Synthesis of Polyfunctionalized 1,2-Disubstituted Cyclopropene Compounds

Kate E. Higgins

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Synthesis of Polyfunctionalized 1,2-Disubstituted Cyclopropene Compounds

Kate E. Higgins

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Chemistry

DEPARTMENT OF CHEMISTRY
COLLEGE OF SCIENCE
ROCHESTER INSTITUTE OF TECHNOLOGY
ROCHESTER, NY
AUGUST, 2010
Approved By:

__________________________

Dr. Michael Coleman (Thesis Advisor)

__________________________

Dr. Christina Collison (Committee Member)

__________________________

Dr. Paul Craig (Committee Member)

__________________________

Dr. Thomas Smith (Committee Member)

__________________________

Dr. L. Paul Rosenberg (Department Head)
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### COMMON ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tr>
<td>$^{13}$C NMR</td>
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</tr>
<tr>
<td>$^1$H NMR</td>
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</tr>
<tr>
<td>ACC</td>
<td>1-AMINOCYCLOPROPANECARBOXYLIC ACID</td>
</tr>
<tr>
<td>Ar</td>
<td>ARYL SUBSTITUENT</td>
</tr>
<tr>
<td>BINAP</td>
<td>2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl</td>
</tr>
<tr>
<td>CDCl$_3$</td>
<td>DEUTERATED CHLOROFORM</td>
</tr>
<tr>
<td>COD</td>
<td>CYCLOOCTODIENE</td>
</tr>
<tr>
<td>DCM</td>
<td>DICHLOROMETHANE</td>
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<tr>
<td>de</td>
<td>DIASTEREOMERIC EXCESS</td>
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<td>dpti</td>
<td>DIPHENYLTRIFLYLIMIDAZOLIDINONE</td>
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<td>EDG</td>
<td>ELECTRON-DONATING GROUP</td>
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<td>ee</td>
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<td>Equiv.</td>
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<td>Et</td>
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<td>EWG</td>
<td>ELECTRON-WITHDRAWING GROUP</td>
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<td>HRMS</td>
<td>HIGH RESOLUTION MASS SPECTROMETRY</td>
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<tr>
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<td>INFRARED</td>
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<td>LIQUID CHROMATOGRAPHY, MASS SPECTROMETRY</td>
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</tr>
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<td>METHYL</td>
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<td>Meaning</td>
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</tr>
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</tr>
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<td>Rh₂(S-DOSP)₄</td>
<td>DIRHODIUM TETRAKIS((S)-N-(DODECYLBENZENESULFONYL)PROLINATE)</td>
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<td>RIT</td>
<td>ROCHESTER INSTITUTE OF TECHNOLOGY</td>
</tr>
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<td>rt</td>
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HRMS Spectrum of [3-Acetyl-3-(4-Bromophenyl)-2-(4-Methoxyphenyl)cycloprop-1-en-1-yl] Methyl Methyl Carbonate (12) ........................................................................................................................................ 36
The objective of this thesis project is to synthesize 1,2-disubstituted cyclopropene compounds from internal alkynes and diazoacetate compounds via [2+1] cycloaddition reactions catalyzed by rhodium acetate (Rh₂(OAc)₄). To date, there is no known synthetic transformation to achieve this substitution pattern. 1,2-disubstituted cyclopropene compounds are versatile synthetic intermediates because their functionalization enables further synthetic manipulation. In this work, three cyclopropene compounds were synthesized using this methodology. Their syntheses are described herein.
INTRODUCTION

Cyclopropane and cyclopropene compounds are of current interest because of their versatility in organic synthesis. Cyclopropene compounds are excellent synthetic intermediates, serving as precursors to a variety of functionalized cyclopropane compounds. Cyclopropene compounds can undergo a number of transition metal-mediated transformations to create functionalized cyclopropane compounds which can be used as is or undergo further functionalization.

The key structural features of cyclopropene compounds are the densely functionalized carbocyclic core and the unique alkene reactivity due to the highly strained nature of the ring system. This increase in reactivity leads to a wide range of novel cyclopropane compounds, as cyclopropene compounds have proven to be useful intermediates in the production of functionalized cyclopropane compounds, in addition to, a variety of other interesting synthetic transformations.

The double bond present in cyclopropene compounds also provides novel reactivity which is otherwise not observed in unstrained alkene compounds due to its small ring structure relative to unstrained alkene compounds. This enhanced reactivity enables cyclopropene compounds to undergo a wider range of known synthetic organic transformations as well as many more that are yet to be discovered.

