A Synthetic Route to Polymeric Carbohelicenes and Cyclic Derivatives

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Abstract

The King group’s interest is in the synthesis of polycyclic aromatic hydrocarbons (PAHs) for their wide range of applications in materials, electronics, and mechanical properties. The primary focus of my own synthetic efforts in PAHs involves the production of polymeric carbohelicenes and their cyclic derivatives.

Traditional methods for synthesizing helicenes structure use cross coupling of two phenanthrenes with desired functional groups. The final synthetic step usually involves a single reaction to close the ring and complete the helicenes such as Diels-Alder, carbenoid couplings, or photocyclisation. Our own approach to synthesizing carbohelicenes is to synthesize a polymer precursor, poly{4,6-di((1E)-(2-2H)-propenyl)-m-phenylene}, followed by a ring closing metathesis reaction (RCM) to stitch up the helicene. Our route is eight synthetic steps starting from commercially available m-xyene. The sequential steps involve bromination of m-xylene by electrophilic aromatic substitution, with a 70-74% yield, followed by a benzylic bromination with a 75-78% yield. Next a hydrolysis is performed using ZnBr₂ in acetic acid yielding the dialdehyde in 75-80%. A double Wittig reaction follows using ethyltriphenylphosphonium bromide to obtain on average 65% yield of a mixture of EE, EZ, and ZZ isomers.

Through optimization, we obtained a 95:5:0 ratio of our Wittig product (EE, EZ, and ZZ, checked by GC-MS). The key to this excellent stereoisomeric composition is the
application of applying an excess of base. Investigating this further we found a general and practical method for the isomerization of cis-β-methyl styrenes to their trans-isomers using potassium tert-butoxide. Our reaction conditions can be applied across a range of β-methyl styrenes and halogen substituted β-methyl styrene compounds that are difficult to isomerize by other methods. Additionally the reaction settings can be applied to a one-pot Wittig synthesis to obtain predominately trans-isomer.

The reaction involves a deprotonation of the terminal carbon of the phenyl alkene to form an allylic carbanion as an intermediate. The allylic intermediate then reforms to the more thermodynamically stable trans-isomer. With this serendipitous discovery we were able to skip our isomerization step of our mixture and obtain predominately our desired EE configuration.

With our desired stereoisomer in hand we borylated via lithium halogen exchange and trapping with isopropylpinacol borate to give monomer for a Suzuki polymerization. Using Pd(P(o-Tol)₃)₄ as our catalyst we obtained a polymer of Mw = 1.38 x 10³ Daltons and PDI = 1.51 analyzed by gel permeation chromatography (GPC). However, with Suzuki polymerization there are competing side reactions that can occur, shortening the polymer chain. Common complications include aryl-aryl exchange, hydrolytic deboronation, and dehalogenation. To help reduce these unwanted side products our catalysts were freshly synthesized. To avoid the side products of Suzuki polymerization we employed a different polymerization method by using Yamamoto coupling. Using the dibromo monomer, 1,5-dibromo-2,4-di[(1E)-2⁻²H]propenylbenzene. This reaction allowed us to skip borylating our monomer and go straight to polymerization. The Yamamoto coupling reactions yielded similar results to the Suzuki polymerization with Mw = 1.30 x 10³ Daltons and PDI = 1.35.
Matrix-assisted laser desorption ionization (MALDI) mass spectrometry of the polymers showed that both linear and cyclic polymers formed up to thirty repeat units. To separate the larger oligomers we used a preparatory recycling gel-permeation chromatography and removed the smaller oligomers from our product.

In a final step we did an ring-closing metathesis RCM reaction with our longer oligomers in an attempt to synthesize our polymeric carbohelicenes. Based on our past research and past literature precedence, we felt that using Grubbs 2nd generation catalysts would be sufficient to close the rings in our polymers. Other catalysts, like Grubbs 1st and 3rd generation or Schrock's catalyst were considered but were not used because the Grubbs 2nd generation is able to undo stilbene-like defects that can occur in the final product.

The RCM reaction was monitored by MALDI TOF mass spectrometry. We looked for a repeat unit of 100 daltons and 56 daltons which is the loss of butene. The loss of butene is from the RCM catalytic cycles reacting with one of the propenyl groups. However, after four days the reaction can no longer be monitored by MALDI spectrometry even when using a various selection of matrixes and cation salts. This is probably due to the increased difficulty in ionizing our product. Normal phase UV-HPLC is able to detect similar UV-vis spectra compared to past helicenes and cyclic derivatives, but do not conclusively confirm product formation. We believe that most of our products may also be insoluble in even our best solvent 1,2,4 trichlorobenzene, which makes standard workups difficult.
Dedication

To my parents for their love and support.
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List of abbreviations

CM : Cross-metathesis

D : Deuterium

ELSD : Evaporative light scattering detector

GCMS : Gas chromatography mass spectrometry

GPC: Gel permeation chromatography

h : Hour

IR : Infrared

J : Coupling constant

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 : Poly aromatic hydrocarbon

RCM : Ring closing metathesis

ROMP : Ring opening metathesis polymerization
s : Singlet

t : Triplet

K'OBu : Potassium tert-butoxide

THF : Tetrahydrofuran

UV-Vis : Ultraviolet-Visable
Chapter 1

Introduction and Background

1.1 Synthetic uses of alkenes

The formation of carbon-carbon double bonds can be found in numerous organic syntheses for natural products, pharmaceuticals, and materials. Most alkenes are stable and are useful synthetic intermediates allowing easy functional group interconversions. Alkenes can also be converted into enantiopure compounds, with steroselective variations via hydroboration, epoxidation, and hydrogenation. The synthesis of new functional groups from alkenes puts them frequently in the center of many synthesis. There are many
well recognized reactions that alkenes can be converted into other synthetically useful products where a brief selection is shown in Figure 1.1

### 1.2 Synthetic approaches to stereoselective alkenes

Alkenes can be generated by standard elimination reactions from alcohols or good leaving groups (e.g. halogens, or tosyl groups) where an E₁, E₂, or E₁cB reaction can occur. These reactions often require strong acids or bases which can affect sensitive functional groups within the molecule and can give poor stereoselectivity and regiochemistry in alkenes generated, ending with a mixture of isomers (Scheme 1.1).

![Scheme 1.1 Example of alkenes prepared by E₁ (eq 1), E₂ (eq 2), and E₁cB (eq 3) elimination reactions.](image)

A literature search reveals better methods for olefin synthesis than the standard elimination reactions. There are many organic reactions that are similar in mechanism and approach but form alkenes from different reactants. A classic organic chemistry alkene reaction is the aldol condensation where it selectively forms an \( \alpha,\beta \)-unsaturated aldehydes or ketones. The reaction combines two saturated \( \alpha,\beta \)-aldehyde or ketone using a base or an
acid to form the aldol addition product. This is followed by a dehydration step to remove water or alcohol by elimination to form the $\alpha,\beta$-unsaturated aldehyde or ketone (Scheme 1.2).\(^9\) This reaction can also use a mixture of aldehydes and ketones to form crossed aldol addition products.

![Scheme 1.2 An Aldol Condensation reaction.](image1)

Another similar reaction for synthesizing alkenes from aldehydes and ketones is known as the Knoevenagel reaction. The main difference between this and the aldol is that the Knoevenagel uses an activated methylene group as the nucleophile. The reaction proceeds by methylene deprotonation by a base to form a stabilized carbanion that nucleophilic attack the electron-deficient carbonyl carbon. The following steps are comparable to the aldol condensation reaction where the final step is elimination to form the alkene. The Knoevenagel reaction was used by Horning and co-workers in 1963 as a key step to synthesize their target molecule ethyl $\alpha$-acteyl- $\beta$-(2,3-dimethoxyphenyl)-propionate in 64-72% yield (Scheme 1.3).\(^{10}\)

![Scheme 1.3 A Knoevenagel Reaction.](image2)
Similar to the aldol reaction, the Perkins reaction was discovered in 1868 serves as another synthetic tool towards olefination. The main difference between the two reactions is that the Perkins uses a carboxylic acid anhydride with an aromatic aldehyde to form α,β-unsaturated carboxylic acid (Scheme 1.4).\textsuperscript{11} Another difference from previous reactions is that the Perkins reactions needs a carboxylic acid anhydride to have two α-hydrogens that can be deprotonated. Past publications show that the reaction will form a mixture of E- and Z-isomers of the α,β-unsaturated carboxylic acid, favoring the E-isomer.\textsuperscript{12,13} Also the reaction yields can be boasted with shorter reaction times with the use of cesium salts.\textsuperscript{14}

Another valuable transformation for the synthesis of alkenes is the Shapiro reaction. The reaction regioselectively eliminates to form alkenes in the least-substituted position.\textsuperscript{15} Evidence of this reaction’s usefulness can be found in the synthesis of Luciduline as shown in (Scheme 1.5).\textsuperscript{16} The reactions only require an aldehyde or ketone to be converted into a tosylhydrazone derivative, followed by the addition of two equivalents of a strong base.
Alkenes can be synthesized from diols as shown by the Corey-Winter reaction. The advantage of using this reaction is that it allows for the synthesis of highly stereospecific alkenes from their corresponding vicinal diols. The two step reaction first forms an intermediate cyclic thionocarbonate, followed by addition of trimethylphosphite to syn-eliminate to the alkene. An example of this reaction’s efficacy was shown in Kuwajima’s total synthesis of taxol in 2000. (Scheme 1.6).\textsuperscript{17}

![Scheme 1.6](image)

Another well-known alkene synthesis finding immense use in organic chemistry is the Wittig reaction. Its wide synthetic application garnered its inventor the Nobel Prize in 1979.\textsuperscript{18} In this reaction an aldehyde or ketone reacts with a phosphorus ylide to yield a regiospecific alkene.\textsuperscript{19} However, it is well established that this olefination reaction can form a mixture of alkene geometric isomers. To form stereospecific alkenes from the Wittig reaction, it is common to use stabilized ylides to yield \textit{E}-selective alkenes and unstabilized ylides to yield \textit{Z}-selective alkenes (Scheme 1.7).\textsuperscript{18}
Scheme 1.7. A Wittig reaction using stabilized ylides (eq 1) and non-stabilized ylides (eq 2)
The limitation of the Wittig reaction is that it forms a mixtures of alkene isomers by means of the erythro betaine intermediate being formed, leading to the Z-alkene.\textsuperscript{20} The Schlosser modification is able to transform the erythro betaine into the threo betaine to form predominately the \textit{E}-alkene. This is done by forming a lithobetaine with a lithium salt then protonating with an acid followed by deprotonation with potassium \textit{tert}-butoxide.\textsuperscript{21} The protonation and deprotonation allows for the erythro betaine to reform into the more thermodynamic stable threo betaine which will convert predominately into the \textit{E}-alkene (Scheme 1.8).\textsuperscript{22}

![Scheme 1.8. A Schlosser modification in the total synthesis of pseudolaric acid B.](image)

There are many variations to the Wittig reaction that focus solely on the synthesis of more geometrically pure alkenes. The Horner-Wadsworth-Emmons reaction is very similar to the Wittig reaction, only differing by the use of a stabilized phosphonate ester ylide. This method leads to exceptional levels of stereoselectivity for \textit{E}-alkenes (Scheme
Another advantage to this reaction is the byproduct of phosphate ester which, unlike triphenylphosphine oxide is water soluble, making it easy to separate during workup. The Julia-Lythgoe olefination reaction is another type of Wittig reaction that favors the formation of E-alkenes. The reaction uses phenyl sulfones with aldehydes or ketones to give alcohol functionalization that is reduced by a strong base forming the alkene (Scheme 1.10). Its E-selectivity is attributed to the formation of the thermodynamically preferred carbanion, which arranges the larger groups further apart. However, this reaction is incompatible with some functional groups like halogens.

