes.

Figure 1-2: Examples of helicenes

The successful synthesis of the first non-racemic helicene phenanthro[3,4-
c]phenanthrene (8) by Newman and Lednicer in 1955 was another noteworthy
contribution in the field.14 These events heralded a cascade of fascinating
discoveries leading to the synthesis of the longest carbohelicene [14]helicene (9) by
Martin and Baes in 1975,10 and a series of functionalized and heterohelicenes.

1.4.1 Nomenclature of helicenes

The classic nomenclature for helicenes is the [n]helicene nomenclature where
n refers to the number of aromatic rings in the helicene.13,15 Compound a below will
be considered a [6]helicene in accordance with this nomenclature. In 2003, Balaban
proposed the n,m,k- nomenclature where n is the number of repeating units, m
represents the number of aromatic rings in the longest linear chain and k defines the
number of layers or width of the helicene.15 This nomenclature is exemplified in
figure 1.3.

Compound a is a [6.2.1]helicene with cis-1,3- butadiene moiety as the repeat
unit. The vinyl styrene group is the repeat unit in compound b. Compounds a and b
are examples of single layered helicenes whereas compound c, a [5.3.2]helicene is a
classic example of a multi-layered helicene with a width of 2. This nomenclature is
considered superior to the [n]helicene nomenclature as it reveals more information
about the helicene and can conveniently be used to name complex helicene
structures like compound c.
**Figure 1-3:** Nomenclature of helicenes

### 1.4.2 Properties of helicenes

Helicenes have received continued attention since the report of the first racemic helicene in 1956. Helicenes are constructed from aromatic rings that adopt a bent conformation resulting in a helical motif. This bent/spiral conformation confers an intrinsic chirality to these compounds. Helicenes therefore exist as $p$ or (+) helicene (helical twist sense is anti-clockwise/left-handed helix) or as $m$ or (-) helicene with a clockwise helical twist sense (right-handed helix), figure 1.4.
Figure 1-4: Chirality of helicenes. (Structures were drawn and optimized on Spartan by Pawel Rempala).

Helicenes possess intrinsic chirality by virtue of their helical conformation and can rotate plane polarized light either to the right or left.

1.4.3 Potential applications of helicenes

Helicenes have been used as biomedical probes. Most biological responses in cells are associated with specific binding of compounds or drugs to unique target receptor sites. Yan and co-workers studied the selective binding of enantiomeric helicenes to B and Z-DNA. The binding affinity to the DNA strands was measured quantitatively using circular dichroism (CD), fluorescence spectroscopy and equilibrium dialysis. They concluded that the specific binding of enantiomeric helicenes to DNA series offers an alternative and innovative rationale for the design
and synthesis of inhibitors for biological systems.\textsuperscript{16} Helicenes can therefore be used as probes in studying receptor site requirements and designing target inhibitor and activator molecules for biological functions.

Owing to their inherent chiral nature, helicenes might find applications in the manufacture of chiroptical devices.\textsuperscript{17} Norel and co-workers reported the first synthesis of a metallahelicene, in 2010.\textsuperscript{18} The compound was synthesized by incorporating Pt into the pi-conjugated framework of the helicene. This heavy metal integration into the helicene backbone resulted in intense metal-helix interactions inducing efficient phosphorescence and large tunable chiroptical properties in the molecule. The metallahelicene synthesized was reported as the first helicene derivative to exhibit phosphorescence at room temperature. The compound produced intense circular dichroism bands whose intensity could be tuned by changing the oxidation state of the metal or changing the metal.\textsuperscript{18}

Their use as ligands in asymmetric catalysis is also well documented.\textsuperscript{19,20} Reetz and co-workers synthesized a rhodium complex from an enantiomeric 2,15-bis(diphenylphosphino)hexahelicene (PHelix) and used it (without purification) in an enantioselective hydrogenation of itaconic acid ester resulting in the formation of 39\% ee of the (s)-enantiomer. This was the first report of the use of helicenes in asymmetric catalysis.\textsuperscript{21} An enantiomeric bis[5]helicene diol was synthesized by Dreher and co-workers in 2000. The compound served as a ligand in the asymmetric catalytic addition of diethylzinc to aldehydes to form the corresponding alcohols. This reaction yielded products with higher enantiomeric excesses (72-81\% ee)
compared to BINOL.\textsuperscript{22}

The extensive pi-conjugated nature of helicenes validates their use in the manufacture of molecular electronic devices, diodes and semi-conductors.\textsuperscript{23} Conductance algorithm calculations performed by Treboux and co-workers on a series of fused conjugated six membered benzene rings revealed the helicene category had the highest band gap.\textsuperscript{24} The calculations estimated a band gap of 2.64 eV for [11]helicene. It was realized that the band gap can be decreased or eliminated in these molecules by increasing the diameter of the helicene as in anthra-helicene (our target product) or by widening the helix ribbon as in benzo-anthracene respectively (figure 1.5).

![Simple helicene](image1.png)

![Anthra-helicene](image2.png)

![Benzo-helicene](image3.png)

**Figure 1-5:** Tuning the structure of helicene to decrease band gap

These compounds can be made semi-conductive or metallic by properly tuning
their structures.\textsuperscript{24}

Simulations suggest that helicenes can contract and expand like a spring in appropriate media. They can be used as target molecules for the design and synthesis of molecular actuators. Molecular dynamic calculations performed by Pawel Rempala revealed that a functionalized helicene bearing amino groups on the outer periphery can expand by 176\% in dilute acid conditions.\textsuperscript{25} This response was explained by electrostatic repulsion between the ions in solution. Protonation at low pH and deprotonation at higher pH values can cause a helicene to expand and contract thus acting as a biological muscle.\textsuperscript{25} Computational calculations also revealed a 190\% elongation of a helicene (1.5 nm to 2.8 nm) following intercalation with 1,3,5-trinitrobenzene. An intimate $\pi - \pi$ stacking interaction was established between the helicene and the nitrobenzene molecule.\textsuperscript{25}

\subsection*{1.4.4 Hetero and functionalized helicenes}

Helicenes were envisaged to have interesting physical and chemical properties for over half a decade following the synthesis of the first helicene, but no actual application was identified. This was probably because the photochemical methods employed in the synthesis yielded small amounts of products and the structures lacked functionalized entities.\textsuperscript{26} As the interest in helicenes soared over the years, scientists began introducing new functional groups (functionalized helicenes) and heteroatoms (heterohelicenes). This was done to improve the synthetic utility and versatility of carbohelicenes.\textsuperscript{26} Heteroatoms such as oxygen,
sulfur and nitrogen were introduced into the backbone of the helicene yielding oxa, thia and azahelicenes respectively.

A myriad of thiahelicenes have been synthesized over the years, culminating in the synthesis of the longest thiahelicene, pentadecacyclic thia[15]helicene [10, (comprising alternating thiophene and benzene rings)] by Yamada and co-workers in 1981.11

![Figure 1-6: Pentadecacyclic thia[15]helicene (10) and thia[11]helicene (11)](image)

In 2005, Rajca and co-workers reported the nonphotochemical synthesis of thia[11]helicene (11) consisting of 11 fused thiophene rings.27

A multitude of carbon-sulfur [n]helicenes have been synthesized over the years and some have been studied for their electronic properties.26,28,29 It was realized that replacing carbons in carbohelicenes with sulfur atoms produced a red shift in the absorption/emission spectra. It was also observed that the HOMO is raised and the LUMO is lowered in most cases leading to smaller band gaps, a requirement for improved conductivity in the molecule.28
Many nitrogen-containing compounds have found applications in biological systems because they form structures or architectures that mimic molecules in biological systems. Nitrogen-containing helicenes (azahelicenes) have not been largely targeted for the synthesis of biological devices. Nevertheless, their use in the synthesis of light-harvesting/light-emitting complexes has been established. When coupled with an appropriate transition metal, these complexes are capable of absorbing visible light and re-emitting light of various colors. This effect was illustrated by Caronna and co-workers.\textsuperscript{30}

Some azahelicenes can act as ‘proton sponge’. The ‘proton sponge’ ability decreases with an increase in the length of the helicene. This is because the molecule loses its planarity as it starts twisting and the distance between the nitrogen atoms increases. The increased distance reduces the electron repulsion on the nitrogen atoms with a consequent reduction in basicity. It becomes more difficult to form a strong linear N...H...N linkage thus reducing the ability to trap protons.\textsuperscript{31} The ‘proton sponge’ affinity reduces from the diaza[4]helicene through the [5]helicene to the diaza[6]helicene. The diaza[4]helicene has a planar structure while the [5]helicene has a helical structure. Even though the distance between the two nitrogens on the diaza[5]helicene seems shorter than in the [4]helicene, the distorted planar geometry disrupts effective N...H...N linkage. The N-N distance is longer in the [6]helicene resulting in a significant reduction in the ‘proton sponge’ affinity.\textsuperscript{31}
Figure 1-7: Examples of diazahelicenes that are proton sponges

Diazahelicenes have been synthesized wherein oxygen atoms have substituted some carbon atoms in five member rings on the outer periphery of the rings. This normally leads to a contraction of the periphery of the helicene. This property was exploited by Eskildsen and co-workers in the synthesis of the dioxa[6]helicene shown below. The contraction in the helicene caused by the introduction of the oxygen atom lowered the barrier of interconversion between the enantiomers.

Dioxa[6]helicene

Many helicenes have been functionalized with oxygen-containing functionalities like alcohols, ethers, ketones, aldehydes, esters and carboxylic acids. These groups have facilitated transformations to more interesting target materials or have endowed the helicenes with new properties such as solubility in
polar solvents.\textsuperscript{33}

\textbf{1.4.5 Synthesis of helicenes}

Photocyclisation of stilbenes is the oldest and most widely used reaction in the synthesis of helicenes. This reaction was employed in the synthesis of the first helicene as well as the synthesis of the longest carbohelicene, [14]helicene.\textsuperscript{9,10} This reaction has also been used in the synthesis of a wide variety of functionalized helicenes.\textsuperscript{34}

\textbf{Scheme 1- 5:} Synthesis of a functionalized helicene via a photochemical reaction\textsuperscript{34}

The nonphotochemical methods used in the synthesis of helicenes include the Diels-Alder reaction, metal-catalysed aryl-aryl couplings, cycloisomerizations and ring closing metathesis reactions. Minuti and co-workers used a Diels-Alder reaction in the synthesis of a pentahelicenequinone shown below.\textsuperscript{33,35}

\textbf{Scheme 1- 6:} Diels-Alder route to pentahelicenequinone
Metal-catalysed aryl-aryl coupling reactions have been used to form one and multiple rings in the synthesis of helicenes.\textsuperscript{36} Tanaka and co-workers used a metal-catalysed coupling reaction on the starting material bearing a chiral auxiliary below, followed by a McMurry coupling reaction to afford an enantioenriched disubstituted [7]thiaheterohelicene.\textsuperscript{37}

![Scheme 1-7: Synthesis of [7]thiahelicene by metal-catalysed coupling reaction](image)

\textbf{Scheme 1-7}: Synthesis of [7]thiahelicene by metal-catalysed coupling reaction

An emerging class of reactions in the synthesis of aromatic systems and helicene-like molecules is cycloisomerization of alkenes and alkynes.\textsuperscript{38,39} Teply and co-workers synthesized [7]helicene shown below via a cycloisomerization of a dienetriyne precursor.\textsuperscript{40}

![Scheme 1-8: Synthesis of [7]helicene by cycloisomerization of a dienetriyne](image)

\textbf{Scheme 1-8}: Synthesis of [7]helicene by cycloisomerization of a dienetriyne\textsuperscript{40}
Ring closing metathesis is one of the most recent reactions used in the synthesis of helicenes. Shawn K. Collins recently synthesized some helicenes via ring closing metathesis reaction. He was able to combine two fragments on the helicene through an RCM and formed one new double bond creating one new benzene ring.\textsuperscript{12}

\textbf{Scheme 1-9}: Synthesis of [5]helicene via RCM reaction

Bonifacio of B.T King group and co-workers reported the synthesis of dibenz[$a,c$]anthracene and dibenz[$a,j$]anthracene via a double RCM reaction using Grubbs catalyst. Details of this reaction including the theoretical calculations are outlined in chapter two.\textsuperscript{41} This reaction served as the raison d’être and logical foundation for our synthetic strategy.

The other synthetic methods described above also lead to the formation of one or two new benzene rings. The difference with our synthetic design lies in the fact we will synthesize helicene through an RCM reaction in which multiple double bonds will be formed, generating multiple fused benzene rings in one reaction.

In our target synthesis, the helicene was synthesized from a suitably designed poly(m-phenylene) polymer via an RCM reaction. Both open chain and cyclic polymers were formed during the polymerization reaction. The open chain
polymers yielded helicene from the RCM reaction while the cyclic analogues afforded kekulenes.

![Polymers and Helicenes](image)

**Figure 1-8:** Synthesis of n-helicene and n-kekulene

Having discussed the helicenes, we will do a brief discussion of kekulenes in the next section.