At the present time, cyclopropene synthetic research has lagged behind because there is no direct method to synthesize both electronically and physically diverse cyclopropene compounds. That is, current methods are needed in order to efficiently synthesize diversely functionalized cyclopropene compounds. The goal of this research will improve upon a straightforward transition metal-catalyzed [2+1] cyclopropanation methodology utilizing diazoacetate compounds and both electronically and physically diverse 1,2-disubstituted acetylenic compounds for the rapid synthesis of a small library of poly-functionalized cyclopropene compounds.
BACKGROUND

PHYSICAL PROPERTIES OF CYCLOPROPANE AND CYCLOPROPENE COMPOUNDS

RING STRAIN

The reactivity of cyclopropane and cyclopropene compounds is attributed to the considerable amounts of ring strain contained within the geometry of the simplest carbocyclic molecular structure (Figure 1).

Figure 1: Cyclopropane and Cyclopropene Carbocyclic Skeleton

The total ring strain observed through the heat of combustion data for cyclopropane (115 kJ/mol) and cyclopropene (228 kJ/mol) is a result of Baeyer (angular) and Pitzer (torsional) strain. According to the work of Adolf von Baeyer, the angular strain arises from the non-ideal triangular carbon-carbon bond geometry of both the cyclopropane and cyclopropene molecular skeleton. The Baeyer strain is a measure of the angular compression of the carbon-carbon bonds forced into a less than optimal angle. The majority of the total ring strain in cyclopropane and cyclopropene compounds is a result of Baeyer strain. There is also considerably more angle strain in the cyclopropene ring system.
due to the deviation of the forced angle from ideality being greater than that for cyclopropane compounds. The optimal bond angles for a sp$^3$-hybridized carbon (109.5°) and sp$^2$-hybridized carbon (120°) are dramatically perturbed. For example, the non-ideal bond angle (60°) of both the cyclopropane and cyclopropene ring structure constitutes nearly 50° and 60° of angular compression, respectively.

The Baeyer strain has a profound impact on the bonding in cyclopropane and cyclopropene compounds as compared to that of straight-chain compounds. In straight-chain alkanes, the bonding orbitals from two carbon atoms overlap to form four (4) equivalent sp$^3$-hybridized orbitals.\(^3\) On the other hand, three membered cyclic alkanes do not have equivalent bonding orbitals. This is most amplified in small cyclopropane and cyclopropene carbocyclic ring systems. For example, the cyclopropane skeleton's bonding orbitals have significantly less s-character, only about 17% of that for a linear carbon-carbon sp$^3$-hybridized bond.\(^4\) Thus, the molecular orbital overlap of the sp$^3$-hybridized bonds in cyclopropane is not as symmetrical, and consequently, not as stable as that of typical carbon-carbon single bonds.\(^5\) This structural phenomenon is often referred to as "bent" bonds (Figure 2).

The weak molecular orbital overlap causes the bonds of cyclopropane to be unstable.\(^5\) For cyclopropene compounds, the Baeyer strain is significantly amplified due to the presence of a highly strained sp$^1$-
hybridized carbon-carbon double bond. The relatively higher $\pi$-bond reactivity of the cyclopropene ring can be attributed to the thermodynamic stability gained by releasing the Baeyer strain of the $\pi$-bond.

Although, the rehybridization from sp$^3$ (cyclopropene) to sp$^3$ (cyclopropane) relieves some Baeyer strain$^7$, sp$^3$-hybridized carbons add an additional component of ring strain called torsional strain$^8$. According to Wiberg$^9$, approximately 50-59 kJ/mol of torsional strain is added to the ring for each sp$^3$-hybridized carbon. Torsional strain, also known as Pitzer strain, results from the eclipsing hydrogen atoms in the cyclopropane ring (Figure 1). The carbon atoms on cyclopropane compound are in a syn coplanar arrangement, which causes the hydrogens to be eclipsed. Each eclipsed hydrogen atom adds about 38 kJ/mol of additional strain. Cyclopropene does not have any torsional strain because the double bond prevents eclipsing interactions between the hydrogens on the ring. The lack of torsional strain in cyclopropene compounds partially offsets the additional angle strain. However, cyclopropene compounds have more total ring strain than cyclopropane compounds. The total ring strain of a cyclopropane compound is about 113 kJ/mol, while the total ring strain of a cyclopropene compound is about 228 kJ/mol.$^{10}$ The total ring strain of three-membered ring compounds, in particular cyclopropene compounds, makes them a challenge to synthesize and an interesting class of compounds to study.