Another attractive method for synthesizing alkenes is the Peterson olefination reaction due to its ability to be able to selectively synthesize either the Z/E-alkene isomers. The reaction uses α-sily carbanions with carbonyls to synthesize β-hydroxysilanes that can be treated with an acid to yield the Z-isomer, while if treated with a base would form the E-isomer. This stereoselective alkene formation is explained by
mechanism of the Peterson reaction, where the acid treated β-hydroxysilane proceeds via an anti-elimination, while the basic treated β-hydroxysilane proceeds by via syn-elimination (Scheme 1.11).26

Scheme 1.11 A Peterson olefination reaction. The intermediate alkoxide can be protonated by aqueous workup and isolated. (eq 1). Each diastereomer of the β-hydroxysilane is treated with acid or base to afford the desired alkene isomer. (eq 2, and 3).

1.3 Isomerizing alkenes

From the previous short discussion about the synthesis of alkenes via different routes, it should be evident that there is an overall goal to obtain geometrically pure alkenes. When a reaction produces a mixture of alkenes, there is often the need to separate the stereoisomers before continuing with the synthesis. However, isolating the different isomers can be difficult and will reduce the total yield of the desired product. There have been vast developments of methods to isomerize mixtures of alkenes to the desire cis or trans conformation, such as radical isomerization,27 base and acid catalyzed reactions,28 and transition metal catalysis.29 The following literature survey will give an overview of methods that have been developed to isomerize alkenes to the desired geometric isomer.
1.3.1 Isomerizing alkenes methods

Acid-catalyzed isomerization have been extensively studied and are used in many key processes.\textsuperscript{30} The isomerization of \textit{cis}-stilbene by the use of a sulfuric acid was reported by Noyce and co-workers in 1964.\textsuperscript{31} They proposed that the initial step was protonation of the alkene followed by hydration at the carbocation that is formed. The reversibility of the reaction allows the alkene to form into the more thermodynamically stable \textit{trans}-stilbene (Scheme 1.12).

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme12.png}
\end{center}

\textbf{Scheme 1.12} An acid-catalyzed isomerization of \textit{cis}-stilbene

Observations of base-catalyzed isomerization of alkenes were first reported in the literature in 1892 by Griner of a 1,4-hexadiene isomerized into 2,4-hexadiene.\textsuperscript{32} Base-catalyzed isomerization is not limited to just dienes, but also can be applied across a wide range of alkene systems like phenylalkenes,\textsuperscript{33} allylic alkenes,\textsuperscript{34} and acetylenes.\textsuperscript{35} An example of base-catalyzed isomerization is that of dipentene, a terpinene that used potassium \textit{tert}-butoxide in DMSO by Naslund and co-workers in 1967.\textsuperscript{36} They reported a
migration of double bonds to give a mixture of alkenes in variant amounts based on their thermodynamically stable ratio (Scheme 1.13).

\[ \text{Scheme 1.13} \text{ A base-catalyzed isomerization of dipentene to form a mixture of regioisomers in 5:3:1 mixture, respective to the product.} \]

Radical isomerization of alkenes is a well-established method that is commonly used in biological systems unsaturated fatty acids radically isomerize to obtain predominately trans-isomer.\textsuperscript{37} Thiol compounds are most often used to do radical chain reaction which can be initiated by \( \gamma \)-irradiation,\textsuperscript{38} thermal decomposition,\textsuperscript{39} or photochemically\textsuperscript{40} (Scheme 1.14). However, radical isomerizations have been reported to produce byproducts and to be unreliable in isomerizing mixtures of alkenes to single alkene.\textsuperscript{37,41}

\[ \text{Scheme 1.14} \text{ A radical isomerization.} \]

A wealth of literature can be found on the use of transition metal-based catalysts for isomerization of alkenes. The vast research on transition metal-based catalysts is due to the many advantages compared to the previous methods in terms of mild reaction
conditions, group tolerance, selectivity, and tunability. Also the use of catalytic systems are more desirable by industrial scale for the advantage of separation and the lower amounts of waste generated. Spencer and co-workers report an example of isomerization of alkenes in 2002 preparing trans-arylalkenes by means of Pd(II) catalysts (Scheme 1.15). Their isomerization method used 10 mol % PdCl$_2$(MeCN)$_2$ as a catalyst to obtain the $E$-isomer. They propose that the isomerization occurs from a reversible addition of PdCl$_2$(MeCN)$_2$ to the alkene bond give a carboxation intermediate, allowing free rotation around the carbon-carbon bond. This free rotation is key for the conversion of $Z$-alkenes being converted into the more thermodynamically stable $E$-alkene.

Another method for the isomerization arylalkenes catalyst was done by Wangelin and co-workers using Fe(acac)$_3$ as their catalyst. The Fe(acac)$_3$ advantages over other metallic isomerization methods is that it is cost effective and non-toxic which make it highly desirable to use for drug synthesis. Their conditions, used phenylmagnesium halide as a reductant and Fe(acac)$_3$ as their pre-catalyst at room temperature to obtain
predominately trans-isomers (Scheme 1.16). The mechanism is very similar to Spencer and co-workers mechanism in that reversible addition of the catalyst to form a carbocation allowing for free rotation about the carbon-carbon bond, then reformation into the more thermodynamically stable trans-alkene.\textsuperscript{43}

![Scheme 1.16](image)

**Scheme 1.16** Wangelin and co-workers isomerization of cis-stilbene to trans-stilbene using Fe(acac)\textsubscript{3}

### 1.4 Conclusion

The vast array of methods allows for different approaches in obtaining desired geometric alkenes. However, there is not a single standard method for synthesizing pure alkenes or isomerizing a mixture to a desired isomer. This is evident by the hundreds of publications that can be found in the literature on alkene isomerization. More studies continue to be published modifying old methods and creating new ones to obtain geometrically pure alkenes for specific reaction conditions.
Chapter 2
Isomerization of β-methyl styrenes using tert-butoxide

2.1 Introduction

The formation of carbon-carbon double bonds can be found in numerous organic syntheses for natural products, pharmaceuticals, and materials. Most alkenes are stable and are useful synthetic intermediates allowing easy functional group interconversions. Alkenes can also be converted into enantiopure compounds, with steroselective variations via hydroboration, epoxidation, and hydrogenation reactions. There are many reported methods for synthesizing geometrically pure alkenes under various conditions to obtain desired product. However, most methods for alkene syntheses, such as condensation, elimination, alkene metathesis, and Wittig olefination, have the possibility of producing a mixture of cis- and trans- alkenes. Extensive research has been dedicated to isomerizing alkenes, often employing organometallic catalysts. Some of these catalysts can undergo bond migration or oxidative addition with halogens making them undesirable for some syntheses. Halogens are synthetically useful and well known throughout organic chemistry for their ability to be used in lithium-halogen exchange, substitution, and cross coupling reactions. The ability to convert a compound containing halogens from its cis- isomer to a predominately trans- isomer without the introduction of a protecting group would be useful to many syntheses and would increase synthetic efficiency.
Previously, we reported the synthesis of septulene which required an isomerization of an intermediate compound 1,5-dibromo-2,4-bis[(2-\textsuperscript{2}H)propenyl]benzene (1i) to the geometrically pure form 1,5-dibromo-2,4-di[(1E)-2-\textsuperscript{2}H]propenylbenzene for later use in a Suzuki coupling and RCM.\textsuperscript{59} Compound (1i) was prepared by conventional Wittig olefination which produced a mixture of \textit{cis}- and \textit{trans}-alkenes. Though there are several alkene isomerization methods, many resulted in oxidative addition and alkene migration. Other methods to obtain enriched \textit{trans}-alkenes, which only a harsh and low yielding radical process was successful.\textsuperscript{60,61} However, we noticed that in our Wittig olefinations the accidental use of excess potassium \textit{tert}-butoxide would yield predominately our desired 1,5-dibromo-2,4-di[(1E)-2-\textsuperscript{2}H]propenylbenzene \textit{trans}-isomer (2i). We used this approach to isomerize \textit{cis}-\textit{β}-methyl styrene to their \textit{trans}-isomer. Here we present our study of this serendipitous discovery for the isomerization of \textit{cis}-\textit{β}-methyl styrenes to predominately \textit{trans}-isomers using potassium \textit{tert}-butoxide.

\textbf{2.2 Results and Discussion}

Since 1887, base-catalyzed isomerizations have been reported in various systems.\textsuperscript{62} Isomerization of phenylalkene systems have been explored mechanistically using potassium \textit{tert}-butoxide by Donald Cram and many others, but their application have not been explored.\textsuperscript{63,64} Mechanistic studies suggest the deprotonation of the terminal carbon of phenylalkene systems to form an allylic carbanion as an intermediate.\textsuperscript{65} This allylic intermediate then reforms to the more thermodynamically stable \textit{trans}-isomer.\textsuperscript{19} Factors
such as solvent, mesomeric effects, inductive and steric effects all play a role in the carbanion stability and affect the rate of formation of the more stable isomer (Figure 2.1).

To test the scope of the base-catalyzed isomerization methodology, we synthesized a variety of β-methyl styrene substrates by conventional Wittig olefination yielding mixtures of cis- and trans-alkenes (1a–1i, 1k). Isomerization of these alkene mixtures were carried out with 20-100 mol % of potassium tert-butoxide in a 0.2 M solution of alkene in dry tetrahydrofuran under an inert atmosphere. In most cases, the reactions were complete in 24-48 h (Table 2.1).
<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Mol %</th>
<th>Time/hrs.</th>
<th>Before ratio</th>
<th>After ratio Isolated yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td></td>
<td>100</td>
<td>72</td>
<td>75:25 (cis:trans)</td>
<td>2:98&lt;sup&gt;a&lt;/sup&gt; 94 (cis:trans)</td>
</tr>
<tr>
<td>1b</td>
<td>Me</td>
<td>100</td>
<td>24</td>
<td>78:22 (cis:trans)</td>
<td>3:97&lt;sup&gt;a&lt;/sup&gt; 90 (cis:trans)</td>
</tr>
<tr>
<td>1c</td>
<td>MeO</td>
<td>100</td>
<td>48</td>
<td>78:22 (cis:trans)</td>
<td>3:97&lt;sup&gt;a&lt;/sup&gt; 93 (cis:trans)</td>
</tr>
<tr>
<td>1d</td>
<td></td>
<td>20</td>
<td>1</td>
<td>71:29 (cis:trans)</td>
<td>4:96&lt;sup&gt;a&lt;/sup&gt; 88 (cis:trans)</td>
</tr>
<tr>
<td>1e</td>
<td>F</td>
<td>20</td>
<td>24</td>
<td>79:21 (cis:trans)</td>
<td>2:98&lt;sup&gt;a&lt;/sup&gt; 92 (cis:trans)</td>
</tr>
<tr>
<td>1f</td>
<td>F&lt;sub&gt;3&lt;/sub&gt;C</td>
<td>20</td>
<td>1</td>
<td>70:30 (cis:trans)</td>
<td>2:98&lt;sup&gt;a&lt;/sup&gt; 68 (cis:trans)</td>
</tr>
<tr>
<td>1g</td>
<td>NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>10-100</td>
<td>1-24</td>
<td>67:33 (cis:trans)</td>
<td>tar</td>
</tr>
<tr>
<td>1h</td>
<td>O&lt;sub&gt;2&lt;/sub&gt;N</td>
<td>10-100</td>
<td>1-24</td>
<td>93:7 (cis:trans)</td>
<td>tar</td>
</tr>
<tr>
<td>1i</td>
<td>Br Br</td>
<td>20</td>
<td>1</td>
<td>31:46:23&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0:7:93&lt;sup&gt;b&lt;/sup&gt; 90</td>
</tr>
<tr>
<td>1j</td>
<td></td>
<td>100</td>
<td>72</td>
<td>99:1 (cis:trans)</td>
<td>no reaction</td>
</tr>
<tr>
<td>1k</td>
<td></td>
<td>100</td>
<td>48</td>
<td>88:12 (cis:trans)</td>
<td>3:94:1:2&lt;sup&gt;c&lt;/sup&gt; 87</td>
</tr>
</tbody>
</table>