1.5. Kekulenes

Closed cycles of angularly annulated benzene rings are called kekulenes. The first synthesis of kekulenes was attempted by Staab A. H. and co-workers in 1968.
They developed a 14 step route that led to small amounts of kekulenes that could not be isolated. Nevertheless, they were confident in their assertion of the fact that kekulene was synthesized based on mass spectroscopic data. The synthesis was abandoned and revived a couple of years later by Staab A. H. and Dieterich F. They synthesized, isolated and characterized kekulene in 1978.\textsuperscript{42} This kekulene has D\textsubscript{6h} symmetry with planar cyclic conjugation. Initially, these molecules were believed to be superaromatic. Computational studies and calculations performed later on revealed a small superaromatic stabilization energy, indicating kekulene is non-superaromatic.\textsuperscript{44}

1.5.1 Benzenoid versus anulenoid nature of kekulenes

![Benzenoid and Annulenoid structures](image)

**Figure 1-9:** Predicted structures for kekulene

The non-annulenoid nature of keulene was confirmed by molecular geometry and \textsuperscript{1}H NMR assignments. Molecular geometry and calculations indicated that the core/inner ring protons in the annulene-like kekulene will be highly shielded and have very low $\delta$ values possibly extending to negative values. Highly deshielded
inner protons were predicted for the benzene-like structure that was in line with observed experimental values (~ 10.45 ppm). This confirms the benzenoid structure.

1.5.2 Nomenclature of kekulenes

Based on the nomenclature rules, kekulenes are named based on the number of anelated benzene rings present in the molecule. For example the benzenoid and annulenoid structures in figure 1.9 are referred to as cyclododecakisbenzenes. Kekulenes with 10 benzene rings will be described as cyclodecakisbenzenes, cyclononakisbenzenes for 9 and cyclooctakisbenzenes for 8 member rings respectively. A more descriptive nomenclature defines the nature of the annelation between adjacent rings as linear denoted by the letter $d$, or $e$ for angular. Examples are illustrated in figure 1.9.

![Figure 1-10: Nomenclature of kekulenes](image)

1.5.3 Properties and potential applications of kekulenes

Kekulenes are polyhexes with cyclic planar conjugation. This makes them suitable candidates for use in the synthesis of electrical conducting devices. Their
exceptionally high thermal and photostability validates their use in the synthesis of electronic materials.\textsuperscript{46}

An intriguing potential use of these compounds lies in the synthesis of new ligands and complexes for chemical and biological use.\textsuperscript{47} A related and very important compound that comes to mind is the porphyrin ring, a major constituent of haemoglobin. It is interesting to note that porphyrin-like kekulenes (aza-kekulenes) might be synthesized with nitrogen atoms replacing the inner ring carbon atoms. Staab and co-workers have attempted the synthesis of hexaazakekulene,\textsuperscript{47} and their synthesis will be discussed in the next section. These nitrogen atoms can be coordinated to different metals to form a variety of coordination complexes similar to heme in haemoglobin. These compounds may posses some interesting physical, chemical and biological properties. This is an appealing facet of kekulene chemistry that has not been exploited and warrants further research.\textsuperscript{1}

\textbf{Figure 1-11:} An aza-helicene coordinated to a metal M (aza-helicene complex)

The peripheral/outer ring hydrogens can be substituted with a variety of functional groups or the carbon atoms replaced with sulfur or oxygen atoms to form
functionalized, thia and oxakekulenes respectively.

1.5.4 Synthesis of kekulene and its derivatives

The first successful synthesis of kekulene was reported in 1978 by Staab A. H. and Dieterich F. They used dehydrogenation and photocyclisation reactions (photocyclodehydrogenation reactions).^48

![Scheme 1-7: Synthesis of kekulene by Staab and Dieterich](image)

There has not been any other report on the complete synthesis of kekulenes or higher analogues. We report in this dissertation our attempts towards the synthesis of higher analogues of kekulene via RCM reaction.

Attempts have been made to synthesize some heterokekulenes following the successful synthesis of kekulenes. Three compounds have been synthesized so far,
dodecahydro-18,21-dioxoniakekulene, dodecahydrohexaazakekulene and 3,9, 15,19,21,23-hexaazakekulene (figure 1.11).

**Figure 1-12:** Examples of synthesized heterokekulenes

The authors used a series of condensation reactions and cyclodehydrogenation reactions to put the fragments together in the synthesis of the heterokekulenes above. We will use RCM reaction in our research to synthesize kekulenes. This is the first report of the use of RCM reaction in the synthesis of kekulenes.
1.6 References


493-497.


Chapter 2: Optimization of monomer

2.1 Introduction

Photocyclisation of stilbenes is the oldest and most widely employed method for the preparation of helicenes.\textsuperscript{1,2} Non-photochemical routes to helicenes include Pschorr cyclization, Diels alder reactions, cycloisomerization and biaryl coupling reactions.\textsuperscript{3-5} Ring closing metathesis was recently used in the synthesis of helicenes. Shawn K. Collins and B.T. King research groups have demonstrated that new aromatic rings can be formed using ring closing metathesis (RCM) reactions.\textsuperscript{6-8}

Our project concerns the synthesis of a helicene polymer through an RCM reaction. In this chapter, we will describe the optimization efforts leading to the synthesis of the monomer ((5), scheme 2-1).

Scheme 2-1 is a retrosynthetic route for the synthesis of polymeric [n]helicenes/[n]kekulenes. The polymeric [n]helicene/[n]kekulenes can be obtained following an RCM reaction of the polyphenylene moiety. The target monomer (14), obtained from a divinyl benzene precursor affords the poly(dipropenyl phenylene) (15) following treatment under Suzuki conditions. Two synthetic routes can be attempted to afford the dibromo dipropenyl benzene (13). Dehydration of a dibromobenzene diol from dibromobenzene dialdehyde affords the divinyl benzene (dehydration route). A Wittig reaction between the benzene carboxydialdehyde and ethyltriphenylphosphonium salt, followed by isomerization to the E,E isomer (13) appears to be a better option because it affords the product in greater yield.
Scheme 2-1: Retrosynthetic route

The benzene carboxyldialdehyde (2) can be obtained from m-xylene (1) following an electrophilic aromatic substitution (bromination) in the dark followed by a photo-assisted benzylic bromination reaction and a subsequent hydrolysis of the product thereof using an ethanolic solution of AgNO₃.
2.2 Synthetic efforts

2.2.1 Bonifacio's synthesis of monomer

Bonifacio optimized the synthesis of the monomer using the dehydration route (scheme 2-2)\(^9\). He obtained the products in good to excellent yields for these reactions, but the dehydration step was a bottleneck. He obtained the dehydration product (3) in at least 44% yield (figure 2-2). Alternative reactions, which will be discussed in the next section, to increase the yield of this reaction were attempted in our current synthesis.

**Scheme 2-2: Bonifacio's synthesis of monomer (dehydration route)**

The following conclusions were drawn from Bonifacio's synthesis of the monomer.

- A single olefin isomer was required to simplify the \(^1\)HNMR spectrum of compound (3) and subsequent products.
• The yield of the dehydration reaction was too low and required improvements.
• Test RCM reactions performed with different substituents on the vinyl substituent revealed that the monomer with propenyl side chains was the best substrate for the RCM reaction. The styrene pendants in poly(4,6-di(E)-styryl-\textit{m}-phenylene were too bulky and could not be easily eliminated after RCM. The ethylene pendant in poly-distyrylbenzene resulted in unwanted radical styrene-like polymerizations. Compound (4) with propenyl substituents was stable and sufficiently reactive for RCM reaction.\textsuperscript{6,9}

With these ideas at hand, our initial objective in the current synthesis of polymeric helicene was to repeat these series of reactions and try to improve the yield of the dehydration reaction.

\textbf{2.2.2 Current synthesis of target borylated monomer (4).}

\textbf{2.2.2.1 Dehydration route}

This route was optimized by Bonifacio of B. T. King group.\textsuperscript{6,9} Our major objective here was to find ways of improving the yield and efficiency of the dehydration reaction [\textit{e}] leading to the synthesis of compound (3), scheme 2-3.
Scheme 2-3: Synthesis of the target monomer via a dehydration route

[a] Br₂, I₂, dark, 0 °C, 16 h, 56.8%; [b] Br₂, 100W lamp, CH₂Cl₂, 9 h, 87.3%; [c] AgNO₃, H₂O, EtOH, reflux, 0.5 h, 95.5%; [d] Mg, ether, EtBr, 87.2%; [e] KHSO₄, P₂O₅, 4-tert-butylcatechol, 230 °C, vacuum, 15 min, 30.5%. Unsuccessful reactions included i) Martin sulfurane reagent, rt, ii) Et₂O, p-toluenesulfonic acid monohydrate, toluene, 130 °C, Na₂SO₄, mole sieves, iii) Dowex 50X-200 ion exchange resin, toluene, 130-150 °C; [f] n-BuLi, THF, isopropyl pinacolborate, -78 °C – rt, 62.8%.

Aromatic bromination of m-xylene (1) with bromine in the dark for 16 hours afforded 2,4-dibromo-m-xylene (1'). Benzylic bromination of (1') under incandescent radiation yielded compound (1''), which was oxidized using an ethanolic solution of AgNO₃ to afford 4,6-dibromobenzene-1,3-dicarbaldehyde 2 in very good yields. Treatment of (2) with ethylmagnesium bromide in ether (Grignard reaction) yielded the diol (2') (mixture of three stereoisomers), which was dehydrated to the corresponding E,E-dipropenylbenzene (3) using P₂O₅, potassium
tert-butoxide under high temperatures and vacuum.\(^7\) The yield obtained was low (30.5\%), triggering the search for an alternative reaction with improved yields.

Attempts to improve the yield for this dehydration reaction included the use of Martin sulfurane reagent, rt, Et\(_2\)O\(^10\); \(p\)-toluenesulfonic acid monohydrate, toluene, 130 °C, Na\(_2\)SO\(_4\), mole sieves; Dowex 50XB-200 ion exchange resin, toluene, 130-150 °C\(^11\); and \(N,N'\)-dicyclohexylcarbodiimide, CuCl, THF (pseudourea-mediated dehydration)\(^12,13\), proved futile. The reaction of (3) with triisopropylborate and n-BuLi furnished the borylated target monomer (4) in good yields. \(^1\)H NMR data for compounds (1') through (4) are in agreement with literature values.\(^6\)

The dipropenylbenzene monomer (3) could be obtained in better yields through a Wittig reaction, albeit as a mixture of isomers. Bonifacio encountered little success in his attempt to isomerize a mixture of this monomer via a Pd (II) catalyzed and thiophenol-mediated isomerizations.\(^14,15\)

Obtaining good yields at this stage of the reaction sequence was paramount because many grams of monomer was required to optimize the polymerization and RCM reactions. We decided to explore the Wittig reaction route with the hope of getting suitable conditions for high yielding isomerization reaction of the mixture of divinylbenzene monomers to the E,E-isomer.

### 2.2.2.2 Wittig reaction route

The dehydration route described above suffered from low percent yields probably due to styrene-like polymerization of the product. The Wittig reaction seemed an attractive option at this point since it furnished the desired monomer in
higher yields, though as a mixture of isomers. A high yielding isomerization reaction following the Wittig reaction was needed to convert the stereoisomers to a single product.

**Scheme 2-4: Wittig reaction route**

[g] CH$_3$CH$_2$PPh$_3$Br, KtOBu, THF, rt, 16 h, 95.3%; [h] PhSSPh, THF, reflux, 70°C, 16 h, or 100W incandescent lamp, 3 h, 70.7%; [i] n-BuLi, THF, triisopropylborate, pinacol, -78°C – rt, 73.7%.

The product (2") was a colorless oil. GC-MS of the product (95%) material revealed the presence of 3 isomers, EE, EZ and ZZ isomers. This reaction was optimized using non-labelled substrates as shown in scheme 2-4.

Having obtained the divinyl benzene precursor as a mixture of isomers in good yields, we proceeded to the isomerization reaction. The isomerization reaction was required to furnish a single isomer to ease characterization of the subsequent products. Our reagent of choice for the isomerization process was diphenyl disulfide.

The S-S bond length is 2.05Å, about 0.5Å shorter than a C-C bond. Compared to the C-C bond with bond dissociation energy of about 80kcal/mol, the S-S bond with dissociation energy of 60 kcal/mol is often considered as weak because of its
relative ease of scission. Cleavage of the S-S bond can be chemically or photochemically induced. The rotational energy barrier for this bond is very low making it a good substrate for isomerization.\textsuperscript{16,17} These properties of the S-S bond have been exploited in the literature in isomerization reactions.\textsuperscript{18,19,20}

Photo-induced isomerization of polybutadiene from cis to trans was achieved using PhSSPh. Kinetic studies revealed that the rate of the reaction was first order with respect to light intensity.\textsuperscript{21} Variation of the concentration of PhSSPh had no effect on the rate of the reaction. An equilibrium mixture was obtained consisting of 80-85\% of the trans product.\textsuperscript{21} These results were in line with our observations. We never obtained a 100\% isomerization of the monomer. Photo-irradiation of pure EE isomer resulted in a mixture of three isomers with \~80-90\% E,E isomer confirming the existence of an equilibrium concentration comprising a mixture of isomers.