**Reactivity of the $\pi$-Bond**

Cyclopropene compounds are excellent synthetic intermediates for the production of highly substituted cyclopropane compounds. The $\pi$-bonds in cyclopropene compounds are shorter than those in a typical straight-chain alkene. This gives the $\pi$-bond in the cyclopropene ring more electron density compared to an unactivated $\pi$-bond making them more reactive than straight-chain alkenes.$^{11}$
Harnessing the reactivity of the cyclopropene π-bond allows several transition-metal mediated transformations to afford a wide range of substituted cyclopropane compounds.\textsuperscript{11}

One type of reaction that cyclopropene compounds can undergo to produce functionalized cyclopropane compounds is the catalytic asymmetric rhodium(I)-catalyzed hydroboration (Scheme 1).\textsuperscript{11}

\[
\begin{align*}
\text{Ph} & \quad \text{Me} \\
\text{Me} & \quad \text{B} & \quad \text{O} \\
\text{Rh-cat.} & \quad \text{THF, rt.} \\
\text{Me} & \quad \text{B} & \quad \text{O} \\
\text{trans} & \quad \text{cis} \\
\text{[Rh}(	ext{COD})\text{Cl}]_2 & \quad \text{(3 mol%)} \quad \text{/ (R)-BINAP (6 mol%)} \quad 97 \quad 3 \quad 65\% (58\% \text{ ee})
\end{align*}
\]

**Scheme 1: Catalytic Asymmetric Hydroboration of Cyclopropenes**

Hydroboration places a boronate group on the cyclopropane ring. This sets up the cyclopropane system to undergo further transition-metal catalyzed reactions. For example, the cyclopropene boronate compound is poised to be utilized in a palladium(0)-catalyzed Suzuki cross-coupling reaction with vinyl or aryl halides to yield a large variety of poly-functionalized cyclopropane compounds (Scheme 2).\textsuperscript{11}

\[
\begin{align*}
\text{Me} & \quad \text{B} & \quad \text{OH}_2 \\
\text{RX} & \quad \text{1.5-2 equiv.} \quad \text{Me} \\
\text{Pd} & \quad \text{0.5-7 h} \quad \text{P}_2 \quad \text{R} \\
84-85\%
\end{align*}
\]

**Scheme 2: Suzuki Cross-Coupling of Cyclopropyl Boronate**

Another powerful example of the versatility of cyclopropene compounds is the chiral rhodium(I)-catalyzed hydrostannation of cyclopropene compounds (Scheme 3).\textsuperscript{11}
Scheme 3: Catalytic Asymmetric Hydrostannation of Cyclopropenes

Hydrostannation reduces the cyclopropene π-bond by the asymmetric addition of tin and a hydride to afford a cyclopropyl stannate. This carbon-metal bond on the cyclopropane ring enables the cyclopropane compound to undergo a palladium(0)-catalyzed Stille coupling to further functionalize the ring. This is an excellent illustration of the versatility of cyclopropene compounds to act as intermediates towards a vast variety of cyclopropane compounds.

1-AMINOCYCLOPROPANECARBOXYLIC ACID

Small ring compounds are important in nature because they offer rigidity and lock compounds into a specific stereo-defined conformation. This characteristic is highly desirable in biochemistry where stereo-defined compounds can act as mechanistic probes. The structural properties of the cyclopropyl group can be used as a scaffold upon which a highly specific molecule can be developed. Several known naturally occurring cyclopropane compounds have demonstrated a wide range of biological activities due to their geometric and electronic constraints. In particular, 1-aminocyclopropanecarboxylic acid (1) (ACC) is a phytohormone used in plants to initiate ripening (Figure 3).

Figure 3: 1-Aminocyclopropanecarboxylic Acid (ACC)
ACC is a precursor to ethylene which serves as an initiator for fruit ripening in plants as well as a regulator of other aspects of plant growth. Recently, several research programs have been developed with the motivation to identify effective derivatives of 1 that prevent the spoilage of produce due to premature ripening. An effective derivative of 1 could have the potential to save numerous lives and billions of dollars for the global economy.

1-Aminocyclopropene carboxylic acid (2) (Figure 4), the unsaturated derivative of 1, has been shown to be an inhibitor of the ethylene-forming enzyme ACC-oxidase. It is postulated that 2 is an extremely poor candidate for acetylene production due to the ready formation of a stabilized cyclopropenone imine which can then undergo nucleophilic attack by an enzymatic residue.

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{COOH} \\
\Delta & \quad 2
\end{align*}
\]

Figure 4: 1-Aminocyclopropene carboxylic Acid

Due to their physiological importance, the synthetic derivatives of compound 1, have received special attention from synthetic organic chemists as interesting targets. Hence, the goal of our research group is to develop new methods for the synthesis of this unique structural class of organic compounds.