Table 2.1<sup>a</sup>Yield reported as mixture \(cis:trans\). Yield reported as mixture of isomers<sup>b</sup> Isomer ratio \(cis/cis\), \(cis/trans\), and \(trans/trans\) respectively. <sup>c</sup> Isomer ratio \(cis\) in conjugated, \(trans\) in conjugation, \(cis\) out of conjugation, \(trans\) out of conjugation.
Styrene substrates with no substituent (entry 1a) or electron donating substituents (entry 1b – 1c) isomerized with good yields. Styrene substrates that are moderately electron deficient and contain groups that stabilized the allylic anion (1d, e,i) exhibited accelerated reaction rates and isomerized in good yields. Styrene substrates with strong electron withdrawing groups, (1f – h) resulted in reduced or no yield of the trans-alkene. Para and ortho-nitro substrates (entry 1g-1h) when introduced to varying mol % of potassium tert-butoxide and temperature ranges, resulted in a tar like product that its structure could not be resolved. The introduction of a trifluoromethyl group in the para position of the aromatic ring (entry 1f) resulted in the trans-isomer in a lower yield of 68%, due to additional purification. We believe that the strong electron withdrawing groups stabilize a quinoidal type of structure, which induces side reactions to occur instead of reforming back into one of the isomers.66 The stilbene substrate (entry 1j) resulted in no change to the cis-isomer in various temperatures and mol % of potassium tert-butoxide. To investigate the possibility of double bond migration, we isomerized 1k using similar conditions to 1a and produced primarily (E)-1-phenylbut-1-ene isomer. A minor amount of bond migration occurred as determined by 1H NMR spectroscopy and GCMS.

To reduce the number of synthetic steps, we investigated the use of excess potassium tert-butoxide in a one-pot Wittig reaction to obtain predominately trans-alkene. We performed a conventional Wittig olefination to synthesize 1d and compared results to our preparation using excess potassium tert-butoxide. In the Wittig olefination without excess potassium tert-butoxide 1d was obtained in 82% yield, with 71:29 (cis:trans) mixture. However, using excess potassium tert-butoxide under similar conditions resulted in 77% yield with 4:96 (cis:trans) ratio. The use of excess potassium tert-butoxide in a
Wittig olefination does not appreciably affect yields while producing primarily the *trans*-isomer and skipping a synthetic step.

We have shown that isomerization of *cis*-β-methyl styrenes to predominately *trans*-β-methyl styrenes can occur in the presence of potassium *tert*-butoxide. This reaction is an attractive method for the preparation of various *trans*-β-methyl styrenes including ones that containing halogens without the need for protecting them or the use of specialized catalysts. We show that strongly deactivating groups such as trifluoromethyl substituent will isomerize with this method to the *trans*-isomer with lower yields after purification, however, nitro substituents will generate many more side products and is unsuitable for this method of isomerization. An appealing option with this method is that it can be used in a one-pot synthesis with conventional Wittig olefination to obtain predominately *trans*-β-methyl styrenes, eliminating the isomerization synthetic step without any significant loss of product.

### 2.3 Experimental Section

**General Information:** $^1$H NMR spectra were recorded in deuterated chloroform, TMS as internal standard, at 500 MHz at 298 K. Chemical shifts are quoted relative to residual solvent (7.26 ppm for $^1$H) and coupling constants (J) are given in Hz. Gas chromatography mass spectral (GCMS) data was recorded on Agilent 7890A GC. *cis*-Stilbene 1j was purchased from Sigma Aldrich assay 96% and used with no further purification. Tetrahydrofuran was freshly distilled before use. Potassium *tert*-butoxide was purchased from AK Scientific 98% purity and used with no further purification. All chromatography was carried out using silica gel Siliaflash P60 40-63 μm.
General Procedure for the Isomerization of cis-Alkenes.

A solution containing mixture of cis- and trans-alkenes and potassium tert-butoxide (20-100 mol %) in dry tetrahydrofuran (10 mL per 1 mmol of substrate) was stirred at 50 °C for the designated time. All reactions were done under inert atmosphere using N\textsubscript{2} inside of a Schlenk flask. The reaction was diluted with hexanes and purified by flash chromatography with silica gel. The solvent was removed under reduced pressure to afford the trans-alkene.

Additional purification of benzene, 1-prop-1-enyl-4-(trifluoromethyl), 2f:

The reaction was diluted with hexanes and purified by flash chromatography with silica gel. The solvent was removed under reduced pressure to afford the trans-alkene and other impurities in colorless oil. Distillation by Kugelrohr was performed at room temperature under reduced pressure of 210 miliitorr using dry ice/acetone bath to collect 2f. The impurities created during the reaction were high boiling but their structure could not be determined by GCMS or \textsuperscript{1}H NMR spectroscopy.

Synthesis of mixture benzene, 1-bromo-2-(1-prop-1-enyl), 1d:

Potassium tert-butoxide (0.72 g, 6.42 mmol) was added to a solution of (1,1\textsuperscript{2}H)-ethyltriphenylphosphonium bromide (2.66g, 7.17 mmol) in dry tetrahydrofuran (125 mL). The resulting orange solution was stirred at 50 °C. 2-Bromobenzaldehyde was added (1.01 g, 5.46 mmol) slowly to the reaction mixture and the solution was stirred overnight at 50 °C. The solvent was then evaporated and the residue was dissolved in hexane and purified
by flash chromatography with silica gel to give an oily liquid containing benzene, 1-bromo-2-(1-prop-1-enyl) (0.88 g, 82 %) as mixture of isomers.

**Synthesis of benzene, 1-bromo-2-(1-prop-1-enyl), in one-pot Wittig, 2d:**

Excess potassium tert-butoxide (0.90 g, 8.02 mmol) was added to a solution of (1,1-2H)-ethyltriphenylphosphonium bromide (2.59 g, 6.98 mmol) in dry tetrahydrofuran (125 mL). The resulting orange solution was stirred at 50 °C for 20 minutes. 2-Bromobenzaldehyde was added (1.09 g, 5.46 mmol) slowly to the reaction mixture. The solution was stirred for four hours at 50 °C. The solvent was evaporated and the residue was dissolved in hexane and purified by flash chromatography with silica gel to give Benzene, 1-bromo-2-(1-prop-1-enyl)(0.84 g, 77 %) as a mixture of isomers in an oily liquid (1,5-dibromo-2,4-di[(1Z,E)-2-2H]propenylbenzene) with crystalline solids (1,5-dibromo-2,4-di[(1E)-2-2H]propenylbenzene).

1a - C9H10, benzene, prop-1-enyl-Propenyl-benzene:

**Before:** 1H NMR (500 MHz, CDCl3) δ = 7.36 – 7.16 (m, 5H, aromatic), 6.47 – 6.42 (dd, J = 11.6 Hz, 1H), 6.42 – 6.37 (dd, J = 15.7 Hz, 1H) 6.28 – 6.20 (dq, J = 15.8 Hz, 1H), 5.83 – 5.75 (dq, J = 11.6 Hz, 1H), 1.92 – 1.90 (dd, J = 7.2 Hz, 3H), 1.89 – 1.87 (dd, J = 6.7 Hz, 3H). GCMS: R.T. min 3.248 peak area 83297310, R.T. min 3.540 peak area 27423352.

2a - After: 1H NMR (500 MHz, CDCl3) δ = 7.36 – 7.16 (m, 5H, aromatic), 6.47 – 6.42 (dd, J = 11.6 Hz, 1H), 6.42 – 6.37 (dd, J = 15.7 Hz, 1H) 6.28 – 6.20 (dq, J = 15.8 Hz, 1H), 5.83 – 5.75 (dq, J = 11.6 Hz, 1H), 1.92 – 1.90 (dd, J = 7.2 Hz, 3H), 1.89 – 1.87 (dd, J =
6.7 Hz, 3H). GCMS: R.T. min 3.256 peak area 3418222, R.T. min 3.540 peak area 136710995.


1b - C\(_{10}\)H\(_{12}\), benzene, 1-methyl-4-(1-prop-1-enyl):

**Before:** \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.23 - 7.07\) (m, 4H, aromatic), 6.44 – 6.38 (dd, 1H, J = 11.7 Hz), 6.40 – 6.36 (dd, 1H, J = 15.8 Hz), 6.23 – 6.15 (dq, 1H, J = 15.4 Hz), 5.78 – 5.70 (dq, 1H, J = 11.6 Hz), 2.35 – 2.33 (s, 3H), 2.34 – 2.32 (s, 3H), 1.91 - 1.88 (dd, 3H, J = 7.1 Hz), 1.87 – 1.85 (dd, 3H, J = 6.6 Hz). GCMS: R.T. min 5.102 peak area 19007699, R.T. min 5.394 peak area 5334628.

**After:** \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.23 - 7.07\) (m, 4H, aromatic), 6.44 – 6.38 (dd, 1H, J = 11.7 Hz), 6.40 – 6.36 (dd, 1H, J = 15.8 Hz), 6.23 – 6.15 (dq, 1H, J = 15.4 Hz), 5.78 – 5.70 (dq, 1H, J = 11.6 Hz), 2.35 – 2.33 (s, 3H), 2.34 – 2.32 (s, 3H), 1.91 - 1.88 (dd, 3H, J = 7.1 Hz), 1.87 – 1.85 (dd, 3H, J = 6.6 Hz). GCMS: R.T. min 5.109 peak area 468151, R.T. min 5.394 peak area 17897275.


1c - C\(_{10}\)H\(_{12}\)O benzene, 1-methoxy-4-(1-prop-1-enyl)

**Before:** \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.27 - 7.22\) (m, 4H, aromatic), 6.89 – 6.86 (m, 2H), 6.84 – 6.81 (m, 2H), 6.39 – 6.35 (dd, 1H, J = 11.6 Hz), 6.37 – 6.31 (dd, 1H, J = 15.9 Hz) 6.13 – 6.05 (dq, 1H, J = 16.0 Hz), 5.74 – 5.65 (m, 1H, J = 11.6 Hz), 3.82 – 3.81 (s,
3H), 3.80 – 3.79 (s, 3H), 1.90 – 1.87 (dd, 3H, J = 7.2 Hz), 1.86 – 1.84 (dd, 3H, J = 6.6 Hz).