A mixture of compound (2") and PhSSPh was dissolved in THF and refluxed at 70 °C overnight under N\textsubscript{2} atmosphere. The solvent was removed and the residue was dissolved in hexane. Column chromatography with SiO\textsubscript{2} and hexane as eluent furnished the EE isomer in 70.7\% yield, 67.4\% over two steps, a 47\% yield greater than the dehydration reaction. This was definitely a beautiful improvement on the dehydration route.

The identity of the purified isomer was confirmed by \textsuperscript{1}HNMR (figure 2-1). A trans-trans coupling constant of 12 Hz was observed for the vinyl protons on the isomer at \~ 6.6 ppm for the non-labelled compound. The observed experimental data was in agreement with values from literature.\textsuperscript{21}
**Figure 2-1:** $^1$HNMR spectrum of unlabeled EE-isomer

The thermal reaction was slow and required chromatography so we looked for a better route. A photo-induced isomerization reaction was attempted. The isomeric mixture and PhSSPh was dissolved in dry THF under N$_2$ atmosphere. The reaction mixture was refluxed under incandescent irradiation for 3 hours. The solvent was removed and the product was recrystallized in hexane. The product was harvested in very good yield, 74%, demonstrating a small but significant improvement on the column chromatography technique. The photoisomerization was faster, and more reliable than the thermal-induced isomerization. We were able to synthesize 23 g of E,E isomer via this route within a very short time. The
synthesis of 23 g of EE isomer via the dehydration route would certainly have been difficult.

The importance of unstabilized THF (which presumably contains small amounts of peroxides) for the isomerization reaction was elucidated. Little isomerization was observed when distilled THF from the still was used. The same reaction with THF from a bottle led to ~ 95% conversion to the E,E-isomer. This observation suggested the importance and role of peroxides in this reaction. The peroxides may have acted as free radical initiators for this reaction.

2.2.3 Labeling the target monomer

In previous studies in our research group, the progress of the RCM reaction was monitored by observing the disappearance of D peaks in labeled polymers in the $^2$HNMRS spectrum. These experiments were complicated by the low solubility of the putative helicene. We decided to use solid state infrared (IR) spectroscopy to circumvent this problem. This required the synthesis of a carefully designed monomer and polymer. Incorporation of two D atoms on the monomer in compound 8 was a breakthrough in our design. The idea behind this approach is that the C-D stretch which occurs at ~ 2244 cm$^{-1}$ is clearly visible in the IR spectrum of the poly(dipropenyl phenylene). The D atoms are lost however, in the RCM step. We could therefore use the disappearance of the C-D stretch to monitor the RCM reaction and helicene formation. The advantages of this approach were twofold. In addition to the fact that the synthesis was relatively cheaper and easier than the incorporation of D atoms in our previous studies, the yields were also better. The
solubility dilemma was eluded since the analysis could be done on a solid sample.

The incorporated D in the monomer and subsequent polymer is lost as part of the butene molecule after RCM reaction. This is a huge advantage because butene is volatile and can easily be eliminated from the reaction, facilitating our observation of the C-D disappearance by infrared spectroscopy.

The synthesis of the labeled monomer commenced by the incorporation of D atoms in ethyltriphenylphosphonium bromide, which is commercially available.

![Scheme 2-5: Synthesis of labeled ethyltriphenylphosphine bromide](image)

[j] D₂O, Et₃N, reflux, 110 °C, 17 h, 99%.

Treatment of ethyltriphenylphosphine bromide with D₂O and triethylamine, a basic catalyst, gave the labeled Wittig precursor in excellent yield (99%), with ~97-99% incorporation of D.²² ¹H NMR spectrum of the product revealed the disappearance of the CH₂ peak. This was also confirmed by ³¹P NMR, which showed only one signal for the product at 27.4 ppm.

A Wittig reaction with the dialdehyde (2) and (1,1⁻²H)-ethyltriphenylphosphonium bromide furnished the divinyl monomer (12) as a mixture of three isomers just like compound (2”).
**Scheme 2- 6**: Synthesis of labeled monomer

[k] CH$_3$CD$_2$PPH$_3$Br, KO'Bu, THF, rt, 16 h, 90.3%; [l] PhSSPh, unstabilized THF, reflux, 100W lamp, 3 h, 81.7%; [m] n-BuLi, THF, triisopropylborate, pinacol, -78$^\circ$C – rt, 73.7%.

The presence of three isomers was confirmed by GC-MS, which showed three peaks with m/z 318, and by $^1$H NMR spectrum, which showed peaks corresponding to a mixture of three isomers. A singlet in our labeled substrate, replaced the doublet observed for the vinyl protons as expected in the non-labeled substrate on the $^1$H NMR spectrum due to the absence of vicinal coupling.

Isomerization using PhSSPh in unstabilized THF and recrystallization from hexane afforded the desired 1,5-dibromo-2,4-di[1(E)-2-2H]propenylbenzene (13) as a single isomer in 78.4% over two steps.
Figure 2-2: $^1$HNMR spectrum of labeled EE-isomer

An IR spectrum of the product showed the characteristic C-D signal at 2244 cm$^{-1}$.

Figure 2-3: IR spectrum of 1,5-dibromo-2,4-di[(1E)-2-$^{2}$H]propenylbenzene (13) showing the isolated C-D stretch at 2244 cm$^{-1}$.
Functionalization of the labeled dibromo-dipropenylbenzene (13) with triisopropylborate and pinacol in the presence of n-BuLi afforded the desired labeled target monomer (10) in good yield (73.7%). The incorporated C-D bond was unaffected in the process and was observed on the IR spectrum as an isolated signal at 2236 cm\(^{-1}\).

![IR Spectrum Image]

**Figure 2-4:** IR spectrum of labeled target borylated monomer (14) showing the isolated C-D stretch at 2236 cm\(^{-1}\).

The structure and identity of compound (14) was confirmed by \(^1\)H NMR spectrum and GC-MS. The singlets observed in the preceding structure (13) were preserved indicating the C-D bonds were not affected in the borylation reaction. GC-MS confirmed the expected mass of this compound at m/z 365.
**Figure 2-5:** $^1$H NMR spectrum of monomer (14).

Worthy of note is the fact that the non-labelled analogue (14) from incomplete deuteration constituted about 5% of the final product. The good news is that both compounds react in the same way in the subsequent reactions giving similar products, the only difference being the D label on one product.

### 2.3 Experimental

**1,5-Dibromo-2,4-dimethylbenzene, (1')**

Bromine (108.9 g, 681.2 mmol) was added dropwise to an ice-cold solution of iodine (0.5 g, 3.9 mmol) in neat xylene (34.6 g, 40 mL) over 1 h in the absence of light. The reaction mixture was stirred at room temperature for 16 h. An aqueous solution of KOH (20%, 50 mL) was added to the reaction mixture. The mixture was warmed
slightly until the yellow color disappeared. A white solid was formed. The aqueous layer was decanted and the resulting solid was washed with distilled water. Recrystallization of the solid from absolute ethanol afforded white crystals (48.9 g, 56.8% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$7.70 (s, 1H), 7.10 (s, 1H). $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta$ 136.9, 134.9, 132.6, 121.9, 22.2. GCMS: $m/z$ 264.

1,5-Dibromo-2,4-bis(dibromomethyl)benzene, (1$^\circ$) $^9$

Bromine (4.47 mL, 56.0 mmol) was added slowly to a solution of 1,5-dibromo-2,4-dimethylbenzene (2.64 g, 10.0 mmol) in refluxing CH$_2$Cl$_2$ for 2 h. Bromine (2.25 mL, 28.0 mmol, 2 eq) was added to the reaction mixture when the color turned yellow. The mixture was stirred over night under incandescent irradiation (100W lamp). The mixture was cooled to room temperature and extracted with an aqueous solution of sodium thiosulfate. The organic layers were combined and dried over anhydrous sodium sulfate. Evaporation of solvent under reduced pressure followed by recrystallization of the resulting crystals in hexane furnished the product as pale brown crystals (4.95 g, 98.8%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.66 (s, 1H), 7.71 (s, 1H), 6.97 (s, 2H). $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta$ 141.2, 135.7, 133.4, 121.1, 37.6. GCMS: $m/z$ 501.
4,6-Dibromobenzene-1,3-dicarbaldehyde, (2)⁹

An ethanolic solution (1200 mL) of 1,5-dibromo-2,4-bis(dibromomethyl)benzene (30.0 g, 51.7 mmol) and an aqueous solution (240 mL) of AgNO₃ (36.8 g, 216.8 mmol) were mixed and refluxed at 85 ºC for 90 min. the reaction mixture was cooled to room temperature, and filtered to remove AgBr. The filtrate was evaporated to dryness under reduced pressure and the residue was washed with copious amounts of water to remove HNO₃. The resulting white amorphous solid was dried under reduced pressure at 80 ºC overnight furnishing the product (14.4 g, 95.6% yield). ¹H NMR (400 MHz, CDCl₃): δ 10.32 (s, 2H), 8.39 (s, 1H), 8.05 (s, 1H). ¹³C NMR (400 MHz, CDCl₃): δ 189.7, 138.9, 133.2, 131.9, 131.1. GCMS: m/z 291.

1-[2,4-Dibromo-5]-1-hydroxy-propyl)-phenyl]-propan-1-ol, (2')⁹

To a dry Schlenk flask containing 4,6-dibromobenzene-1,3-dicarbaldehyde (5.05 g, 17.3 mmol) was added anhydrous diethyl ether (150 mL).The mixture was stirred for 5 min. Ethylmagnesium bromide (13.3 mL, 2.3 eq) was added slowly to the reaction mixture in an ice bath with continuous stirring. The reaction mixture was stirred over night under N₂ atmosphere. The mixture was quenched with an aqueous solution of ammonium chloride and extracted with diethyl ether. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo to afford a white amorphous solid (5.46 g, 89.7% yield) as a mixture of 2 stereoisomers. ¹H NMR (500 MHz, CDCl₃): δ 7.61 (s, 1H), 7.56 (s, 1H), 7.54 (s, 1H), 7.52 (s, 1H), 4.81 (2H, dd), 4.61 (2H, dd), 3.14 (s, OH), 1.75 (m, 4H), 1.56
(m, 4H), 0.93 (t, 6H). \(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \(\delta\) 143.8, 134.8, 126.2, 119.9, 72.9, 72.8, 30.4, 30.3, 9.0, 8.8. GCMS: \(m/z\) 352.

**1,5-Dibromo-2,4-di[(1E)-propenyl]benzene, (3)**

1-[2,4-Dibromo-5]-1-hydroxy-propyl]-phenyl]-propan-1-ol (5.05 g, 14.2 mmol), potassium hydrogen sulfate (0.592 g, 4.35 mmol), phosphorus pentoxide (0.254 g, 1.79 mmol), and 4-tert-butyl catechol (0.002 g, 0.014 mmol) were transferred to a 10 mL Schlenk flask fitted with a small Liebig condenser and attached to a vacuum line. The mixture was heated at 230 °C under reduced pressure. The product sublimed and was collected as a liquid in the receiving flask, which solidified upon cooling to room temperature. The solid was washed with CH\(_2\)Cl\(_2\) and recrystallized from EtOH to afford white needle-like crystals (1.37 g, 30.5% yield). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.69 (s, 1H), 7.54 (s, 1H), 6.64 (d, 2H, \(J = 20\) Hz), 6.22 (dd, 2H, \(J = 20\) Hz, 7 Hz), 1.92 (d, 6H, \(J = 7\)Hz).\(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \(\delta\) 136.9, 135.8, 129.4, 129.1, 124.4, 121.1, 18.6 GCMS: \(m/z\) 316.

**{(1,1-^{2}\)H)-Ethyltriphenylphosphonium bromide (CH\(_3\)CD\(_2\)PPh\(_3\)Br)**

Triethylamine (5 drops) was added to a solution of ethyltriphenylphosphonium bromide (3.55 g, 9.56 mmol) in D\(_2\)O (10 mL). The mixture was heated under reflux at 110 °C for 16 h under N\(_2\) atmosphere. The solvent was removed under reduced pressure to yield (1,1-^{2}\)H)-ethyltriphenylphosphonium bromide (3.23 g, 90.4 %) as a white solid. mp 204-206 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.91 - 7.76 (m, 8H), 7.70
(ddd, \(J = 2.5, 3.4, 7.6, 5H\)), 1.39 (d, \(J = 20.1, 3H\)). \(^{31}\)P NMR (400 MHz, CDCl\(_3\)): \(\delta 27.4\). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)): \(\delta 135.1, 135.0, 133.6, 130.6, 130.4, 118.3, 117.5, 6.6\). El-MS: \(m/z 373\).