CLASSIC PREPARATION OF CYCLOPROPENE COMPOUNDS
In one example of a classic cyclopropanation reaction, a halogenated carbene (such as dibromocarbene) is reacted with an alkene to produce a dibrominated cyclopropane compound. The dibromocyclopropane can then be debrominated to produce the monobrominated species. Subsequent attack using a strong base will abstracted a hydrogen from a carbon adjacent to the brominated carbon, pushing the electrons into the ring to form a double and displace the bromine, producing a cyclopropene compound (Scheme 4).13

Another classic method for synthesizing a halogenated cyclopropane is through use of the Simmons-Smith reagent (ICH2ZnI) in the presence of alkenes (Scheme 5).14

The Simmons-Smith reagent is prepared from the reaction of diiodomethane and zinc powder.14 Only the trans product is formed because a singlet carbene is used. A singlet carbene has a filled \( p \) orbital and two empty \( p \) orbitals. When a singlet carbene is used to affect cyclopropanation, the reaction is concerted. Both electrons in the filled \( p \) orbital attack one carbon of the alkene double bond while the electrons of the other double bond carbon simultaneously enter an empty \( p \) orbital on the carbene (Scheme 6).
Alternatively, a triple carbene could be used to affect cyclopropanation. In the case of a triplet carbene, there are two unpaired electrons, one in each of two different half-filled p orbitals, along with an empty p orbital. The cyclopropanation proceeds with a step-wise radical mechanism. In the first step, one unpaired electron from the carbene combines with one electron from a carbon of the alkene double bond to form a new carbon-carbon single bond, while the other electron from the alkyl carbon moving to form a radical on the other alkyl carbon. In a second step, the other unpaired electron of the carbene combines with the radical electron to form a second carbon-carbon single bond to close the cyclopropane ring. Since the cyclopropanation with a triple carbene is a step-wise reaction, there is time between the two steps when rotation can occur around the first formed carbon-carbon single bond. This rotation allows for formation of the cis product (Scheme 7).\textsuperscript{15,16}

An example of a classic method for the synthesis of cyclopropene compounds is the dehydrohalogenative cyclization, which proceeds as illustrated in Scheme 6.
Both of the methods discussed above for the synthesis of cyclopropene compounds have significant disadvantages. First of all, both occur under strongly basic conditions, which limit the functionality on the cyclopropene ring since most functional groups would be too sensitive to withstand a strong base. This synthetic method is particularly unattractive for the synthesis of amino acids. In order for an amine and carboxylic functionality to be installed on the ring, several additional transformations are necessary. Moreover, the precursors for these cyclopropene compounds are not readily available and their synthesis is often highly complex.

PHOTOCHEMICAL AND THERMAL DECOMPOSITION

To avoid the use of harshly basic conditions, photochemical and thermal decomposition methods of diazo compounds as carbene precursors were thought to be a synthetic alternative. Carbenes are quite reactive because the carbon center is ambiphilic, meaning the carbene can exhibit both electrophilic and nucleophilic properties. Carbenes consist of an uncharged carbon atom that is bonded to two substituents and has two very reactive nonbonding electrons which give it an incomplete octet. Singlet carbenes (Figure 5a) have both the nonbonding electrons in the same orbital, whereas triplet carbenes (Figure 5b) have one nonbonding electron in each of two orbitals.
In classic cyclopropanation reactions, ultraviolet light and heat were used to decompose a diazo compound (such as diazomethane) in the presence of an alkene to non-selectively produce a cyclopropane compound along with a significantly larger amount of byproducts (Scheme 7). This process is only selective in the way that singlet carbenes react to produce a product with the same geometry as the starting material\textsuperscript{17}, while triplet carbenes react through a radical mechanism which allows for isomerization.\textsuperscript{18}

During the decomposition of the diazo compound, nitrogen gas (N\textsubscript{2}) is released and is the thermodynamic driving force for the reaction (Scheme 8). Upon release of nitrogen gas, methylene, a carbene, is formed which then preferably reacts with the electron rich ethylene in the cyclopropanation step.
However, the photochemical and thermal decomposition of diazo compounds was found to be (1) extremely nonselective due to carbene dimer formation, and (2) violently explosive. Both the photochemical and thermal methods are not amenable to stereoselective transformations.

**TRANSITION METAL-CATALYZED [2+1] CYCLOPROPENATION**

One pivotal approach used to control the reactivity and the selectivity of carbene chemistry was the use of transition-metal catalysts with chiral ligands. A wide variety of coordinatively unsaturated transition-metals, in the third and fourth periods of the periodic table, are capable of stabilizing the metal-bound carbene. These transition metal-stabilized complexes with the general formula, $L_nMCRR'$, are often described as ‘metal-carbenoid’ complexes (Scheme 9).