GCMS: R.T. min 6.337 peak area 11026145, R.T. min 6.597 peak area 3481292.

2c - After: $^1H$ NMR (500 MHz, CDCl$_3$) $\delta = 7.27 – 7.22$ (m, 4H, aromatic), 6.89 – 6.86 (m, 2H), 6.84 – 6.81 (m, 2H), 6.39 – 6.35 (dd, 1H, J = 11.6 Hz), 6.37 – 6.31 (dd, 1H, J = 15.9 Hz) 6.13 – 6.05 (dq, 1H, J = 16.0 Hz), 5.74 – 5.65 (m, 1H, J = 11.6 Hz), 3.82 – 3.81 (s, 3H), 3.80 – 3.79 (s, 3H), 1.90 – 1.87 (dd, 3H, J = 7.2 Hz), 1.86 – 1.84 (dd, 3H, J = 6.6 Hz).

GCMS: R.T. min 6.349 peak area 206322, R.T. min 6.597 peak area 11585026.


1d - C$_9$H$_9$Br, benzene, 1-bromo-2-(1-prop-1-enyl)

Before: $^1H$ NMR (500 MHz, CDCl$_3$) $\delta = 7.58 - 7.01$ (m, 8H, aromatic), 6.75 – 6.70 (dd, 1H, J = 15.7 Hz), 6.50 – 6.45 (dd, 1H, J = 11.5 Hz), 6.23 - 6.13 (dq, 1H, J = 15.6 Hz), 5.93 – 5.85 (dq, 1H, J = 11.5 Hz) 1.95 - 1.88 (dd, 3H, J = 6.7 Hz), 1.79 – 1.77 (dd, 3H, J = 7.1 Hz). GCMS: R.T. min 5.307 peak area 35753648, R.T. min 5.735 peak area 15807103.

2d - After: $^1H$ NMR (500 MHz, CDCl$_3$) $\delta = 7.58 - 7.01$ (m, 8H, aromatic), 6.75 – 6.70 (dd, 1H, J = 15.7 Hz), 6.50 – 6.45 (dd, 1H, J = 11.5 Hz), 6.23 - 6.13 (dq, 1H, J = 15.6 Hz), 5.93 – 5.85 (dq, 1H, J = 11.5 Hz) 1.95 - 1.88 (dd, 3H, J = 6.7 Hz), 1.79 – 1.77 (dd, 3H, J = 7.1 Hz). GCMS: R.T. min 5.301 peak area 4972548, R.T. min 5.741 peak area 117646352.


1e - C$_9$H$_9$F, benzene, 1-fluoro-4-(1-prop-enyl)
**Before:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.31 - 7.22$ (m, 4H, aromatic), 7.02 – 6.94 (m, 4H, aromatic), 6.41 - 6.36 (dd, 2H, $J = 15.8$ Hz), 6.38 – 6.33 (dd, 1H, $J = 11.4$ Hz), 6.18 – 6.10 (dq, 1H, $J = 15.8$ Hz), 5.81 – 5.73 (dq, 1H, $J = 11.6$ Hz), 1.89 – 1.85 (dd, 3H, $J = 7.4$ Hz). GCMS: R.T. min 3.267 peak area 25282644, R.T. min 3.552 peak area 826088.


**2e - After:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.31 - 7.22$ (m, 4H, aromatic), 7.02 – 6.94 (m, 4H, aromatic), 6.41 - 6.36 (dd, 2H, $J = 15.8$ Hz), 6.38 – 6.33 (dd, 1H, $J = 11.4$ Hz), 6.18 – 6.10 (dq, 1H, $J = 15.8$ Hz), 5.81 – 5.73 (dq, 1H, $J = 11.6$ Hz), 1.90 – 1.87 (dd, 3H, $J = 6.4$ Hz). GCMS: R.T. min 3.267 peak area 25282644, R.T. min 3.552 peak area 826088.

**1f - C$_{10}$H$_9$F$_3$, benzene, 1-prop-1-enyl-4-(trifluoromethyl):**

**Before:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.59 - 7.35$ (d, 8H, aromatic), 6.47 – 6.42 (dd, 1H, 11.1 Hz), 6.44 - 6.39 (dd, 1H, $J = 15.5$ Hz), 6.38 – 6.29 (dq, 1H, 15.8Hz), 5.94 – 5.86 (dq, 1H, $J = 11.6$ Hz), 1.93 – 1.89 (dd, 3H, $J = 6.4$ Hz), 1.90 – 1.88 (dd, 3H, $J = 7.3$ Hz). GCMS: R.T. min 4.333 peak area 39359434, R.T. min 4.650 peak area 18010169.

**2f - After:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.55 - 7.50$ (d, 4H, aromatic), 7.42 – 7.38 (d, 4H aromatic) 6.47 – 6.42 (dd, 1H, 11.1 Hz), 6.44 - 6.39 (dd, 1H, $J = 15.5$ Hz), 6.38 – 6.29 (dq, 1H, 15.8Hz), 5.94 – 5.86 (dq, 1H, $J = 11.6$ Hz), 1.93 – 1.89 (dd, 3H, $J = 6.4$ Hz), 1.90 – 1.88 (dd, 3H, $J = 7.3$ Hz). GCMS: R.T. min 4.333 peak area 2663841, R.T. min 4.656 peak area 104947556.

1g - C₉H₉O₂ benzene, 1-nitro-2-(1-prop-1-enyl)

**Before:** ¹H NMR (500 MHz, CDCl₃) δ = 8.02 – 7.98 (dd, 2H, aromatic), 7.88 – 7.85 (dd, 2H, aromatic), 7.59 – 7.31 (m, 4H, aromatic), 6.89 – 6.83 (dt, 1H, J = 13.8 Hz), 6.75 – 6.71 (dt, 1H, J = 11.4 Hz), 6.30 – 6.22 (dq, 1H, J = 15.5 Hz), 5.99 – 5.92 (dq, 1H, J = 11.5 Hz), 1.97 – 1.94 (dd, 3H, J = 6.7 Hz), 1.75 – 1.72 (dd, 3H, J = 7.1 Hz). GCMS: R.T. min 7.003 peak area 15914423, R.T. min 7.300 peak area 7421647.


1h - C₉H₉O₂, benzene, 1-nitro-4-(1-prop-1-enyl)

**Before:** ¹H NMR (500 MHz, CDCl₃) δ = 8.21 – 8.13 (dd, 4H, aromatic), 7.45 – 7.40 (dd, 4H, aromatic), 6.51 -6.46 (dd, 1H, J = 11.7 Hz), 6.04 – 5.97 (dq, 1H, J = 11.7 Hz), 1.95 -1.91 (dd, 3H, J = 7.3 Hz). GCMS: R.T. min 6.907 peak area 50866579, R.T. min 7.230 peak area 3833867.


1i - C₁₂H₁₂Br₂, Benzene, 1,5-dibromo-2,4-di-(1-prop-1-enyl)

**Before:** ¹H NMR (500 MHz, CDCl₃) δ = 7.81 (s, 1H, aromatic), 7.75 (s, 1H, aromatic), 7.69 (s, 1H, aromatic), 7.54 (s, 1H, aromatic), 7.37 (s, 1H, aromatic), 7.22 (s, 1H, aromatic), 6.68 – 6.58 (m, 1H, J = 16.0 Hz), 6.42 – 6.36 (m, 1H), 6.26 – 6.12 (m, 1H), 5.95 – 5.87 (dqd, 2H, J = 11.4 Hz), 1.96 – 1.88 (dd, 6H, 6.7 Hz), 1.80 – 1.77 (dd, 12H, J = 7.1 Hz).


2i - After: $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.81 (s,1H, aromatic), 7.75 (s, 1H, aromatic), 7.69 (s, 1H, aromatic), 7.54 (s, 1H, aromatic), 7.37 (s, 1H, aromatic), 7.22 (s, 1H, aromatic), 6.68 – 6.58 (m, 1H, J = 16.0 Hz), 6.42 – 6.36 (m, 1H), 6.26 – 6.12 (m, 1H), 5.95 – 5.87 (dqd, 2H, J = 11.4 Hz), 1.96 – 1.88 (dd, 6H, 6.7 Hz), 1.80 – 1.77 (dd, 12H, J = 7.1 Hz).


1j – C$_{12}$H$_{14}$, Cis-stilbene

Before: $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.27 – 7.16 (m, 10H, aromatic) 6.60 – 6.59 (s, 2H) GCMS: R.T. min 7.509 peak area 144535106, R.T. min 8.154 peak area 2579803.


1k – C$_{10}$H$_{12}$, (E)/(Z)-1-phenylbut-1-ene

Before: $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.36–7.16 (m, 5H, Aromatic) 6.40 – 6.36 (dt, 1H, J = 11.7 Hz, 1.9 Hz), 6.30–6.24 (dt, 1H, J=15.5, 6.4Hz) 5.69–5.62 (dt, 1H, J = 11.6, 7.3 Hz) 2.38 – 2.31 (m, 2H, J = 7.4 Hz, 1.8 Hz), 2.27 – 2.20 (m, 2H, J = 15.4 Hz, 6.4 Hz) 1.10-
1.07 (t, 3H), 1.08 – 1.04 (t, 3H) GCMS: R.T. min 4.873 peak area 46027512, R.T. min 5.276 peak area 6073350.


2k After: ¹H NMR (500 MHz, CDCl₃) δ = 7.36–7.16 (m, 5H, Aromatic) 6.40 – 6.35 (d, 1 H, J = 15.6 Hz), 6.31–6.23 (dt, 1H, J=15.7), 3.42 – 3.40 (d, 2H, J = 5.1 Hz), 3.33 – 3.30 (d, 2H J = 6.3 Hz), 2.27 – 2.20 (qdd, 2H, J = 7.4 Hz), 1.73 – 1.72 (d, 1H, J = 4.6 Hz), 1.70 – 1.67 (d, 1H, J = 6.1 Hz), 1.10 – 1.07 (t, 3H). GCMS: R.T. min 4.793 peak area 144535106, R.T. min 4.878 peak area 2579803, R.T. min 4.916 peak area 12382, R.T. min 5.279 peak area 2579803.
Chapter 3

3.1 Introduction to helicenes

My research has focused on the synthesis and characterization of polycyclic aromatic hydrocarbons (PAHs). These compounds are composed of fused benzene rings where all the carbon atoms are $sp^2$ hybridized. PAHs may be found naturally in oil, generated as by-products from fuel combustion, and even in meteorites. Helicenes have been my focus towards synthetic PAHs. These compounds are helicoidally shaped and have chiral features that have been explored since the early 20th century. Helicenes is a general name used interchangeably to refer to similar types of compounds such as thio-helicenes, aza-helicenes, dioxo-aza-helicenes, and carbohelicenes (Figure 3.1). My research focuses on carbohelicenes, which from here on out all use of helicene will refer to an “all-carbon skeleton with delocalized $\pi$-system”, contrasting to $\sigma$-helicenes joined in a helix such as spiro-annulated cyclobutanes and diamantine.
The name of carbohelicenes is generated by a number in brackets associating to the number fused aromatic rings. The direction of the helical twist clockwise is noted as P-(+), and anti-clockwise as M-(−). An example of this nomenclature can be found in (Figure 3.2).