**1,5-Dibromo-2,4-bis[(2-\(^2\)H)propenyl]benzene, (12)**

Potassium tert-butoxide (2.83 g, 25.2 mmol) was added to a solution of (1,1-\(^2\)H)-ethyltriphenylphosphonium bromide (9.87 g, 26.5 mmol) in tetrahydrofuran (350 mL). The orange solution was stirred at room temperature for 20 min. A solution of 4,6-dibromobenzene-1,3-dicarbaldehyde (3.50 g, 12.02 mmol) dissolved in 200 mL of tetrahydrofuran was slowly added to the reaction mixture. The solution was stirred overnight at room temperature. The solvent was removed and the residue dissolved in hexane. The mixture was subjected to flash chromatography using hexane to afford 1,5-dibromo-2,4-bis[(2-\(^2\)H)propenyl]benzene (3.64 g, 96 %) as an oily liquid. The product constituted a mixture of three isomers (EE, ZZ, EZ), which could not be separated by column chromatography. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.80\) (s, 1H), 7.74 (s, 1H), 7.68 (s, 1H), 7.52 (s, 1H), 7.36 (s, 1H), 7.25 (s, 1H), 7.21 (s, 1H), 6.62 (d, \(J = 11.6, 3H\)), 6.38 (d, \(J = 8.1, 3H\)), 1.90 (s, 6H), 1.77 (s, 12H). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)): \(\delta 136.9, 136.5, 136.4, 135.7, 135.5, 131.9, 129.4, 129.3, 129.2, 129.1, 129.0, 128.6, 128.5, 128.1, 124.3, 122.4, 122.2, 121.1, 121.0, 87.7, 18.6, 14.5, 14.4, 14.3. GCMS: \(m/z 318\).
1,5-Dibromo-2,4-di[(1E)-2-²H]propenylbenzene, (13)

Diphenyl disulfide (0.17 g, 0.78 mmol) was added to a solution of 1,5-dibromo-2,4-bis[(2-²H)propenylbenzene (1.38 g, 4.34 mmol) in unstabilized, unpurified tetrahydrofuran (150 mL). The solution was stirred under reflux at 70 °C under N₂ atmosphere overnight. The solvent was removed under reduced pressure and the residue was re-dissolved in hexane. The solution was purified by column chromatography using hexane as the eluent to afford 1,5-dibromo-2,4-di[(1E)-2-²H]propenylbenzene (1.02 g, 81.7 %) as white crystals. mp 55-58 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.68 (s, 1H), 7.52 (s, 1H), 6.60 (s, 2H), 1.90 (s, 6H). ¹³C NMR (500 MHz, CDCl₃): δ 136.9, 135.7, 129.1, 128.8, 124.3, 121.0, 18.5. IR (cm⁻¹): 3025, 2966, 2929, 2909, 2842, 2723, 2244, 1628, 1427, 1371. UV (THF, 256 nm): EI-MS: m/z 318.

2-{5-Bromo-2,4-di[(1E)-(2-²H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. (14)

1,5-dibromo-2,4-di[(1E)-2-²H]propenylbenzene (3.27 g, 10.3 mmol) was dissolved in dry, degassed tetrahydrofuran (145 mL). The solution was stirred for 5 min at -78 °C. n-BuLi (6.22 mL, 10.4 mmol) was added dropwise to the solution under N₂ atmosphere. The solution was stirred for 10 min prior to the addition of triisopropylborate (2.13 g, 11.3 mmol). The solution was stirred overnight and gradually warmed up to room temperature. Pinacol (1.34 g, 11.3 mmol) was added to the solution followed by stirring for 5 min. The solvent was removed and the
residue dissolved in CH₂Cl₂. The mixture was flash chromatographed on silica gel with CH₂Cl₂. The solvent was removed from the filtrate and the residue was recrystallized in absolute ethanol to afford 2-{5-bromo-2,4-di[(1E)-{(2-H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.09 g, 55.7 %) as a yellow solid. mp 87-90 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.87 (s, 1H), 7.59 (s, 1H), 7.06 (s, 1H), 6.69 (s, 1H), 1.94 – 1.82 (m, 6H), 1.37 – 1.28 (m, 12H) ¹³C NMR (400 MHz, CDCl₃): δ 143.2, 139.9, 139.6, 130.8, 130.0, 122.9, 120.8, 83.8, 24.9, 18.6. IR (cm⁻¹): 3045, 2980, 2931, 2909, 2848, 2727, 2235, 1633, 1585, 1477, 1444, 1383. UV (THF, 261 nm). EI-MS: m/z 366.

2.4 References


(9) Bonifacio, M.C. Towards Polymeric Helicenes. The Chemistry of Poly(divinyl-


Chapter 3: Development of polymerization reaction

3.1 Introduction

Polyphenylenes can have ortho, para or meta connections giving rise to polymers or macrocycles with different conformational and structural motifs and different properties.¹

![Structures of polyphenylenes](image)

**Figure 3-1:** Structures of polyphenylenes with \(a, p, m\)-connections

Poly-\(p\)-phenylenes are the most common polyphenylenes in literature. They have linear structures and form rigid systems due to efficient packing. Rapson²³ and co-workers and Wittig⁴ have reported poly-\(o\)-phenylene systems.⁵ There has been increasing interest in the study and synthesis of poly-\(m\)-phenylenes. Studies have shown that a poly-\(m\)-phenylene of appropriate length will adopt a helical shape in solution.⁶ The helical motif is mostly random and can be ordered by introducing intramolecular attractions through side chain interactions.⁷

Our synthesis of an extended polymeric helicene and kekulene required a suitable poly-\(m\)-phenylene precursor (figure 3-2).
**Poly(dipropenyl phenylene)**

*Figure 3-2*: Structure of dipropenyl phenylene polymer, the precursor polymer

We envisioned that the polymer would be constructed from an appropriate monomeric phenylene unit shown above.

The successful application of the Suzuki polycondensation reaction in the synthesis of polyphenylenes was a breakthrough in the polyphenylene chemistry. This reaction and related coupling reactions like Yamamoto and Heck reactions have been used in the synthesis of many polyphenylenes.

Having obtained a structural design of our target polymer, we proceeded to search for an appropriate reaction for its synthesis. We opted for Suzuki polycondensation reaction because it is well developed.

**3.2 Suzuki Polycondensation reaction**

The Suzuki polymerization reaction is a palladium-catalyzed cross coupling reaction between an aryl or vinyl halide and an aryl or vinyl boronic acid or ester.\(^8\) It constitutes one of the most important C-C bond forming reactions in chemistry and is a versatile method for the synthesis of new aryl-aryl bonds. The most appealing facet of this C-C bond forming process is the mild reaction conditions employed in the process. It came as no surprise that Akira Suzuki was a co-recipient of the 2010
Nobel Prize in Chemistry (awarded jointly to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki) for their work on transition metal-catalyzed cross couplings in organic synthesis.

The scope and utility of this reaction has been broadened and now incorporates alkyls, alkenes and alkynes.\textsuperscript{2,10} Modifications to the reaction include among others not listed here, the use of nickel catalyst, microwave-assisted solvent-free reactions and asymmetric reactions.\textsuperscript{11,12,13}

![Scheme 3-1: General Suzuki polycondensation reaction](image)

Suzuki polycondensation is normally carried out in basic medium, which activates the boronic acid/ester and facilitates the transmetallation process in the catalytic cycle. Recently, base-free reactions have been developed using cesium fluoride or tetrabutylammonium fluoride, which have been shown to activate boronic acids in the coupling reaction.\textsuperscript{14} In 2007, John R. R. and co-workers reported the synthesis of an acid-functionalized polyfluorene via a base-free Suzuki polymerization reaction.\textsuperscript{5}

Suzuki polycondensation reaction has found a wide application in the synthesis of polymers and pharmaceuticals.\textsuperscript{15,16} This reaction exhibits a high tolerance to a huge variety of functional groups and the by-products are generally non-toxic.\textsuperscript{17,18} A majority of the boronic esters are stable, easy to handle, commercially available and are easily synthesized thereby increasing the synthetic utility of this reaction.
Pinacol boronic esters have been shown to be easier to handle than the free boronic acids.\textsuperscript{17} They are easily generated from the acids via the addition of pinacol at room temperature. Schlüter reported the first use of a phenyl boronic ester in Suzuki polycondensation.\textsuperscript{19} This report triggered the synthesis of a multitude of conjugated polyphenylenes with very interesting physical and chemical properties. Synthesis involving \textit{p}-phenylenes are more popular than \textit{m}-phenylenes in the literature.

\textbf{3.2.1 Side reactions in Suzuki polycondensation reactions and their impact on polymerization}

Hydrolytic deboronation, dehalogenation and aryl-aryl exchange reactions are major side reactions that limit the molecular weight and chain length of the polymer/macromolecule by initiating premature termination of the chain growth.\textsuperscript{17} Examples of these chain termination processes are illustrated in scheme 3-2.
Scheme 3-2: Deboronation, dehalogenation, and aryl-aryl exchange reactions

The chain termination processes described above can be controlled by utilizing appropriate catalysts and reaction conditions. Jayakannan and co-workers observed significant hydrolytic deboronation and deiodination with Pd(Ph$_3$)$_4$ and Pd[P(o-Tol)$_3$]$_4$ catalysts in the synthesis of poly(p-phenylene)s. These catalysts promoted the deboronation reaction before the polymerization reaction leading to lower molecular weight polymers. This effect was very evident with aged catalysts. Using freshly made catalyst prepared in situ ameliorated this effect, culminating in higher molecular weight polymers.$^{16,17,19}$ Guillerez and Bidan proved that these hydrolytic deboronation reactions can be suppressed by using a phosphine-free catalyst such as Pd(OAc)$_2$. $^{20}$ Bauerle and co-workers observed and reported a suppression of hydrolytic deboronation by using a non-aqueous medium (THF instead of THF/water mixture) and CsF as the base.$^{21}$
Aryl-aryl exchange reactions were observed, in which a Ph group was transferred from Pd(PPh₃)₄ or a tolyl group from Pd[P(o-Tol)₃]₄ to the polymer via a Pd complex. This process stops chain growth. It was also noted that the aryl-aryl transfer reaction was not possible with Pd(OAc)₂ catalyst.¹⁶,²²

3.3 Results and discussions

3.3.1 Synthesis of Poly-propenyl-m-phenylene via Suzuki polymerization reaction.

A consequence of the Carother’s equation (Xn = 1/1-p; where Xn is the number average value of the degree of polymerization, p is the extent of conversion to polymer) is that highly pure monomers can give adequate molecular weight polymers. ¹H NMR, ¹³C NMR and GCMS data were used to determined the purity of our monomer. We were able to synthesize 23 g of monomer following the optimization of the monomer synthesis. This was essential for our synthetic strategy because although the polymerization reaction is high yielding, more than 70% of the mass is lost in the polymerization and subsequent RCM reaction. Much starting material was also required to optimize the polymerization and subsequent RCM reactions.

With a reasonable amount of clean monomer available, we proceeded to the optimization of the polymerization reaction. Our reaction of choice was the Suzuki polycondensation reaction. Precedent for this reaction was obtained from Bonifacio’s work. He carried out test polymerization reactions using Yamamoto coupling and Suzuki coupling reactions on the synthesis of poly-1,3-dimethyl
poly(\textit{m}-phenylene). The Suzuki polymerization yielded higher molecular weight polymers (Mw = 8.33 x 10^3, PDI = 4.54) compared to the Yamamoto reaction (Mw = 6.2 x 10^3, PDI = 1.62). He carried out this reaction on our target borylated monomer (4) and obtained the product in 77\% yield. The polymer had a molecular weight Mw = 16690 with PDI = 5.10. The optimized conditions for this reaction consisted of refluxing the reactants in dimethoxyethane (DME) in the presence of Pd(PPh₃)₄ and sodium carbonate.

3.3.2 Polymerization reaction with Pd(PPh₃)₄ catalyst

The Pd catalyst was washed with MeOH before use in the Suzuki polymerization to remove impurities that gave chain termination and isomerized the olefins.

In Bonifacio's work, the product was treated with hydrogen peroxide to remove traces of triphenyl phosphine, which is believed to have an adverse effect on the subsequent RCM reaction. In our synthesis, we realized that this treatment was not necessary, as we did not observe any traces of residual triphenyl phosphine in the polymer. The RCM reaction worked just fine with untreated polymer.

The optimized conditions were applied in the Suzuki polymerization of labeled bromo dipropenyl phenyl pinacolborate (14) affording the product, poly\{4,6-di[(1E)-(2-2H)-propenyl]}-\textit{m}-phenylene in 87\% yield. The monomer was dissolved in DME and refluxed for 27 h in the presence of an aqueous solution of sodium carbonate and Pd(PPh₃)₄. The product was extracted with CH₂Cl₂ and filtered through SiO₂ and magnesium sulfate.²³ Removal of the solvent afforded a
yellow solid. In contrast with Bonifacio, we did not treat the product with H₂O₂. This reaction is illustrated in scheme 3-3.