Figure 3.1 Example of previously synthesized carbohelicenes.
Interest in synthesizing helicenes has been sparked by the variety of innovative uses which include biological,\textsuperscript{76} physiochemical,\textsuperscript{77} chemical,\textsuperscript{78} and electronic.\textsuperscript{79} One of the first reports to exhibit the use of helicenes in a reaction were chiral auxiliaries to obtain highly diastereoselective products.\textsuperscript{80} Carlson and co-workers used a variety of \(\alpha\)-ketoesters auxiliaries to test diastereoselective reductions with NaBH\(_4\). The carbohelicene auxiliary outperformed other smaller auxiliaries in terms of reduction yield and diastereoselectivity. Success of this diastereoselection reduction is most likely due to steric effects in the transition state where the helicene is positioned in a way to force a single face attack of the carbonyl group (Scheme 3.1).\textsuperscript{73}
Okamoto and co-workers reported in 1983 another use for helicenes by incorporating [5] and [6]helicene derivative into crown-ethers for the differential transport of enantiomeric chiral amino acids.\textsuperscript{81} Their method allowed for liquid-liquid chiral extractions to occur using sterically hindered chiral (P)- or (M)-helicene crown ethers to obtain enantiomer in excess of 77\% (Scheme 3.2).\textsuperscript{82}

![Scheme 3.2 Oktamoto and co-workers optically active crown ethers for transport of enantiomeric chiral amino acids.](image)

Helicenes have also been reported by Katz and co-workers in 2000 to be able to determine the enantiopurity of amines and alcohols.\textsuperscript{83} This determination was achieved by adding a chlorophosphite onto the helicene and using \textsuperscript{31}P NMR to analyze the enantiomeric composition. This use of chlorophosphite with helicenes was able to analyze the enantiomeric purity of complex molecules and extend the length of the alkyl chains. This means that the absolute configuration of stereogenic centers can be detected from three carbons up to seven atoms away (Scheme 3.3).\textsuperscript{84}
3.2 Synthesis of helicenes

The traditional method for helicene synthesis consists of coupling two phenanthrenes with desired functional groups together followed by using a single reaction to stitch up the helicenes. Past syntheses of helicenes used a variety of methods to close up the rings, like Diels-Alder reactions,\textsuperscript{85} carbenoid couplings,\textsuperscript{86} radical cyclizations,\textsuperscript{87} cyclotrimerizations of acetylenes,\textsuperscript{88} and ring-closing metathesis.\textsuperscript{89}

The first report of any helicene was in 1913 by Lieb and Weitzenboöck where they synthesized [4]helicene using a Pschorr reaction followed by a decarboxylation.\textsuperscript{90} This synthesis would be used again by Weitzenboöck five years later to synthesize mixture of racemic [5]helicene (Scheme 3.4).\textsuperscript{91}
The Gingras group reported a non-photochemical method for helicenes. They synthesized [5]helicene using a benzylic-type of coupling to close up the final benzene ring. They were also able to use similar reaction conditions to synthesize a racemic mixture of [7]helicene in multiple-gram reactions with little purification needed (Scheme 3.5).

Martin and co-workers reported a well-known synthesis of helicenes in 1967 report using oxidative photocyclodehydrogenation to form the remaining benzene ring and obtain racemic [7]helicenes (Scheme 3.6). In 1975 he would again publish using the same oxidative photocyclodehydrogenation step to close the benzene ring in his procedure to synthesize racemic [11], [12], and [14] helicenes, one of the longest helicenes published to date.
Most helicenes synthesis usually provide a racemic mixture, but Bestmann and Both were able to use electrooxidative cyclization to obtain enantioenriched [5]helicene. Their synthesis used triphenylphosphonium periodate where they proposed that the oxidation occurs it generates a stabilized benzylic-type of radical cation, which favors the formation of (+)-(P)-[5]helicene (Scheme 3.7).

Ring-closing metathesis is a well-known regioselective reaction that has been used in numerous organic synthesis including, helicenes. It has been reported by Bonifacio and King that the ring-closing metathesis is a suitable reaction for helicenes synthesis. This comes from the formation of polyaromatic hydrocarbons being more thermodynamically favored than common defects. The ring-closing metathesis is a reversible reaction and can remove defects overtime until the more thermodynamically stable helicene product is formed.
Collins and co-workers used RCM in their own synthesis to stitch up their helicenes-precursors into the more thermodynamically favored helicenes. They were able to synthesized [5]-, [6], and [7]helicenes using RCM with a variety of catalysts and conditions (Scheme 3.8).99

![Scheme 3.8](image)

King and co-workers attempted to synthesize helicenes from a poly(m-phenylene) polymer via RCM reaction, and serendipitously synthesized kekulenes. Their polymer precursor formed both cyclic and linear products. The cyclic polymers when RCM is performed closes all the rings synthesizing kekulenes while all the linear polymers synthesizes helicenes (Scheme 3.9).100
Scheme 3.9 King and co-workers synthesis towards polymeric helicenes
3.3 Kekulenes

Kekulene is a well-known polycyclic aromatic hydrocarbon that was synthesized by Staab and Dieterich and named in honor of August Kekulé. It consists of twelve cyclic fused benzene rings and was synthesized to answer a fundamental question about aromaticity; is aromaticity in a kekulene localized or delocalized throughout the molecule like annulene. Staab and Dieterich reported on their synthesis of kekulene in 1978, showing that it could be synthesized by photocyclodehydrogenation (Scheme 3.10).\(^\text{101}\) Also they reported that kekulene itself had localized aromaticity by experimental \(^1\text{H}\) NMR data showing the inner protons to be \(~10.45\) ppm.

The only other known entirely carbon and hydrogen based kekulene to date is the seven memebred homologue, septulene which consists of fourteen cyclic fused benzene rings. King and co-workers reported septulene in 2012 and was synthesized using poly(m-phenylene) polymer precursor followed by RCM reaction.\(^\text{100}\) However, septulene is different than kekulene due to an has an odd number of carbon atoms in the outer and inner carbon ring making the only way to resolve the septulene’s Kekulé structure is by including a radial \(\pi\)-bond. If that radial bond was added it would break the symmetry in the molecule.
giving the molecule different properties. If proposed with a Clar representation, septulene should have similar properties to kekulene. With $^1$H NMR and x-ray crystallography they concluded that septulene’s and all PAHs can only be accurately represented with Clar circles since it’s properties are strikingly similar to kekulenes (Figure 3.3).

![Figure 3.3 Septulene unique radial bond with Kekulé structure (right) compared with Clar circle (left).](image)
Chapter 4: Synthesis towards helicenes

4.1 Introduction to synthetic route.

Traditional methods for synthesizing helicene structures start by coupling two phenanthrenes with desired functionality. The final synthetic step, usually involves a single reaction to close the ring and complete the helicenes with a Diels-Alder,\textsuperscript{102} carbenoid couplings,\textsuperscript{103} or photocyclisation.\textsuperscript{104}

Our own approach to synthesizing carbohelicenes is to synthesize a polymer precursor, poly\{4,6-di((1E)-(2-H)-propenyl)-m-phenylene\} followed by a ring-closing metathesis reaction (RCM) to stich up the helicene. Our route is eight synthetic steps starting from the commercially available chemical, \textit{m}-xyene. This route is taken from our previous synthesis of septulene with a few modifications (\textbf{Scheme 4.1}).\textsuperscript{105}

\textbf{Scheme 4.1} Synthetic route used towards septulene
The sequential steps involve bromination of $m$-xylene (1) by electrophilic aromatic substitution, with a 70-74% yield; followed by a benzylic bromination with a 75-78% yield (2). This followed by using AgNO$_3$ in ethanol yielding the dialdehyde in 90-95% (3). A double Wittig reaction follows, using deuterated ethyltriphenylphosphonium bromide to obtain on average 65% yield of a mixture of $EE$, $EZ$, and $ZZ$ isomers (4). Deuterium labeling was necessary in this step to give a spectroscopic handle for the planned RCM reaction dependent on the disappearance of the C-D stretch in the IR, indicating the completion of the reaction. In order to isomerize the mixture to the more thermodynamically stable EE isomer, diphenyl disulfide was used with a 100W lamp for a radical isomerization (5). Yields were inconsistent with this reaction, a best of around 70% yield mixture predominantly is of the EE isomer. With geometrically pure (5) we borylated via lithium halogen exchange and trapping with isopropylpinacol borate to give monomer (6) in 55-65% yield. Suzuki polymerization was used to make the polymeric helicenes both cyclic and linear polymers (7). Final step of the reaction was a RCM reaction using Grubbs 2$^{nd}$ generation catalysts over three day reactions to get a 3% yield of septulene (Figure 4.1).
4.2 Synthetic route to monomer

4.2.1 Optimization to monomer route

The synthesis of kekulenes and septulene, gives us confidence that we could get the non-cyclic oligomers from the same synthetic route (Scheme 4.1). However, use of the same route would require large amounts of our monomer to be synthesized in order to obtain our carbohelicenes. Certain parts of the synthesis would have to be optimized to prevent bottlenecks in the synthesis by either low yields or availability of materials and to make mass spectrometry of our molecules easier.

The hydrolysis reaction (3) using AgNO₃ in an ethanolic solution to transform our hexabromo compound to our dialdehyde was changed to using ZnBr₂ with refluxing acetic acid. This was modified because ZnBr₂ is more readily available than AgNO₃ while at the same time providing similar yields, 85-88%. Also, using ZnBr₂ allowed us to scale up our reaction from a ~30g scale using AgNO₃ to a ~60g reaction. With this change in reaction

Figure 4.1 Septulene and kekulene were both synthesized with the synthetic route from scheme 1.
conditions, we were able to synthesize over 350 grams of our dialdehyde in a relatively short time (Scheme 4.2).

![Scheme 4.2 Routes to the dialdehyde. Previous route (eq 1) was switched out for a larger scale reaction (eq 2).](image)

Another modification we made was with our double Wittig reaction (4) where we decided to replace deuterated ethyltriphenylphosphonium bromide with non-deuterated ethyltriphenylphosphonium iodide. This modification allowed for better high resolution atmospheric pressure photoionization (APPI) and matrix-assisted laser desorption ionization (MALDI) results since the prior Wittig product would not be completely 100% deuterium labeled, making isotopic distributions difficult to interpret. Removing deuterium labeling would lose our ability to monitor our RCM reaction by IR spectroscopy, but with the recently arrived MS-MALDI TOF we believed we could track the progress by MALDI TOF. Also with the use of MALDI TOF, we could monitor our polymerization reactions more reliably for a better understanding what type of polymers we were making.

The last optimization we made was with our Wittig product (4) was to change the radical isomerization step (5), which had been the bottleneck of our monomer synthesis. Compound (4) was prepared by conventional Wittig olefination, which produced a mixture...
of cis- and trans-alkenes. We needed to isomerize our intermediate compound 1,5-dibromo-2,4-bis[(2⁻²H)propenylbenzene (4) to the geometrically pure form 1,5-dibromo-2,4-di[(1E)-2⁻²H]propenylbenzene. Other isomerization methods were tested, including Fe(acac)$_3^{106}$ and PdCl$_2$(MeCN)$_2^{107}$ but did not produce our desire alkene. The only isomerization method that showed any results for us was a harsh and unreliable photo-initiated radical isomerization reaction using diphenyl disulfide.

However, we noticed that in our Wittig olefinations the use of excess potassium tert-butoxide would serendipitously yield predominately our desired 1,5-dibromo-2,4-di[(1E)-2⁻²H]propenylbenzene trans-isomer (Scheme 4.3). We used this approach to isomerize cis-β-methyl styrene to the trans-isomer and allowed us to replace step (5) from our synthesis. Additionally the reaction settings can be used in a one-pot Wittig synthesis to obtain predominately trans-isomer by using an excess of potassium tert-butoxide. This finding allowed us to remove the isomerization step (5) from our synthesis and remove the bottleneck in our synthesis of the monomer.

Scheme 4.3 Different routes of isomerization used. Radical isomerization (eq 1) was switched out for base isomerization (eq 2).
4.2.2 Experimental for monomer synthesis

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

Bromine (54.45 g, 340.6 mmol) was added dropwise with a dropping funnel into 0°C solution of iodine (0.25 g, 1.95 mmol) in m-xylene (17.3 g, 20 mL) over 2 h in the absence of light with stirring. The solution was allowed to warm to room temperature and continued stirring for 16 h. An aqueous solution of KOH (20%, 50 mL) was added to the reaction mixture and the resulting solid was filtered. Continued washes with water were performed until the yellow color disappeared and a white solid remained. Recrystallization from absolute ethanol obtain white crystals (24.45 g, 56.8% yield). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.69 (s, 1H), 7.09, (s, 1H), 2.43, (s, 6H).

1,5-Dibromo-2,4-bis(dibromomethyl)benzene, (2)

Bromine (2.24 mL, 28 mmol) was added by a dropping funnel to a solution of 1,5-Dibromo-2,4-dimethylbenzene (1.32 g, 5 mmol) in refluxing dichloromethane for 2 h. The mixture was stirred overnight under 100W lamp. Afterwards, the reaction was cooled to room temperature and extracted with aqueous solution of sodium thiosulfate. The organic layer was separated from the aqueous layer and removed under pressure to produce a dark solid. The solid was recrystalize with hexanes to obtain pale brown crystals. (2.48 g, 97.9%).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.64 (s, 1H), 7.71, (s, 1H), 6.95, (s, 6H).

4,6-Dibromobenzene-1,3,-dicarbaldehyde, (3)
In an acetic acid solution (600 mL), 1,5-Dibromo-2,4-bis(dibromomethyl)benzene (40 g, 69.1 mmol) was refluxed with ZnBr$_2$ (31.1 g, 138.2 mmol) and 10 mL of water overnight. The mixture was cooled to room temperature and a copious amount of cold water was added to crash out an off white solid. This mixture was filtered and washed with plenty of water to furnish the product (17.7 g, 88.1% yield). $^1$H NMR (500 MHz, CDCl$_3$): δ 10.32 (s, 2H), 8.38 (s, 1H), 8.04 (s, 1H).

**Ethyltriphenylphosphonium iodide**

Triethylamine (5 mL) was added to a mixture of neat iodoethane (11.9 g, 76.3 mmol) and triphenylphosphonium (20 g, 76.3 mmol). The mixture was heated to 100 °C overnight under nitrogen. The solids were crushed up and washed with hot toluene to remove yellow impurities. White solids were obtain (28.7 g, 89.8%) 1H NMR (400 MHz, CDCl$_3$): δ 7.94 – 7.71 (m, 8H), 3.68 (m, 2H), 1.40 (d, 3H).

**1,5-dibromo-2,4-bis(2-2H)propenylbenzene, (4)**

Potassium tert-butoxide (2.88 g, 25.7 mmol) was added to a solution of ethyltriphenylphosphonium iodide (8.61 g, 20.6 mmol) in dry tetrahydrofuran (350 mL). The resulting orange solution was stirred at room temperature for 15 min. 4,6-dibromobenzene-1,3-dicarbaldehyde (3) (3g, 10.3 mmol) was added to the reaction mixture and stirred overnight at 50°C under nitrogen. Following the reaction the solvent was evaporated. The residue was dissolved in hexane and passed through a plug of silica to give a white solid. Recrystallization with absolute ethanol afforded white crystals of 1,5-dibromo-2,4-bis((2-2H)propenylbenzene (2.27 g, 70%).
$^1$H NMR (500 MHz, CDCl$_3$) δ = 7.81 (s, 1H), 7.75 (s, 1H), 7.69 (s, 1H), 7.54 (s, 1H), 7.37 (s, 1H), 7.22 (s, 1H), 6.68 – 6.58 (m, 1H, $J = 16.0$ Hz), 6.42 – 6.36 (m, 1H), 6.26 – 6.12 (m, 1H), 5.95 – 5.87 (dqd, 2H, $J = 11.4$ Hz), 1.96 – 1.88 (dd, 6H, 6.7 Hz), 1.80 – 1.77 (dd, 12H, $J = 7.1$ Hz).

2-{5-bromo-2,4-di[(1E)-(2-H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, (6)

1,5-Dibromo-2,4-di[(1E)-2-H]propenylbenzene (4) (3.84 g, 11.2 mmol) was dissolved in dry, degassed tetrahydrofuran(200 mL) and stirred for 5 min. To this, $n$-BuLi (7.2 mL, 11.5 mmol) was added dropwise at $-78$ °C under nitrogen. After addition of $n$-BuLi, the solution was stirred for 15 min followed by addition of pinacolisopropylborate (2.32 g, 12.4 mmol). The reaction mixture was warmed to room temperature overnight. The solvent was removed and the residue was passed through silica using flash chromatography in dichloromethane. The solvent was removed and the crude product was recrystallized from 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 (2.39 g, 62 %) as a off white solid.

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.85 (s, 1H), 7.58 (s, 1H), 7.05 (s, 1H), 6.67 (s, 1H), 1.94 – 1.82 (m, 6H), 1.37 – 1.28 (m, 12H)

4.3 Introduction to polymer synthesis

One of the most important steps in our synthesis towards polymeric helicenes was to synthesize the polymer for our helicenes. The polymer synthesis would control the length of our helicene or the size of our cyclic derivative, kekulenes. Choosing our
polymerization reaction was crucial in our synthesis and many different types of cross-coupling reactions have been performed by my predecessors to find the optimal polymer reaction.\textsuperscript{108,109} The Suzuki polycondensation reaction was the most successful in our past polymerizations and even used in our own synthesis for septulene (Scheme 4.4).\textsuperscript{105}

4.4 Side reactions for Suzuki reaction

The Suzuki polymerization reaction has major side reactions that can limit the length of our polymer. This premature termination of chain growth, identified by Schlüter, can result from aryl-aryl exchange, hydrolytic deboronation, and dehalogenation (Scheme 4.5).\textsuperscript{110}

Jayakannan and co-workers reported significant hydrolytic deboronation and dehalogenation when using Pd[P-(o-Tol)\textsubscript{3}]\textsubscript{4} and Pd(PPh\textsubscript{3})\textsubscript{4} in their reported polymerization reactions. They believe that this was due to their aged catalysts and report that the use of freshly synthesized catalyst in situ increased their polymer length and yields.\textsuperscript{111} It was also reported that hydrolytic deboronation can be reduced by using phosphine-free catalysts like Pd(OAc)\textsubscript{2}. This would prevent aryl-aryl transfer reactions using the same catalyst.\textsuperscript{112,113}
With this information we knew that we had to keep using our phosphine based ligands and bare the major side products that can occur from the Suzuki polycondensation.

### 4.5 Characterization of our polymer

![Scheme 4.5](image)

**Scheme 4.5** Major side products that can occur during Suzuki polymerization.

Characterization of polymers is a challenging process especially when a polymer is made from a new type catalyst, formulation process, or a novel synthesis. Luckily, there are a large number of analytical techniques that may be used for polymeric systems. Techniques used vary from X-ray,\(^{114}\) microscopy,\(^{115}\) nuclear magnetic resonance (NMR),\(^{116}\) gel permeation chromatography (GPC),\(^{117}\) spectroscopic,\(^{118}\) separations,\(^{119}\) to mass spectrometry (MS).\(^{120}\) No single technique mentioned above will be a perfect solution to elucidating complex polymer structures and often multiple techniques are used in combination to afford detailed information.
Analytical GPC and mass spectrometry were the primary sources used in our characterization of the polymer due to the dependable results and ease of instrumental use. A big part of our own synthetic route to polymeric helicenes involved removing deuterium labeling to improve the characterization process of our polymer. This change was done to allow better analytical acquisition with APPI-TOF and MALDI-TOF mass spectrometry.

4.6 Polymerization reactions

4.6.1 Polymerization with Pd(dba)$_2$ and PPh$_3$

To aim for longer polymers we decided to do our Suzuki polymerization in situ as recommended by Jayakannan and co-workers to reduce major side reactions. We added 2-(5-bromo-2,4-di[(1E)-(2-2H)prop-1-enyl]phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in dry toluene and slowly added it with syringe pump over 4h to a boiling mixture of Pd(dba)$_2$ and PPh$_3$ in 2M Na$_2$CO$_3$, THF, and toluene. The reaction progression was monitored by APPI-TOF daily to check the progression of the reaction. After six days the reaction was complete and was worked up to obtain poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.210 g).

If the reaction is not completed then additional time, catalysts, or even a change in method may be required. For us to check our reaction we took aliquots each day and check by APPI-TOF-MS to watch the progression of the reaction. APPI-TOF-MS was the choice of characterization for our polymer, on its well-established use in literature for characterizing PAHs and its ability to offer superior data on reaction progression.$^{120}$ The
size of our polymer can be tracked by the addition of the repeat unit (156 g/mol) and by adding on a possible terminal end like halogen, boronic ester, or hydrogen (Figure 4.2).

After the first day of the reaction an aliquot was taken, and we found evidence of polymer growth from the monomer 2-{5-bromo-2,4-di[(1E)-(2-2H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, to have formed 2-5 unit oligomers with a boronic ester and bromide as the terminal ends (Figure 4.3). Small amounts of reduction product could be observed, but due to the incomplete nature, the reaction was not worked up.
On the third day of the polymerization reaction, we once again checked for completion and found that our polymer has advanced and synthesized many products including dehalogenated, deborylated, and increased polymer size up to 9mers. The polymerization was not complete, but we could see the increasing size of our polymer. We also the same time observed side products (Figure 4.4).

**Figure 4.3** APPI-TOF data on day 1 of the Suzuki polymerization using Pd(dba)$_2$ and PPh$_3$. 

![Graph showing molecular weights and intensity distribution](image)
On the sixth day of polymerization the reaction was completed based on the disappearance of the boronic ester and halogens in the APPI-TOF spectra. Also, the appearance of our polymeric helicenes and the cyclic derivatives can be observed in the spectra, showing that our desired product has been synthesized (Figure 4.5).
After the reaction was complete and worked up, analytical gel permeation chromatography tests were done to check length and polydispersity of the polymer synthesized. We found that our Suzuki polymerization synthesized a polymer of $M_w = 960 \times 10^2$, $M_n = 8 \times 10^2$, with a PDI of 1.15. This information lets us know that the overall polymer chain was made up of short oligomers up to around 8mers which matches what we obtain in our APPI-TOF-MS data. However, when comparing GPC results to polystyrene standards, we noticed that we should have had longer oligomers up to about 30mers (Figure 4.6).
Using the high resolution APPI-TOF-MS we were able to observe that our polymer chain growth was up to 9mers and were able match their predicted isotopic distribution. However, the APPI-TOF-MS was not able to ionize the higher oligomers that GPC shown to have been synthesized and that a different analytical mass spectrometry technique would be required. In order to ionize higher oligomers a MALDI-TOF with appropriate matrix was used to characterize the terminal ends of our oligomers. With the MALDI-TOF we were able to confirm our GPC findings; the presence of oligomers longer than 9mers and up to a 33mer chain with our Suzuki polymerization (Figure 4.7).