![Scheme 3-3: Polymerization reaction using Pd(PPh₃)₄ catalyst.](image)

[a] Pd(PPh₃)₄, NaHCO₃, H₂O, dimethoxyethane, 90°C, 16 h, 87%.

The use of commercially available Pd(PPh₃)₄ catalyst furnished pure product (Mw = 6874, Mn = 1899 and PDI = 3.62). The values from ¹H NMR are in accordance with the values observed from literature.²⁴

### 3.3.3 Isomerization of polymerization product

When the same Pd catalyst was used a couple of months later following its purchase, the product generated from the polymerization reaction had some extra peaks in the aromatic region of the ¹H NMR spectrum. These extra peaks were attributed to olefin isomerization products resulting, possibly from impurities in the Pd catalyst. The ¹H NMR spectrum is shown below in fig. 3-2. This unwanted isomerization confirms the fact that freshly prepared catalysts should be used for this polymerization.
**Figure 3- 3:** $^1$HNMR spectrum of poly dipropenyl-$m$-phenylene showing evidence of olefin isomerization.

We attempted to purify the catalyst by recrystallization in methanol but it was unsuccessful. The catalyst was insoluble in methanol. Following Prof. Schlüter’s advice, we decided to use freshly synthesized catalyst, Pd[P($p$-Tol)$_3$]$_3$ prepared from tri-$p$-tolylphosphine.

**3.3.4 Polymerization with Pd[P($p$-Tol)$_3$]$_3$ catalyst**

**3.3.4.1 Synthesis of Pd[P($p$-Tol)$_3$]$_3$ catalyst.**

Caution should be exercised when carrying out this reaction because the product is air and moisture-sensitive. The solvents used for this reaction, EtOH and MeOH were thoroughly degassed by the freeze-pump-thaw method. Again, caution should be exercised when degassing MeOH because it expands on freezing. The
round-bottomed flask cracked during the process and we resorted to degassing MeOH under vacuum without freezing it.

Tri-\textit{p}-tolylphosphine and PdCl$_2$ were transferred to a dry Schlenk flask. Dry, degassed DMSO was added to the flask and the mixture was heated at 150 °C under reflux. The temperature was reduced to 120 °C and hydrazine hydrate was added to the reaction mixture. The mixture was stirred for 10 min and cooled down to room temperature. Degassed EtOH was added to the mixture to precipitate the catalyst. A yellow precipitate was formed and collected by vacuum filtration. The product was washed with degassed MeOH and dried under vacuum.$^{25,26}$ It was used immediately for the polymerization reaction. The excess catalyst was stored in sealed ampoules under vacuum. This reaction is illustrated in scheme 3-4.

\begin{center}
\includegraphics[width=0.7\textwidth]{scheme}
\end{center}

**Scheme 3- 4:** Synthesis of Pd[P(\textit{p}-Tol)$_3$)$_4$.

[b] PdCl$_2$, P(\textit{p}-Tol)$_3$, N$_2$H$_4$, XH$_2$O, EtOH, MeOH, 150°C-rt.

### 3.3.4.2 Suzuki polycondensation with Pd[P(\textit{p}-Tol)$_3$)$_4$ catalyst

The polymerization reaction was performed immediately following the synthesis of the catalyst. The labeled monomer (14) was transferred to a round-bottomed flask containing distilled THF and an aqueous solution of NaHCO$_3$. The
content of the flask was stirred for 10 min followed by addition of Pd[P(p-Tol)]₄. The reaction mixture was refluxed at 90 °C for 4 days. The reaction mixture was cooled down to room temperature, extracted with CH₂Cl₂, and filtered through a pad of SiO₂ and anhydrous magnesium sulfate. The solvent was reduced to 4 mL and the product was precipitated with MeOH. The white amorphous polymer was collected by vacuum filtration and dried under reduced pressure.²⁷,²⁸

**Scheme 3-5:** Polymerization reaction using Pd[P(p-Tol)]₄ catalyst.

![Scheme 3-5](image)

[c] NaHCO₃, THF, H₂O, Pd[P(p-Tol)]₄, 90 °C, 4 days, 75%.

### 3.4 Polymer characterization

The purity of the product was determined by ¹H NMR (fig. 3-4) and ¹³C NMR (fig. 3-5). The results indicated the polymer was clean. IR spectrum of the product (figure 3-6) showed the characteristic and isolated signal for the C-D vibration frequency at 2231 cm⁻¹. The presence of this peak is essential for monitoring the progress of our ensuing RCM reaction.
Figure 3-4: $^1$HNMR spectrum of poly{4,6-di[(1E)-(2-^2H)-propenyl]}-m-phenylene synthesized with Pd[P(p-Tol)$_3$]$_4$ catalyst.

Figure 3-5: $^{13}$CNMR spectrum of poly{4,6-di[(1E)-(2-^2H)-propenyl]}-m-phenylene synthesized with Pd[P(p-Tol)$_3$]$_4$ catalyst.
Figure 3-6: IR spectrum of poly{4,6-di[(1E)-(2-H)-propenyl]}-m-phenylene synthesized with Pd[P(p-Tol)]_4 catalyst.

A MALDI spectrum (figure 3-7) of the polymer was obtained using dithranol/Ag matrix. The spectrum showed the 156 repeat unit pattern as expected for the non-deuterated monomer.
**Figure 3-7:** MALDI-TOF spectrum of poly{4,6-di[(1E-propenyl)]-m-phenylene showing 156 repeat unit.

Some polymer samples were run using trans-2-[3-(4-t-butyl-phenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) matrix.

GPC analysis was performed for polymers obtained from Suzuki polycondensation reactions under different conditions.
<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Condition</th>
<th>Mw</th>
<th>Mn</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd(PPh₃)₄</td>
<td>Dilute reaction</td>
<td>6874</td>
<td>1899</td>
<td>3.62</td>
</tr>
<tr>
<td>Pd[P(p-Tol)₃]₄</td>
<td>Dilute reaction</td>
<td>6201</td>
<td>3217</td>
<td>1.93</td>
</tr>
<tr>
<td>Pd[P(p-Tol)₃]₄</td>
<td>Concentrated reaction</td>
<td>9244</td>
<td>4903</td>
<td>1.89</td>
</tr>
</tbody>
</table>

**Table 3- 1:** Comparison of average molecular weight and PDI values for different polymers synthesized from different catalysts.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Mw</th>
<th>Mn</th>
<th>PDI/RU</th>
<th>Reaction scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRL4-33A</td>
<td>9839</td>
<td>2312</td>
<td>4.25/15</td>
<td>500mg scale Dilute</td>
</tr>
<tr>
<td>VRL4-33B</td>
<td>9244</td>
<td>4903</td>
<td>1.89/31</td>
<td>500mg scale Conc</td>
</tr>
<tr>
<td>VRL4-43</td>
<td>24567</td>
<td>5683</td>
<td>4.32/36</td>
<td>3g scale Dilute</td>
</tr>
<tr>
<td>VRL4-41</td>
<td>2023</td>
<td>1666</td>
<td>1.21/11</td>
<td>3g scale Conc</td>
</tr>
<tr>
<td>VRL4-52</td>
<td>24354</td>
<td>5580</td>
<td>4.36/35</td>
<td>3g scale Dilute</td>
</tr>
</tbody>
</table>

**Table 3- 2:** Comparison of average molecular weight and PDI values for different polymers synthesized with Pd[P(p-Tol)₃]₄ catalyst.

A PDI of 3.62 and average chain length of 12 repeat units was obtained when old Pd(PPh₃)₄ was used. The old catalyst probably promotes the undesirable deboronation and dehalogenation reactions, which were most likely responsible for limiting the growth of the polymer chain. The fact that the reaction was run for only 27 hours is another plausible explanation why we obtained short polymer chains.
The reaction time was not long enough for the polymers to react and form longer chains compared to 4 days for Pd[P(p-Tol)_3]_4 catalyst.

When freshly prepared Pd[P(p-Tol)_3]_4 was used under dilute (0.018M) conditions, a PDI of 1.93 and average chain length of 20 repeat units was obtained. A slightly longer chain length, 31 repeat units, and a PDI of 1.89 was obtained for the polymer synthesized under higher concentrations (0.036M) using Pd[P(p-Tol)_3]_4 catalyst (table 1). An extended study of the concentration effect on the polymerization revealed that polycondensation reactions under dilute conditions generally afforded polymers with higher PDIs (table 2). This could be due to the formation of macrocycles of different ring sizes under dilute conditions. It has been reported that dilute reaction conditions favor formation of macrocycles in polymerization reactions.²⁹

A monomer of high purity was required to obtain a high molecular weight polymer with a PDI value between 1 and 2. The purity and age of the catalyst as well as the duration of the reaction are very important aspects to consider when running these reactions. No reaction occurred at room temperature. Refluxing conditions was required for polycondensation reaction to occur. The polymerization reaction was optimized leading to product yields greater than 75% and 36 repeat units.

Pd[P(p-Tol)_3]_4 catalyst was used for the polymerization reaction under concentrated conditions resulting in the formation of a polymer with PDI of 1.21 (figure 3-8).
Figure 3-8: Normalized distribution curves for polymer sample

3.5 Formation of macrocycles

During the polycondensation reaction, macrocycles were formed together with the open chain polymers. The presence of macrocycles was confirmed by end-group analysis performed on MALDI-TOF data. Extrapolation of the linear curve revealed a molecular weight of 1044g/mol at the intercept corresponding to six repeat units (936 g/mol) plus Ag\(^+\) ion (108 g/mol) from the matrix (figure 3-9).
**Figure 3-9**: End group analysis for non-labeled polymer

This means there were no extra groups on the ends of the polymer suggesting a cyclic structure. The macromolecule is a precursor for kekulenes.

**Scheme 3-6**: Macrocyle formation via Suzuki polycondensation reaction

With a halogen on one end of the polymer chain and a boronic ester functional group on the other, it is likely for these two ends to react, so long as they
can come together and the resulting ring is large enough to accommodate ring strain in the resulting product. It may be possible to tune the reaction conditions to favor formation of macrocycles.

3.6 Experimental

Materials and methods: All the reactions were carried out under inert atmosphere under nitrogen. The catalysts were weighed out in the glove box under nitrogen atmosphere and transported in a sealed vial to the reaction flask. Tetrakis(triphenylphosphine) palladium(0) was washed with hot EtOH in an attempt to purify it. Tris(tri-p-tolylphosphine)palladium was synthesized in the glovebox and used immediately following its preparation. Excess catalyst was stored in sealed ampoules at -20°C in the glovebox. THF was purified and dried by treatment with sodium and benzoquinone under refluxing conditions. All NMR data (1H and 13C) were recorded either on a MR400 MHz, varian 400 MHz or 500 MHz instrument. The IR data was obtained on the Thermo-nicolet Nexus 470 FT-IR and the Nicolet 6700 FT-IR spectrophotometers. Gel permeation chromatography (GPC) was measured on a system consisting of a Waters 515 pump, Waters styragel HR 3 column, Perkin Elmer LC-95 UV/visible spectrophotometer detector, Sedere Sedex 75 evaporative light scattering detector (ELSD) and a SRI model 302 Peak Simple chromatography data system.
3.6.1 Synthesis of Tris(tri-\(p\)-tolylphosphine)palladium

To a 100 mL Schlenk flask was added tri-\(p\)-tolylphosphine (1 g, 3.29 mmol) and \(\text{PdCl}_2\) (116 mg, 0.654 mmol). Degassed DMSO (10 mL) was added to the flask under \(\text{N}_2\) atmosphere. The mixture was heated at 150 \(^\circ\text{C}\) under refluxing conditions to dissolve all the compounds. The temperature was reduced to 120 \(^\circ\text{C}\) and hydrazine hydrate (0.14 mL, 2.87 mmol) was added to the flask. The solution turned dark orange with the evolution of \(\text{N}_2\) gas. The reaction mixture was stirred for 10 min and cooled down to room temperature. Ethanol (8 mL) degassed by the freeze-pump-thaw was added to the flask followed by gentle stirring at room temperature. A yellow solid precipitated out of the solution. The solid was collected by vacuum filtration under \(\text{N}_2\) atmosphere and washed with degassed MeOH (25 mL). Drying under reduced pressure afforded tris(tri-\(p\)-tolylphosphine)palladium (502 mg, 44.8\%). The catalyst was used immediately for polymerization reaction. The excess catalyst was stored by sealing it in ampoules under vacuum. Note should be made of the fact that caution should be exercised throughout the synthesis to avoid air or moisture because this catalyst is very air and moisture-sensitive.