Figure 4.6 Normalized GPC curve of Suzuki polymer. Mw = 958 is around the average oligomer length of six repeat units long. Triphenylphosphine oxide is most likely impurity shown around 11 min.
From our analytical GPC data we know that we have a majority of short oligomers like 6mers, than our desired longer oligomers like 33mers. This can be seen in our MALDI-TOF spectra. One of our goals for the synthesis of polymeric heliecnnes is to make longer heliecnnes. To target the longer polymers from our reactions, we needed a way to separate out the shorter oligomers from the longer ones. We choose to use gel permeation chromatography, a common chromatography technique used for separating molecules base on their size difference. This technique was used on our polymeric material with recycling pump to get better separation over time. We collected the front fractions of our polymer to target the longer oligomers to use in the final step of our synthesis. (Figure 4.8).
4.6.2 Polymerization using different catalysts and conditions

We performed different polymerization reactions and conditions to obtain the longest polymers possible for use in the final step. This was achieved by switching our catalyst and conditions for the Suzuki polymerization. Also, we tried using a Yamamoto coupling that would use our 1,5-dibromo-2,4-bis(2H)propenylbenzene as the monomer.

The main change for conditions in the polymerization reaction was modifying the concentrated of the reactions reactions. Dilute conditions are known to favor more cyclic products while more concentrated reactions will form longer polymers.121

Many of the catalysts and conditions used, yielded similar polymer products when evaluated by analytical GPC and MALDI-TOF as shown in Table 4.1.
Using Pd(dba)$_2$ and PPh$_3$ as an in situ catalyst to help reduce major side reactions and form longer polymers did not outperform the similar catalyst Pd(PPh$_3$)$_4$. Also, the reaction time take 6 days before the reaction is complete compared to only one to two days using the more reactive catalysts such as Ni(COD)$_2$.

Pd(PPh$_3$)$_4$ in both dilute and concentrated conditions had good overall yields, but the concentrated conditions was favored since it formed longer oligomers with up to 36mer. However, the main problem with this reaction is that triphenylphosphine oxide can be created during the workup of the reaction and can cause difficulty for separation.

The best catalyst for our Suzuki polymerization is Pd[P(p-Tol)$_3$]$_4$ in concentrated conditions. Yields of the polymer were around 80% and by MALDI-TOF and observed up to the 40mer polymer. Also, removal of the catalyst from our polymer product was easier than any other catalyst since flash chromatography with silica gel can remove the catalyst.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conditions</th>
<th>Mn</th>
<th>Mw</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd(dba)$_2$</td>
<td>Dilute reaction</td>
<td>836</td>
<td>958</td>
<td>1.15</td>
</tr>
<tr>
<td>Pd(PPh$_3$)$_4$</td>
<td>Dilute reaction</td>
<td>781</td>
<td>1055</td>
<td>1.35</td>
</tr>
<tr>
<td>Pd(PPh$_3$)$_4$</td>
<td>Concentrated reaction</td>
<td>795</td>
<td>1288</td>
<td>1.62</td>
</tr>
<tr>
<td>Pd[P(p-Tol)$_3$]$_4$</td>
<td>Dilute reaction</td>
<td>911</td>
<td>1194</td>
<td>1.31</td>
</tr>
<tr>
<td>Pd[P(p-Tol)$_3$]$_4$</td>
<td>Concentrated reaction</td>
<td>948</td>
<td>1432</td>
<td>1.51</td>
</tr>
<tr>
<td>Ni(COD)$_2$</td>
<td>Dilute reaction</td>
<td>963</td>
<td>1301</td>
<td>1.35</td>
</tr>
</tbody>
</table>

Table 4.1 Different polymerization catalysts and conditions used including average molecular weight and PDI values for comparison.
The downside with working with this catalyst is that it is air sensitive, requiring careful degassing of solvents.

The most convenient catalyst for the polymerization was Ni(COD)₂. It performs aryl-aryl coupling between halogens which allows us to skip borylating via lithium halogen exchange and trapping with isopropylpinacol borate. It also allows to use another products 1,5-dibromo-2,4-bis(2-2H)propenylbenzene as the monomer. The yields and polymer lengths were similar to using Pd[P(p-Tol)₃]₄. As the catalyst, the workup does require removal of 1,5 cyclooctadiene which can be removed by vacuum overnight. This catalyst is extremely air and moisture sensitive requiring careful degassing of solvents.

4.6.2 Experimental for polymer synthesis

Synthesis of tris(tri-p-tolylphosphine)palladium

PdCl₂ (120mg, 0.66 mmol) and tri-p-tolylphosphine (1g, 3.29mmol) were transferred to a dry schlenk flask. Dry, degassed (10 mL) DMSO was added and stirred at 120°C for 5 minutes. Hydrazine hydrate (0.15mL, 2.88mmol) was slowly added to the mixture over 5 minutes. This is allowed to stir for 10 minutes and was cooled down to room temperature. Degassed ethanol (20 mL) was added to precipitate yellow crystals affording tris(tri-p-tolylphosphine)palladium (552 mg, 45.6%) which was collected by vacuum filtration. Degassed methanol (50 mL) was used to wash the solid. The solid was dried under vacuum and store under nitrogen at -20°C.

Synthesis of poly(4,6-di[(1E)-(2-2H)-propenyl]-m-phenylene using Pd(dba)₂ and PPh₃
A solution of 2-{5-bromo-2,4-di[(1E)-(2-2H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 g, 1.39 mmol) in dry toluene (24 mL) was added with a syringe pump over 4h to a boiling mixture of Pd(dba)$_2$ (20 mg, 10 mol%) and PPh$_3$ (36mg, 0.139mmol) in 2N Na$_2$CO$_3$ (100 mL), THF (300 mL), and toluene (100 mL). The organic phase was separated, washed, and dried. The solids were passed through a silica plug with dichloromethane. Cold methanol (50 mL) was added and solids were filtered to give poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.210 g). The mixture was used for the next step without further purification.

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.66-7.59 (br, 1H), 6.90-6.84 (br, 1H), 6.15-6.10 (br, d, 2H, $J= 27$ Hz), 1.71-1.52 (br, 6H).

**Synthesis of poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene using Pd(PPh$_3$)$_4$**

A solution of 2-{5-bromo-2,4-di[(1E)-(2-2H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 g, 1.39 mmol) in dry toluene (24 mL) was added with a syringe pump over 12h to a boiling mixture of Pd(PPh$_3$)$_4$ (10 mg, 5.0 mol%) in 2N Na$_2$CO$_3$ (180 mL), THF (200 mL), and toluene (100 mL). The organic phase was separated, washed, and dried. The solids were passed through a silica plug with dichloromethane. Cold methanol (50 mL) was added and solids were filtered to give poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.210 g). The mixture was used for the next step without further purification.$^1$H NMR (500 MHz, CDCl$_3$): δ 7.70-7.60 (br, 1H), 6.89-6.82 (br, 1H), 6.19-6.12 (br, d, 2H, $J= 27$ Hz), 1.73-1.51 (br, 6H).
Synthesis of poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene using [Pd(P(p-tol)₃)₄]

A solution of 2-{5-bromo-2,4-di[(1E)-(2-2H)prop-1-enyl]phenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 g, 1.39 mmol) in dry toluene (24 mL) was added with a syringe pump over 3 days to a boiling mixture of [Pd(P(p-tol)₃)₄] (10 mg, 5.0 mol%) in 2N Na₂CO₃ (180 mL), THF (200 mL), and toluene (100 mL). The organic phase was separated, washed, and dried. The solids were passed through a silica plug with dichloromethane. Cold methanol (50 mL) was added and solids were filtered to give poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.180 g). The mixture was used for the next step without further purification.

¹H NMR (500 MHz, CDCl₃): δ 7.68-7.65 (br, 1H), 6.87-6.84 (br, 1H), 6.18-6.11 (br, d, 2H, J= 26 Hz), 1.74-1.52 (br, 6H).

Synthesis of poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene using Bis(cyclooctadiene)nickel(0)

A solution of 1,5-dibromo-2,4-bis(2-2H)propenylbenzene (1 g, 3.17 mmol) in dry toluene (24 mL) was added with a syringe pump over 24h to a boiling mixture of bis(cyclooctadiene)nickel(0) (1.74 g, 6.32mmol),1,5 cyclooctadiene (0.68 g, 6.28 mmol) and 2,2’-bipyridiene (1 g, 6.40mmol) in dry degassed DMF (25 mL) and toluene (200 mL). The organic phase was separated, pumped down and washed with 50 mL of 6M HCl. The solids were passed through a silica plug with dichloromethane and then dried down to afford a pale yellow solid, poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.410 g). The solid was dried overnight on high vacuum to remove any remaining 1,5cyclooctadiene.
4.7 RCM to form polymeric helicenes

4.7.1 Introduction to RCM

Ring closing metathesis (RCM) is a powerful reaction that has been utilized in many syntheses because of the regioselectivity, stability, and tolerance to many different functional groups. The powerful feature of the RCM can be traced to its mechanism, where the driving force of this reaction is the release of small alkene, often ethylene gas (Scheme 4.6).

Scheme 4.6 Example of ring closing metathesis reaction (RCM).

Ring opening metathesis polymerization (ROMP) and cross-metathesis (CM) are possible side reactions that can occur under the same conditions as RCM. The can cause problems because there are instances where ROMP and CM are the preferred products and the RCM is the undesired product. An example of a ring-opening and a cross metathesis being used in one reaction is Hoveyda and co-workers use of a chiral catalyst for the total Synthesis of Baconipyrone C (Scheme 4.7).

Scheme 4.7 Example of a ring-opening followed by cross-metathesis using a chiral ruthenium catalyst.
4.7.2 Synthetic route to carbohelicenes using RCM

With copious amounts of polymer synthesized, we were able to run dozens of RCM reactions in attempt to synthesize polymeric helicenes using Grubbs 2nd generation catalyst. The choice of catalyst and conditions stems from previous group members’ studies and from published septulene results from.\textsuperscript{105,108,109}

In the RCM reaction, we used our polymer poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene as the precursor in making the targeted helicenes and kekulenes with 2,6-dichloro-1,4-benoquinone in 1,2,4-trichlorobenzene. Adding 2,6-dichloro-1,4-benzoquinone acts as an inhibitor for unwanted isomerization of the propenyl unit. This isomerization contributes to the increased concentration of seven membered rings defects (Scheme 4.8).\textsuperscript{125}

Grubbs 2\textsuperscript{nd} generation catalyst was chosen as our catalyst for its robustness and reversibility in a reaction to remove possible defects unlike other RCM catalysts like Schrock's or Grubbs 1\textsuperscript{st} generation.\textsuperscript{115} The robustness of the catalyst was important since we needed to elevate the temperature of the reaction because of possible solubility issues. An example would be septulene, a relatively insoluble product of this synthesis. The
solubility of septulene was measured to be 1 mg per 20 mL 1,2,4-trichlorobenzene at 100 °C.\textsuperscript{105}

Previous syntheses for our polymeric helicenes were monitored by IR spectroscopy by observing for the disappearance of C-D stretch at 2236 cm\textsuperscript{-1}. In lieu of adding deuterium labels, we monitored our reaction using MALDI-TOF. The MALDI-TOF can be used with ease and can give more detailed data showing the course of the reaction.