3.6.2 Synthesis of Poly\{4,6-di[(1E)-(2,2H)-propenyl]\}-m-phenylene with Pd(PPH\(_3\))\(_4\)

To a mixture of 2-{5-bromo-2,4-di[(1E)-(2-\(^2\)H)prop-1-ethyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane \(\textbf{14}\) (2.15 g, 5.89 mmol) and Pd(PPH\(_3\))\(_4\) (0.34 g, 0.295 mmol) was added dry dimethoxyethane (24 mL). The mixture was stirred
under N₂ at room temperature for 10 min. A 2M aqueous solution of Na₂CO₃ (32 mL) was added to the reaction mixture. The mixture was stirred vigorously under reflux at 90 °C for 27 h. The reaction mixture was cooled down to room temperature. Water was added and the mixture extracted 3 times with CH₂Cl₂. The organic layer was passed through a pad of MgSO₄ and silica gel. The filtrate was concentrated in vacuo to afford a yellow product (0.874 g, 93.8%). Mp 232 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.68 (br, 1H), 6.87 (br, 1H), 6.18–6.11 (br, d, 2H, J = 28 Hz), 1.74–1.52 (br, 6H). ¹³C NMR (400 MHz, CDCl₃): δ 138.0, 135.2, 132.4, 129.4, 125.4, 121.2, 18.5. IR (cm⁻¹): 3018, 2953, 2923, 2845, 2229, 193934, 1688, 1628, 1455, 1260, 1090, 1027, 892, 806. UV (tetrahydrofuran, nm): λmax 270 (ε 33,040).

3.6.3 Synthesis of Poly{4,6-di[(1E)-(2⁻²H)-propenyl]⁻m-phenylene with Pd[P(p-Tol)₃]₄

2-{5-Bromo-2,4-di[(1E)-(2⁻²H)prop-1-enyl]phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (500 mg, 1.37 mmol) and NaHCO₃ (1.15 g, 13.7 x 10⁻³ mmol) were transferred to a dry 50 mL Schlenk flask. To the flask was added purified water (4 mL) under N₂ atmosphere. The content of the flask was degassed and filled with N₂ three times. Tris(tri-p-tolylphosphine)palladium (8.3 mg, 3.14 x 10⁻³ mmol) dissolved in THF (3 mL) was added to the flask and the degassing process repeated. The mixture was refluxed at 70 °C under N₂ for 4 days. The reaction mixture was cooled down to room temperature and extracted with CH₂Cl₂. The combined organic layer was filtered through a column packed with SiO₂ and anhydrous MgSO₄. The solvent was reduced to 2 mL and the product was precipitated with MeOH (10 mL).
Poly{4,6-di[(1E)-(2-²H)-propenyl]}-m-phenylene (162 mg, 75 \%) was collected by vacuum filtration as an off-white powder. Mp 230 °C, \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta \) 7.68 (br, 1H), 6.90 (br, 1H), 6.19–6.11 (br, d, 2H, J = 30 Hz), 1.75–1.53 (br, 6H). \(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \(\delta \) 137.1, 135.5, 132.8, 129.5, 125.8, 121.3, 18.6. IR (cm\(^{-1}\)): 3016, 2959, 2909, 2850, 2727, 2232, 1634, 1469, 1445, 1373, 906, 865, 678. UV (tetrahydrofuran, nm): \(\lambda_{\text{max}} \) 270 (\(\varepsilon 20,524\)).

### 3.7 References


2676.


Chapter 4: Optimization of the Ring Closing Metathesis (RCM) reaction

4.1 Background

The advances in recent years in metal carbene catalysts gave birth to a class of reactions known as olefin metathesis reactions. These reactions involve the swapping of substituents on an olefin. It can be described simply as a dance in which partners are exchanged. Olefin metathesis reactions have been classified based on the nature of the substrates and the products formed from the reaction. Ring opening metathesis (ROM) and ring opening metathesis polymerization (ROMP) reactions from cyclic alkenes, acyclic diene metathesis reaction (ADMET) and ring closing metathesis (RCM) reactions from acyclic precursors.1,2

Metathesis reactions are also known for alkynes. Examples of this reaction include acyclic alkyne metathesis and acyclic diyne metathesis (ADIMET). When an alkyne is reacted with an alkene, the reaction pathway is believed to pass through a metallocyclobutene intermediate furnishing a diene product. Alkyne metathesis was first utilized in polymer chemistry in the synthesis of highly conjugated and rigid polymers like poly(para-phenyleneethynylene)s.3,4 These reactions were later applied to natural product chemistry for the synthesis of symmetrical and unsymmetrical alkynes.5 One common setback with olefin metathesis reaction is the generation of a mixture of geometric isomers (E and Z) following the formation of large ring systems. Alkyne metathesis reaction has been used to circumvent this dilemma. The product formed from alkyne metathesis is treated with Lindlars cat.
or hydroboration followed by protonation to yield exclusively the Z-isomer. This idea has been applied in the synthesis of many natural products.6-8

![Scheme 4-1](image)

**Scheme 4-1**: Generalized olefin metathesis reaction

### 4.2 Ring closing metathesis reactions

The RCM reaction leads to the formation of cycles while the other reactions furnish acyclic dienes and polymeric alkenes.1

Ring closing metathesis (RCM) reaction is a versatile reaction involving the reaction of a suitable catalyst and two alkenes to make a new double bond with exchange of substituents, ultimately resulting in the formation of a ring. This reaction generally leads to the generation of 5 to 30-membered cyclic alkene structures. The reaction mechanism involves the generation of a metallocyclobutane intermediate, which undergoes cycloreversion to the product and back to the reactants.9 The equilibrium state can be tuned to favor product formation by the generation of volatile by-products, which can be removed from the reaction mixture as soon as they are produced.

The RCM reaction has been widely employed in the synthesis of a huge variety of macrocycles in the synthesis of some natural products.10,11 The reaction was recently applied to the formation of strained cyclic aromatic systems.12,13 The most prominent setback with this reaction is the lack of stereospecificity of the new
double bond in the ring. The stereochemistry is usually ill-defined and depends to a large extent on the ring strain/size, with larger rings producing mixtures of geometric isomers. One of the most beautiful aspects of this reaction is the high tolerance to a myriad of functional groups. This makes the RCM reaction particularly useful in the synthesis of pharmaceuticals which generally bear multiple and varied functionalities.\textsuperscript{1,14,15} The reaction is well behaved and non-invasive and has found application in a wide array of polymer synthesis.\textsuperscript{16} The chemical industry has also benefitted tremendously from this award-winning reaction. Robert H. Grubbs, Richard R. Schrock and Yves Chauvin were awarded the 2005 Nobel prize in Chemistry for their work on olefin metathesis reactions. This underscored the importance of this reaction in industry and academia.

\textbf{Scheme 4- 2:} Generalized ring closing metathesis reaction (RCM) reaction.

Shawn and co-workers reported the first synthesis of helicenes via RCM reaction in 2006. They were able to construct a 7-helicene by a ring closing metathesis of two ethylene-containing fragments.\textsuperscript{17} Only one aromatic ring was formed in this process.
Thermodynamics calculations performed by Bonifacio indicated an exergonic reaction with -28 kcal/mol for the synthesis of phenanthrene via RCM reaction (scheme 4-3).\textsuperscript{18,19}

![Scheme 4-3: Exergonic reaction for the formation of phenanthrene via RCM reaction](image)

Calculations estimated the enthalpy of formation of dibenz[a,j]anthracene and dibenz[a,h]anthracene form 2,4',6',2''-tetravinyl-[1,1';3',1'']terphenyl and 2,2',5',2''-tetravinyl-[1,1';4',1']terphenyl at -57.12 kcal/mol and -60.08 kcal/mol respectively. These values were almost equal to twice the value for the enthalpy of formation of phenanthrene (scheme 4-4) indicating the process can proceed by multiple cyclizations.\textsuperscript{18}
Scheme 4-4: Calculated enthalpies of formation of dibenzanthracenes by RCM

Results from calculations also revealed that the ring closing metathesis was a more favorable process compared to the dimerization. These results were later justified by the successful synthesis of these compounds (dibenzanthracenes) by Bonifacio of B.T. King group by RCM reaction using Grubbs catalyst.\textsuperscript{18,19}

Our research presents the synthesis of multiple fused aromatic rings in the synthesis of polymeric helicenes and kekulenes via an RCM reaction. The formation of a volatile by-product which can be removed as the reaction progresses, and the stabilization energy gained by forming new aromatic rings compensate for the unfavorable thermodynamic energy involved in moving from a relatively more stable, less strained open chain system to a strained helical and cyclized product.
4.3 Results and Discussions

We were able to synthesize an appreciable amount of the polymer in good yield following our optimization efforts. With a bunch of the polymer on hand, we set out to optimize the RCM reaction. Note should be made of the fact that we obtained both the open chain and cyclized polymers which are precursors for the polymeric helicene and kekulene respectively.

4.3.1 Development of a spectroscopic signature (C-D stretch) to monitor the RCM reaction

In the design of the target polymer for the RCM reaction, a deuterium label was strategically incorporated into the polymer to assist in monitoring the progress of the RCM reaction. The RCM reaction will culminate in a transfer of the C-D bond to the butene molecule, which is lost as a volatile by-product. The loss of D can be detected by infrared spectroscopy and used to monitor the RCM reaction and helicene/kekulene formation.

The generalized equation for the synthesis of [n]helicene is shown below.

Scheme 4-5: Generalized equation for synthesis of extended polymeric n-helicene
The C-D bond was incorporated into the monomer and it was preserved during the synthesis of the polymer.

4.3.2 Monitoring the RCM reaction

As demonstrated in the equation in scheme 4-5, deuterium-labeled butene, the volatile by-product of the RCM reaction, is lost from the reaction mixture during the RCM reaction. The loss of this C-D label from the starting polymer indicates the extent of the reaction and can be monitored by the disappearance of the C-D resonance from the IR spectrum. This is easily observed by the loss in intensity of the unique and isolated C-D vibration signal at ~2230 cm\(^{-1}\).

This process is more effective than the \(^1\)HNMR experiments for monitoring the reaction because we can study insoluble compounds. No expensive deuterated solvents are required. Only a minuscule amount of solid material is needed to obtain a good IR spectrum and we do not have to worry about the solubility of the putative helicene/kekulene.

The 1,2,4-trichlorobenzene solvent from an aliquot was removed under reduced pressure. A tiny amount of the residue, about 1 mg was used to obtain an IR spectrum. The process was done repeatedly and more catalyst was added as needed until a significant reduction of the C-D vibration signal was observed. The reaction was quenched when the C-D signal was sufficiently reduced to a constant value. Fig. 4-1 is a spectrum of over-laid IR spectra showing the disappearance of the C-D vibration signal over a period of five days.
Figure 4-1: IR spectrum of reaction mixture showing the disappearance of the C-D stretch signal over time.

Several factors were considered in optimizing the RCM reaction:

- Overcoming the obstacle of solubility,
- Choosing an appropriate catalyst,
- Controlling catalyst loading,
- Optimizing the reaction temperature,
- Controlling unwanted isomerizations,
- Tuning work-up and catalyst removal.

These factors will be discussed in detail in the subsequent sections.
4.3.3 Optimization of the RCM reaction

Many small-scale reactions were performed under different conditions in an attempt to optimize the RCM reaction. The extent of the reaction was determined and monitored by IR spectroscopy as described in the previous section.

4.3.3.1 Overcoming the obstacle of solubility

**Solvent:** We realized in our earlier screens that the reaction mixture became cloudy after a few hours following the onset of the reaction. Subsequent studies indicated that the partially reacted material was in insoluble in the solvents used. This was an unfavorable observation because the partially reacted polymer precipitates and does not react further. Getting an appropriate solvent in which the product was soluble was essential.

Dichloromethane is a popular solvent for RCM reactions. We used dichloromethane in our early reactions and registered some degree of success. The major problems with this solvent included the fact that the reaction progress was limited by the reflux temperature (40 °C) and the partially reacted material was insoluble which halted the reaction. Toluene was a better solvent than dichloromethane. With toluene, we were able to increase the reaction temperature to 90 °C and the catalysts used were soluble. The lack of solubility of the product in toluene precludes its use. With tetrachloroethylene, we were able to use temperatures as high as 140 °C, but this solvent still failed to fix the issues. 1,2,4-Trichlorobenzene proved to be our solvent of choice. The fact that we were able to achieve product solubility in this solvent outweighed its high boiling point (213 °C).
This solvent was used widely in this project. It was the solvent for the RCM reaction, treatment of the product with tris(hydroxymethyl)phosphine, and column chromatographic separation using polymer-based bio-beads.

4.3.3.2 Choosing a catalyst

A host of different catalysts were screened in our optimization efforts.

Shrocks catalyst is known to be more active than Grubbs catalyst and it works better on sterically hindered substrates. Unfortunately, it is expensive and very sensitive to air and moisture. It produced positive results in our test runs at 50 mol% catalyst concentration. Most of the reactions failed due to improper handling and high sensitivity of the catalyst.

Hoveyda-Grubbs 2nd gen. catalyst produced positive results under microwave conditions at high catalyst concentrations, 20 mol%. No product was observed when the catalyst concentration was reduced to 15 mol% under microwave irradiation. No product was also formed at lower temperatures, 40 °C in CH₂CH₂. Product formation was observed with Hoveyda-Grubbs catalyst under microwave irradiation at 30 mol% catalyst concentration. Hoveyda-Grubbs catalyst required high catalyst loadings and high temperatures.

Grubbs 2nd generation catalyst produced the best results. Product formation was observed under many conditions. This catalyst is stable and has a high functional group compatibility. The reaction worked in toluene, in the presence and absence of microwave irradiation. Product formation was observed with Grubbs 2nd generation catalyst (15 mol%) in toluene and microwave irradiation (temperature =
150 °C, 35 min). Reaction with Grubbs 2nd generation catalyst in CH₂CH₂ required 50 mol% of catalyst and 4 days. The best result was obtained when the catalyst was dissolved in toluene and added to a solution of the polymer in 1,2,4-trichlorobenzene.

Some analogues of Grubbs 2nd gen catalyst [[1,3-Bis(2-methylphenyl)-2-imidazolidinylidenedi]dichloro(2-isopropoxyphenylmethylene)-ruthenium II and 1,3-Bis(2-methylphenyl)-2-imidazolidinylidenedi]dichloro(benzylidene)(tricyclohexylphosphine)-ruthenium II] which are efficient for sterically hindered and tetrasubstituted olefins were also tested and they furnished the product at 5 mol% catalyst concentration in toluene, refluxing at 80-85 °C. Zhan catalyst-1B failed to initiate any reaction. Schrock-Hoveyda catalyst (10 mol%) furnished no product in CH₂Cl₂ at 40 °C.

Figure 4-2 shows structures of all the catalysts that were used in the optimization studies.
**Figure 4-2:** Structures of olefin metathesis catalysts used in the optimization studies

### 4.3.3.3 Controlling catalyst loading

We started off with 50 mol% catalyst loading at the beginning of the optimization process. This was expensive. Monitoring the progress of the reaction was also made difficult because of too much catalyst. Getting rid of all the catalyst
during the work-up process was a problem. We had to search for conditions that will lead to our desired products at lower catalyst concentrations. When we used 1,2,4-trichlorobenzene as solvent, we achieved product solubility and we were able to reduce the catalyst (Grubbs 2nd generation) loading from 50 mol% to 5 mol%.

4.3.3.4 Optimization of temperature

It has been reported in the literature that the catalyst is deactivated at high temperatures, so we had to strike a balance between getting the reaction temperature hot enough for the reaction without destroying the catalyst. The reaction worked for all the trial temperatures but the amount of conversion was mostly limited by product solubility in the other solvents. The reaction temperature ranged from 40 °C in dichloromethane, through 90 °c in toluene, 150 °C in tetrachloroethylene, and 175 °C in 1,2,4-trichlorobenzene. We realized that a very high temperature was not required with 1,2,4-trichlorobenzene. The reaction worked well, at 70 °C with 1,2,4-trichlorobenzene as solvent but failed at 40 °C.

4.3.3.5 Suppressing unwanted isomerizations

One of the major problems with olefin metathesis reactions is the formation of unwanted isomerization products, which are generally difficult to separate via standard experimental procedures and constitute impurities, which reduce the quality and yield of the product. Olefin isomerization has been reported with Ru-based olefin metathesis catalysts. Grubbs and co-workers reported that the isomerization was due to metal hydride species resulting from the decomposition of the catalyst.
In our project, the unwanted isomerization resulted in the formation of terminal alkenes on the propenyl side chains giving rise to products with non-aromatic, 7-membered rings (scheme 4-6). This was a defect in the RCM reaction.

**Scheme 4-6:** Unwanted isomerization in the RCM reaction

A search for additives to act as scavengers of the metal hydride species led to the discovery of compounds like quinones, vitamin E, BHT, halogenated alkanes, halogenated aromatics, halogenated quinones as well as utilizing low temperatures. Recently it was reported that low molecular weight organic acids e.g formic, benzoic and acetic acids can serve as effective acidic metal hydride scavengers or inhibitors of unwanted isomerization in olefin metathesis reactions.\(^\text{23}\) 2,6-Dichloro-1,4-benzoquinone, a halogenated quinone, was used as the metal hydride scavenger to prevent unwanted isomerization during the RCM reaction. The halogenated quinone (5 mol\%) was added at the beginning of the reaction. It was removed at the end of the reaction during work-up.

**4.3.3.6 Tuning work-up and catalyst removal**

**Quenching the reaction:** Vinyl ethers have been reported to deactivate olefin metathesis catalysts\(^\text{24}\) and are used to quench RCM reactions. The resulting unreactive/deactivated catalyst can be removed by chromatographic separation.
Diethylene glycol monovinyl ether, a commercially available vinyl ether was used to deactivate the olefin metathesis catalyst following the completion of the RCM reaction.

**Catalyst removal:** One of the major shortcomings with Grubbs and other metathesis catalysts is getting rid of the catalyst after the reaction. There is an absolute need to eliminate the deactivated and decomposed catalyst after the metathesis reaction as they constitute impurities in the product which alter product stability, impart unwanted color to the product and increase the toxicity of the product. The importance of this aspect is highlighted in the synthesis of pharmaceutical products where ruthenium contamination levels of < 10 ppm is required for pharmaceutical applications. Several systems have been developed over the years to remove residual catalyst post olefin methathesis reactions. They include and are not limited to treatment with tris(hydroxymethyl)phoshine,$^{25}$ Pb(OAc)$_2$, activated carbon,$^{26}$ DMSO or triphenylphoshine oxide,$^{27}$ mesoporous silicates,$^{28}$ polar isocyanide,$^{29}$ and modified catalysts.$^{30}$ In 2007, Grubbs and Hong synthesized a polyethylene glycol-supported catalyst that was removed by simple aqueous treatment of the reaction mixture. Five aqueous washes followed by treatment with activated carbon led to a significant reduction of the ruthenium contamination level (< 0.04 ppm), an appropriate level for pharmaceutical applications.$^{31}$

In our RCM reaction protocol, the crude product was treated with tris(hydroxymethyl)phosphine in basic medium under refluxing conditions for 16
hours. The reaction mixture was flash column chromatographed with 1,2,4-trichlorobenzene as solvent to remove residual ruthenium catalyst. This furnished a relatively pure and catalyst-free product mixture.

4.3.3.7: Other attempted reaction conditions and their outcomes

These conditions included microwave-assisted reactions at various temperatures ranging from 70 °C to 150 °C, and cross metathesis reactions.

Microwave-assisted reactions: Most of the microwave reactions conducted at high temperatures (90 °C – 150 °C) with Grubbs 2\textsuperscript{nd} generation catalyst furnished the product as a green solid. The reactions carried out in the microwave reactor were done under refluxing conditions. This process was abandoned because it did not yield reproducible results.

Cross metathesis reaction: Our motivation for attempting the cross metathesis reaction stemmed from our desire to synthesize a less sterically hindered polymer precursor to facilitate the RCM reaction (figure 4-7). Ethylene gas was bubbled through the reaction mixture in tetrachloroethylene, toluene and 1,2,4-trichlorobenzene to facilitate cross metathesis reaction. This cross metathesis reaction furnished the product but required temperatures above 40 °C. The preferred catalyst for cross metathesis reaction was Grubbs 2\textsuperscript{nd} generation catalyst. The reaction scheme for the cross metathesis reaction is illustrated in scheme 4-6. This process was effective in furnishing the product. The main issue with the process was the fact that we were losing the deuterium label during the first step of the cross metathesis process. This precluded measuring the extent of the actual ring
forming process because the deuterium signal was ethylene by-product during the cross metathesis in the first step. The cross metathesis reaction was abandoned and we concentrated our efforts on the regular ring closing metathesis reactions.

Scheme 4-7: Cross metathesis reaction.

It is likely that the cross metathesis and the ring closing metathesis occur concurrently. The figure is only schematic.
A summary of the optimization efforts and results is presented in the table below.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Conditions</th>
<th>Conditions</th>
<th>Conditions</th>
<th>Optimized conditions</th>
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<td>toluene/1,2,4-trichlorobenzene</td>
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<td>Zhan</td>
<td>Hoveyda-Grubbs, 20 mol%</td>
<td>Grubbs 2nd gen., 4 – 6 mol%</td>
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<td>no CH₂CH₂</td>
<td>CH₂CH₂, cross metathesis</td>
<td>No cross metathesis</td>
</tr>
</tbody>
</table>

**Table 4-1**: Summary of RCM optimization conditions

**4.4 Synthesis of polymeric [n]helicenes and [n]kekulenes using optimized reaction conditions**

RCM reaction of the polymer using our optimized conditions furnished [n]helicenes and [n]kekulenes from the mixture of acyclic and cyclic precursors. The generalized equation for these reactions and the optimized reaction conditions is illustrated on scheme 4-8.
Scheme 4-8: Generalized optimized equations for the synthesis of polymeric [n]helicenes and [n]kekulenes

[a] Grubbs 2nd generation catalyst, toluene, 1,2,4-trichlorobenzene, 2,6-dichloro-1,4-benzoquinone, diethylene glycol monovinyl ether (quench), 90 °C, 1-3 days.

We succeeded in optimizing conditions for the RCM reaction. The best conditions generated included:

- Grubbs 2nd generation catalyst,
A mixture of toluene and 1,2,4-trichlorobenzene as solvent,
- 2,6-Dichloro-1,4-benzoquinone as a hydride scavenger to prevent unwanted isomerizations,
- Diethylene glycol monovinyl ether to quench/deactivate the catalyst,
- Reaction temperature 70-90 °C.

The product was obtained as a mixture. The experimental procedure leading to the synthesis of the product is described in the experimental section. The separation of this mixture will be described in chapter 5.

4.6 Experimental

4.6.1 RCM Reaction with Grubbs 2nd gen catalyst

Poly{4,6-di[(1E)-(2-^2\text{H})-propenyl]}-m-phenylene (1.00 g, 1.58 mmol) and 2,6-dichloro-1,4-benzoquinone (0.06 g, 0.316 mmol) were transferred to a 50 mL Schlenk flask. Distilled and degassed 1,2,4-trichlorobenzene (20 mL) was added to the flask under N\textsubscript{2}. Grubbs 2\textsuperscript{nd} generation catalyst (256 mg, 0.043 mmol), dissolved in degassed toluene (10 mL) was added to the flask in three portions over 3 days. The mixture was refluxed at 70 °C and monitored by IR spectroscopy. The extent of completion of reaction was determined by the disappearance of the C-D label at 2232 cm\(^{-1}\). Vinyl ethers have a high affinity for ruthenium metal in the catalyst. They have been used to terminate ring opening metathesis reactions by cleaving the metal in the catalyst. Diethylene glycol monovinyl ether (1.5 mL) was added to the flask to deactivate the catalyst. Refluxing was resumed overnight. The solvent was
reduced to 3 mL and the product mixture was precipitated with MeOH (8 mL). The crude product, a greenish precipitate (881 mg) was collected by vacuum filtration.

**4.6.2 Treatment of RCM product with tris(hydroxymethyl)phosphine**

The crude product always contained residual catalyst and was treated with tris(hydroxymethyl)phosphine, Et$_3$N and SiO$_2$ to remove the catalyst. The green precipitate was dissolved in 1,2,4-trichlorobenzene (20 mL). EtN$_3$ (2 mL), SiO$_2$ (2 g) and tris(hydroxymethyl)phosphine (2 g) were added to the flask. The reaction mixture was heated at 70 °C overnight. The mixture was cooled down to room temperature, flash chromatographed on a column packed with SiO$_2$ and eluted with 1,2,4-trichlorobenzene. The solvent was removed in vacuo, and afforded a yellow solid (446 mg, 70.5%). Column chromatography on a column packed with polymer-based bio-bead (biorad s-x1) with 1,2,4-trichlorobenzene as eluent afforded 12 fractions. The first five fractions had a greenish-yellow fluorescence (predominantly helicene). Fractions 6 and 7 had a bluish-green fluorescence (mixture of helicenes and kekulenes) while fractions 7 – 12 (predominantly kekulene fractions) had a bright blue fluorescence. Fractions 7-12 were combined and re-chromatographed on a bio-bead column. [7]kekulene was obtained as a yellow solid following removal of the solvent. Its characterization is discussed in chapter 5.

**4.6.3 Matrix-assisted laser desorption ionization- Time of flight (MALDI-TOF)**

The samples were run on an Applied Biosystems 4700 MALDI TOF/TOF, in Positive ion reflecting mode, with voltage of 20 kV. Mass range 500 – 5000 Da. The instrument was calibrated using Applied Biosystems 4700 Calibration mixture. Up
to 2500 shots were accumulated per spectrum. Trans-2-[3-(4-tert-butyl(phenyl)-2-methyl-2-propenyliden]malononitrile (DCTB) was prepared as 10 mg/mL in dichloromethane. Samples were dissolved in dichloromethane to be 0.5 mg/500 uL. 1% silver triflate was prepared in acetone. The sample was mixed in the ratio 50:5:5 (matrix:sample:AgOTf). 1 uL of the mixture was spotted on the target.