Removal of the catalyst is an important step after the reaction was complete, since the ruthenium catalyst can give impurities in our product. To make removal of the catalyst more suitable to chromatographic separation, we first quench any active catalyst we are using with ethylene glycol monovinyl ether\textsuperscript{126} and followed it by addition of tris(hydroxymethyl)phosphine.\textsuperscript{125} Without these two steps large portions of ruthenium catalyst would be left over and would make further purification extremely challenging.

4.7.3 Monitoring RCM reaction

In place of using IR spectroscopy to monitor the progression of the RCM reaction we opted for MALDI-TOF for multiple reasons; such as the data gathered is more detailed for the reactions progression and we can observe possible products that may be in the mixture.

The best results for all aliquots for MALDI-TOF were dried down and combined with AgTFA with dithranol in a 1:5:50 respective mixture to be applied onto the plate as a dry sample. Another matrix mixture that gave similar results was DCTB and AgTFA, in same 1:5:50 respective mixture. Many other matrixes and conditions such as wet
application of the sample were attempted, but did not give good results and were discarded in favor of dry loading.

Monitoring the RCM reaction was performed by taking aliquots of our mixture at different times to observe the progression of the reaction. Aliquots taken out were not purified in attempt to remove any residual ruthenium from the sample. Previous attempts of aliquot purification before obtaining a MALDI-TOF spectra did not yield better results than taking the sample without purification. Also, we were concern that if we attempted to purify our aliquot we could be losing insoluble product on silica gel columns.

We obtained a MALDI-TOF spectra on our reaction at 24h after the catalyst was added and found that our reaction had not progressed much. In the spectra we could see evidence of our polymer still intact, and a repeat unit of 156 g/mol could be seen throughout the spectra (Figure 4.9).
Looking closer at the same spectra we could see evidence that RCM reactions have been occurring. Throughout the spectra a repeat unit of 100 g/mols for formation of new rings and 56 g/mol the loss of butene can be observed (Figure 4.10). This observation can be seen through the entire spectra for many different peaks. This shows that the RCM reactions work but there are many products formed and it is difficult to discern what type of product we actually have.
Allowing the reaction to continue for a couple more days, we took another aliquot after 72h and observed noteworthy differences in the products formed. From our observations we could see a significant decrease in the presence of unreacted polymer and the increase of reacted polymers that formed many closed rings. Repeat units of a 100 g/mol can be observed throughout the entire spectra which signify the formation of the new rings and the loss of butene, showing that the reaction is progressing forward (Figure 4.11).

**Figure 4.10** MALDI-TOF of the RCM reaction 24h after catalyst addition. Progress with the RCM can be seen with the presence of 56 and 100 repeat units.
It is noticeable that many experiments, around three days after the catalyst has been added, that resolution and ionization of the solids becomes increasingly difficult.

Monitoring the reaction by MALDI-TOF after 84h from when the catalyst was added and beyond, we lose the ability to see any recognizable masses that could be our product or polymer with different amount of closed cycles (Figure 4.12). Changes to the matrix, methods, and ionizing power did not yield discernable product on the MALDI-TOF spectra. Attempts with APPI-TOFMS even failed to produce any reliable results.

**Figure 4.11** MALDI-TOF of RCM 72h after catalyst addition. Repeat unit of 100g/mol can be seen throughout the sample.
From what we can tell after 72h after the catalyst was added from the aliquot and MALDI-TOF spectra is that the material that forms more closed cycles becomes increasingly difficult to ionize. The polymers we could see before were no longer visible on the spectra which makes us assume that all of the polymer has been reacted either by forming cycles, or that we may be getting ROMP occurring, both of which would increase the difficulty in ionizing a molecule on the MALDI-TOF.

**Figure 4.12** MALDI-TOF of RCM 84h after catalyst was added.
4.7.4 Experimental

Poly(4,6-di[(1E)-(2-2H)-propenyl])-m-phenylene (0.1 g, .63 mmol) and 2,6-dichloro-1,4-benzoquinone (6 mg, 0.03 mmol) were transferred to a 50 mL Schlenk flask. Distilled and degassed 1,2,4-trichlorobenzene (10 mL) and toluene (10 mL) were added to the flask under N2. The solution was heated to 70 °C. Grubbs catalyst (2nd generation) (24 mg, 0.004 mmol) was added in three batches over three days. The reaction was monitored by MADLI-TOF using AgTFA and dithranol as the matrix. Ethylene glycol monovinyl ether (0.2 mL) was added to quench the catalyst and reaction was poured into methanol (100 mL). The green solid residue was filtered and dried on high vacuum. The residue was dissolved in 1,2,4-trichlorobenzene (10 mL). To the solution, triethylamine (1.0 mL), silica gel (1.0 g) and tris(hydroxymethyl)phosphine (1.0 g) were added. The reaction was heated to 70 °C overnight. The mixture was chromatographed on silica using boiling 1,2,4-trichlorobenzene (100 mL). The solvent was removed under reduced pressure and solid residue was washed with chloroform (50 mL). Attempted purification of the crude mixture was by HPLC (1,2,4-trichlorobenzene:hexane 4:6).
4.8 References


14 Koepp, E; Vogtle, F. Synthesis. 1987, 177.


Appendix

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2.1 NMR and GCMS spectra........................................pg 79
1a - C₉H₁₀, Benzene, prop-1-enyl-Proenyl-benzene: Before: $^1$H NMR (500 MHz, CDCl₃)
1a - C₉H₁₀, Benzene, prop-1-enyl-Propenyl-benzene: Before: GCMS
2a - C9H10, Benzene, prop-1-enyl-Propenyl-benzene: After: $^1$H NMR (500 MHz, CDCl₃)
2a - C9H10, Benzene, prop-1-enyl-Propenyl-benzene: After: GCMS
1b - C_{10}H_{12}, Benzene, 1-methyl-4-(1-prop-1-enyl): Before: $^1$H NMR (500 MHz, CDCl$_3$)
1b - C₁₀H₁₂, Benzene, 1-methyl-4-(1-prop-1-enyl) : Before: GCMS
2b - C_{10}H_{12}, Benzene, 1-methyl-4-(1-prop-1-enyl): After: $^1$H NMR (500 MHz, CDCl$_3$)
2b - C_{10}H_{12}, Benzene, 1-methyl-4-(1-prop-1-enyl) : After: GCMS
1c - C_{10}H_{12}O Benzene, 1-methoxy-4-(1-prop-1-enyl) Before: $^1$H NMR (500 MHz, CDCl$_3$)
1c - C_{10}H_{12}O Benzene, 1-methoxy-4-(1-prop-1-enyl) Before: GCMS
2c - C$_{10}$H$_{12}$O Benzene, 1-methoxy-4-(1-prop-1-enyl) After: $^1$H NMR (500 MHz, CDCl$_3$)
2c - C_{10}H_{12}O Benzene, 1-methoxy-4-(1-prop-1-enyl) After: GCMS
1d - C₉H₉Br, Benzene, 1-bromo-2-(1-prop-1-enyl) Before: $^1$H NMR (500 MHz, CDCl₃)
1d - C₉H₉Br, Benzene, 1-bromo-2-(1-prop-1-enyl) Before: GCMS
2d - C₉H₉Br, Benzene, 1-bromo-2-(1-prop-1-enyl) After: $^1$H NMR (500 MHz, CDCl₃)
2d - C₉H₉Br, Benzene, 1-bromo-2-(1-prop-1-enyl) After: GCMS
1e - C₉H₉F, Benzene, 1-fluoro-4-(1-prop-enyl) Before: $^1$H NMR (500 MHz, CDCl₃)

1e: Before Isomerization
500 MHz in CDCl₃
1e - C₉H₉F, Benzene, 1-fluoro-4-(1-prop-enyl) Before: GCMS
2e - C9H9F, Benzene, 1-fluoro-4-(1-prop-enyl) After: $^1$H NMR (500 MHz, CDCl$_3$)
2e - C₉H₉F, Benzene, 1-fluoro-4-(1-prop-enyl) After: GCMS
1f - C_{10}H_{9}F_{3}, Benzene, 1-prop-1-enyl-4-(trifluoromethyl): Before: $^1$H NMR (500 MHz, CDCl$_3$)
1f - C\textsubscript{10}H\textsubscript{9}F\textsubscript{3}, Benzene, 1-prop-1-enyl-4-(trifluoromethyl): Before: GCMS
2f - C_{10}H_{9}F_{3}, Benzene, 1-prop-1-enyl-4-(trifluoromethyl): After: $^1$H NMR (500 MHz, CDCl$_3$)

2f: After Isomerization
500 MHz in CDCl$_3$
2f - C_{10}H_{9}F_{3}, Benzene, 1-prop-1-enyl-4-(trifluoromethyl): After: GCMS

[Graph showing GCMS data with peaks labeled and retention times]
1g - C₉H₉O₂: Benzene, 1-nitro-2-(1-prop-1-enyl) Before: $^1$H NMR (500 MHz, CDCl₃)
1g - C₉H₉O₂: Benzene, 1-nitro-2-(1-prop-1-enyl) Before: GCMS
1h - C₉H₉O₂, Benzene, 1-nitro-4-(1-prop-1-enyl) Before: ¹H NMR (500 MHz, CDCl₃)
1h - C₉H₉O₂, Benzene, 1-nitro-4-(1-prop-1-enyl) Before: GCMS
$\text{1i} - \text{C}_{12}\text{H}_{12}\text{Br}_{2}$, Benzene, 1,5-dibromo-2,4-di-(1-prop-1-enyl) Before: $^1\text{H}$ NMR (500 MHz, CDCl$_3$)
1i - C_{12}H_{12}Br_{2}, Benzene, 1,5-dibromo-2,4-di-(1-prop-1-enyl) Before: GCMS
2i - C\textsubscript{12}H\textsubscript{12}Br\textsubscript{2}, Benzene, 1,5-dibromo-2,4-di-(1-prop-1-enyl) After: \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3})

2i: After Isomerization
500 Mhz in CDCl

Hexane grease
2i - C$_{12}$H$_{12}$Br$_2$, Benzene, 1,5-dibromo-2,4-di-(1-prop-1-enyl) After: GCMS
1j – C_{14}H_{12}, Cis-stilbene, Before: $^1$H NMR (500 MHz, CDCl$_3$)
1j – C_{14}H_{12}, Cis-stilbene, Before: GCMS
1k – C_{10}H_{12}, (E)/(Z)-1-phenylbut-1-ene  Before: ^1H NMR (500 MHz, CDCl$_3$)
1k – C_{10}H_{12}, (E)/(Z)-1-phenylbut-1-ene Before: GCMS
2k – C₁₀H₁₂, (E)/(Z)-1-phenylbut-1-ene After: $^1$H NMR (500 MHz, CDCl₃)
2k – C₁₀H₁₂, (E)/(Z)-1-phenylbut-1-ene After: GCMS