4.7 Conclusion

RCM reaction of poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene furnished a mixture of kekulenes and polymeric helicenes from the cyclic and acyclic precursors respectively. The separation and characterization of this mixture will be discussed in chapter 5.

4.8 References


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Chapter 5: Separation and characterization of helicenes and kekulenes

5.1 Separation of n-helicenes and n-kekulenes

5.1.1 Silica gel separation of helicene/kekulene mixture

The product obtained from the RCM reaction following treatment with tris(hydroxymethyl)phosphine was subjected to silica gel chromatographic separation to remove the deactivated catalyst and inorganic impurities. The column was eluted with 1,2,4-trichlorobenzene. Tris(hydroxymethyl)phosphine is soluble in THF and it was therefore not a suitable solvent for this separation. The filtrate was evaporated to dryness on the kugelhorr to afford a yellow solid which was a mixture of helicenes and kekulenes. This mixture was chromatographed on an open column using gel permeation chromatographic separation to separate the helicenes from the kekulenes.

5.1.2 Open column gel permeation chromatography (GPC) separation

This chromatographic separation was achieved using polymer-based biobeads (biorad s-x1 and biorad s-x3) as the stationary phase and 1,2,4-trichlorobenzene as solvent/eluent. The biobead was washed with copious amounts of hot THF and flushed with hot 1,2,4-trichlorobenzene to remove polystyrene, which was contaminating the column fractions. Separation on the biobead column was based on the mass of the analyte.

The chromatographic separation afforded mixtures of kekulenes and mixtures of helicenes. The helicenes with relatively larger molecular weights were
eluted first from the column followed by the kekulenes. The kekulene fractions displayed an intense bluish fluorescence when viewed under long wavelength while the helicene fractions had a greenish-yellow fluorescence.

The most predominant kekulene was the [7]kekulene. Higher kekulenes were also identified on the MALDI-TOF spectrum. [7]Kekulene was isolated following multiple chromatographic separations on the open GPC column. This dissertation reports the first synthesis of kekulenes higher than cyclo[d.e.d.e.d.e.d.e.d.e]dodecaakisbenzene commonly referred to as ‘kekulene’, via RCM reaction.

The kekulenes and helicenes were characterized using information from literature, spectroscopic and other analytical data. Unfortunately we did not have enough pure material to fully characterize the helicenes and the kekulenes.

5.2 Characterization of helicene: Towards proof of helicene structure

5.2.1 MALDI-TOF mass spectrum of helicenes

The mass spectrum was obtained for the helicenes using the matrix-assisted laser desorption/ionization- time of flight (MALDI-TOF) mass spectrum. The spectrum obtained shown in figure 5-1 shows 100 repeat unit as expected. The identity of the end groups could not be identified from the end group analysis. No further separations were carried out on the helicenes and it was characterized as a mixture.
Figure 5-1: MALDI-TOF spectrum of helicene

5.2.2 Nuclear magnetic resonance (NMR) of helicenes

The $^1$HNMR spectrum of helicenes in figure 5-2 was obtained in THF-d$_8$. The peaks between 6 – 7.2 ppm corresponds to polystyrene impurities that were introduced from the biobead column. The peaks around 1 – 2 ppm corresponds to residual deuterated THF and some small impurities. The peaks around 7.2 – 7.5 ppm correspond to the solvents CHCl$_3$ and 1,2,4-trichlorobenzene. The broad peaks around 10 ppm, 7.5 – 8.5 ppm corresponds to the helicene. These peaks are broadened because the protons in the helix are in slightly different chemical environments. The $^1$HNMR spectrum of the helicenes was obtained in THF-d$_8$ solvent.
Figure 5-2: The $^1$HNMR spectrum of helicenes

5.2.3 IR of helicenes

Figure 5-3: IR spectrum of helicenes
The IR spectrum above shows the diminished C-H aliphatic signals below 3000 cm\(^{-1}\). The emergence of a prominent stretch at 884 cm\(^{-1}\) for the C-H out-of-plane deformation band was also evident.

5.3 Characterization of kekulenes: Towards proof of kekulene structure

5.3.1 MALDI-MS of kekulenes

![MALDI-MS spectrum](image)

**Figure 5-4**: MALDI-TOF spectrum of a mixture of n-kekulenes

For higher kekulenes, we expect increments of 100 mass units corresponding to the mass of a repeat monomer unit e.g 700 for [7]kekulenes, 800 for [8]kekulenes
etc. We observed 7, 8, 9, 10, 11, 12, 13, and 14 kekulenes as seen on the MALDI-TOF spectrum above (figure 5-4).

For a start, we directed our focus towards the isolation and characterization of [7]kekulene. This was achieved by repeated gel permeation chromatographic separation using a polymer-based resin (biorad s-x1). The mass spectrum of [7]kekulene is shown in figure 5-5.

![Mass spectrum](image)

**Figure 5-5:** Mass spectrum of [7]kekulene

[7]Kekulene was insoluble in all regular organic solvents but was sparingly soluble in THF. The mass spectrum showed a mass of m/z 700.24 with a calculated mass for $C_{56}H_{28}$ m/z 700.22.
5.3.2 NMR of [7]kekulene

[7]-Kekulene

| = [7]kekulene
| = [6]kekulene
★ = THF-d₈

**Figure 5-6:** ¹H NMR spectrum of [6]kekulene and [7]kekulene in THF-d₈

[7]Kekulene isolated from our project has a structure similar to [6]kekulene isolated by Staab and Dietrich in 1978.¹ We expect to have similar chemical shift values on the ¹H NMR spectrum with the same ratio of 2:1:1. The ¹H NMR spectrum of [7]kekulene obtained in THF-d₈ is shown in figure 5-6.

The ¹H NMR spectrum [(THF-d₈), fig. 5-6] of [7]kekulene shows 3 singlets at 7.99, 8.56 and 10.51 ppm in the ratio 2:1:1. These peaks correspond to the two protons on the newly formed double bond (7.99 ppm), the external proton on the benzene rings (8.56 ppm) and the core/inner deshielded proton (10.51 ppm). The peak at 7.2 ppm is CHCl₃. The peaks between 0.5 and 1.4 ppm probably result from
grease. Some unknown impurity in the solvent was identified at \( \sim 10.7 \) ppm and 6 ppm. The aliphatic signals between 1.5 and 3.7 ppm are residual THF signals.

**Figure 5-7:** Comparing \(^1\)HNMR values for [6]kekulene (left) and [7]kekulenenes (right)

The distribution, values and ratios of proton chemical shifts observed for [7]kekulene are similar to those obtained for [6]kekulene (figure 5-7).

### 5.3.3 UV-Vis of [7]kekulene

A solution of kekulene prepared by Staab and co-worker in 1,2,4-trichlorobenzene showed the following absorptions: \( \lambda_{\text{max}} \) 388 (log\( e \) 4.22), 347 (4.74), 326 (4.93).\(^1\) A solution of our isolated [7]kekulene in THF was analyzed and the following \( \lambda_{\text{max}} \) values were obtained, (UV (tetrahydrofuran, nm): 332, 294, and 260. The [7]kekulene was only partially soluble in THF so a true concentration and molar absorptivity values could not be obtained. The UV-Vis spectrum of [7]-  kekulene is shown on figure 5-8. We also had insufficient quantities to weigh.
Figure 5-8: UV-vis spectrum of [7]kekulene
5.3.4 Infrared (IR) spectrum of kekulenes

The IR spectrum of the kekulene(s) shows major peaks at 3024 cm\(^{-1}\) (corresponding aromatic C-H vibrations), 1454, 1494 cm\(^{-1}\) (aromatic C=C vibrations), 893, 778 and 698 cm\(^{-1}\). The aliphatic vibrations below 3000 cm\(^{-1}\) (2955, 2904, 2850 cm\(^{-1}\)) were greatly reduced indicating the loss of the aliphatic protons in the product. This IR spectrum was obtained for a mixture of kekulenes. We did not have enough material to get the IR spectrum of the isolated [7]kekulene.

![IR Spectrum Graph](image)

**Figure 5-9:** IR spectrum of kekulenes
**Figure 5-10:** Optimized structure and electron density distribution of [7]kekulene

### 5.4 Conclusion

Repeated column chromatographic separation using biobead S-x1 and S-x3 polymer resins afforded kekulenes (blue fluorescence) and polymeric helicenes (green fluorescence). The helicene was isolated and characterized as a mixture. The kekulene fractions were further separated on the biobead column to afford [7]kekulene and mixtures of [8], [9] and higher kekulenes. [7]Kekulene was not isolated in sufficient quantities to enable complete characterization of the compound. The mass, $^1$H NMR spectrum, UV spectrum and an IR of the kekulene mixture were obtained. This is the first report of the synthesis of a higher analogue of kekulene by ring closing metathesis reaction.

Having optimized the reactions leading to the synthesis of polymeric helicenes and kekulenes, these reactions can be repeated on a larger scale in order to obtain enough material for complete characterization.
5.5 References


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Chapter 2

2.1 NMR spectra

\[ \text{\textsuperscript{1}HNMR (400 MHz, CDCl\textsubscript{3}) spectrum of 1,5-dibromo-2,4-dimethylbenzene (1')} \]
$^{13}$C NMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-dimethylbenzene (1')
$^1$HNMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-bis(dibromomethyl)benzene (1'')
$^{13}$C NMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-bis(dibromomethyl)benzene (1'')
$^1$HNMR (400 MHz, CDCl$_3$) spectrum of 4,6-dibromobenzene-1,3-dicarbaldehyde (2)
$^{13}$CNMR (400 MHz, CDCl$_3$) spectrum of 4,6-dibromobenzene-1,3-dicarbaldehyde (2)
$^{1}$HNMR (400 MHz, CDCl$_3$) spectrum of CH$_3$CD$_2$PPh$_3$Br
$^{13}$CNMR (400 MHz, CDCl$_3$) spectrum of CH$_3$CD$_2$PPh$_3$Br
$^{31}$PNMR (400 MHz, CDCl$_3$) spectrum of CH$_3$CD$_2$PPh$_3$Br
$^1$H NMR (400 MHz, CDCl$_3$) spectrum of a mixture of 1,5-dibromo-2,4-bis[(2-$^2$H)propynyl]benzene (2$^{''}$) from the Wittig reaction
$^{1}$HNMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-bis[(2-$^2$H)propenyl]benzene (12)
$^{13}$CNMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-bis[(2-$^2$H)propenyl]benzene (12)
$^1$HNMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-di[(1E)-propenyl]benzene (3)
$^{13}$CNMR (400 MHz, CDCl$_3$) spectrum of 1,5-dibromo-2,4-di[(1E)-propenyl]benzene (3)
$^1$HNMR (400 MHz, CDCl$_3$) spectrum of 2-{5-bromo-2,4-di[(1E)-(2-$^2$H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (14)
IR spectrum of 2-{5-bromo-2,4-di[(1E)-(2-^2^H)prop-1-etyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (14)
$^{13}$CNMR (400 MHz, CDCl$_3$) spectrum of 2-{5-bromo-2,4-di[(1E)-(2-$^2$H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (14)
Chapter 3

3.1 NMR spectra, GPC chromatograms, MALDI-TOF spectra

$^{1}$H NMR (400 MHz, CDCl$_3$) spectrum of poly{4,6-di[(1E)-(2-$^2$H)-propenyl]}-$m$-phenylene
$^{13}\text{C} \text{NMR} \ (400 \text{ MHz, CDCl}_3) \text{ spectrum of poly}(4,6\text{-di}[(1\text{E})\text{-}(2\circledast\text{H})\text{-propenyl}])\text{-}m\text{-phenylene}$
IR spectrum of poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene (to 400 cm⁻¹)
IR spectrum of poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene
MALDI-TOF (Dithranol matrix/Ag*, solvent: THF) spectrum of non-deuterated poly{4,6-di[(1E)-(2-2H)-propenyl]}-m-phenylene
Gel permeation chromatography (GPC) chromatogram of poly{4,6-di[(1E)-(2H)-propenyl]}-m-phenylene
Chapter 5

5.1 NMR spectra, MALDI-TOF spectra

MALDI-TOF (Dithranol matrix/Ag+, solvent: THF) spectrum of [n]kekulenes
MALDI-TOF (Dithranol matrix/Ag⁺, solvent: THF) spectrum of [7]kekulene
\[ ^1 \text{HNMR (500 MHz, THF-d}_8 \text{)} \text{ spectrum of [7]kekulene after multiple separations on biobead column} \]
IR spectrum of [n]kekulenes
IR spectrum of [n]helicenes
$^1$HNMR (500 MHz, CDCl$_3$) spectrum of [n]helicenes after separation on biobead column
MALDI-TOF spectrum of [n]helicenes