Transition metal-stabilized carbenoids do not react like photochemically/thermally generated free carbenes. Generally, they are generated from diazoacetate compounds and demonstrate much higher levels of selectivity. Diazoacetate compounds are defined according to their reactivity and are classified...
broadly as three general types used to catalytically generate transition metal-stabilized carbenoids (Figure 6).

Figure 6: Classification of Carbenoid Species

a) acceptor-only substituted carbenoid, b) acceptor/acceptor substituted carbenoid, and c) donor/acceptor substituted carbenoid

The activities of transition-metal catalysts towards diazoacetate decomposition (loss of nitrogen gas) are dependent on both the electrophilicity of the metal catalyst and on the stability of the diazoacetate compound. The transition metal assists the decomposition of the diazoacetate compound, forming an intermediate transition metal-carbenoid species (Scheme 10).

Scheme 12: Transition-Metal Catalyzed Decomposition of Diazoacetate Compounds

Electron-donating (donor) groups and electron-withdrawing (acceptor) groups influence the reactivity of the carbenoid towards cyclopropenation. The electron-withdrawing nature of the acceptor group tends to increase the reactivity of the carbenoid species by making the central carbon atom more electrophilic, while a donor group stabilizes the carbenoid and makes the reactions involving this type of carbenoid more chemoselective.

The acceptor-only class of diazo compounds (Figure 6a, EWG = CO₂R, COR, NO₂, PO(OR)₂, SO₂R) are the most highly reactive class and are the most widely used in organic synthesis. The electron-
withdrawing nature of the acceptor-only substituted diazoacetate compound enhances the reactivity of the already electrophilic carbenoid. Because they are so reactive, they are often found to be less selective. They decompose relatively quickly in the presence or even absence of transition-metal catalysts. There is a wide range of catalysts that are capable of decomposing these diazo compounds into transition metal-carbenoid species. A major drawback of using this class of diazo compounds is inhibition of cyclopropenation due to dimerization of the diazo compound.

Decomposition of the acceptor/acceptor-substituted class of diazo compounds (Figure 6b, EWG = CO₂R, COR, NO₂, SO₂R, CN) are the least reactive and it takes a very reactive transition metal catalyst to decompose them into metal-carbenoid species. The presence of a second acceptor group stabilizes the diazo compound, making a very reactive catalyst necessary for decomposition into a highly electrophilic carbenoid species. Again, a major drawback of using this class of diazo compounds is inhibition of cyclopropenation due to dimerization of the diazo compound; however, this class allows for more selectivity in cyclopropanation reactions.

The newest class of carbene precursors to be developed are the donor/acceptor-substituted diazo compounds (Figure 6c, EWG = CO₂R, COR and EDG = vinyl, alkynyl, aryl, heteroaryl). The donor group stabilizes the diazo compound making a highly reactive catalyst necessary for decomposition into a resonance stabilized carbenoid. Generally, it is found that donor/acceptor diazoacetate compounds are more stable and selective towards transition metal-catalyzed decomposition in to a resonance stabilized carbenoid. For example, comparison experiments for the cyclopropanation of styrene demonstrated that the donor/acceptor-substituted carbenoid affords higher yields and diastereoselectivities. Furthermore, donor/acceptor-substituted diazoacetate compounds reduced syringe pump addition times by 4-10 fold because less dimerization of the diazoacetate compound was observed. In all cases, the judicious choice of transition metal-complexes and carbene precursors are needed to effect a successful reaction.
When transition metals catalyze the decomposition of diazoacetate compounds in the presence of an electron-rich substrate, such as an alkene or alkyne, a [2+1] concerted asynchronous cyclopropanation or cyclopropenation results (Scheme 11).

![Scheme 13: Transition-Metal Catalyzed Cyclopropanation Cycle](image)

COPPER(I)-CATALYZED CYCLOPROPA NATION

Copper(I) revolutionized carbene selectivity by offering the first example of transition metal-mediated carbene decomposition into a copper-stabilized carbenoid complex. Copper is attractive due to its low cost relative to other transition metals.

The first major accomplishment in the field of copper-catalyzed cyclopropanations was made by Salomon and Kochi in 1973 (Scheme 12).²⁶

![Scheme 14: Salomon and Kochi’s Cyclopropanation](image)

Initially, copper(II) was used in these catalysts, but Salomon and Kochi discovered that copper(I) was the actual active catalytic form of the transition metal. Copper(II) permitted successful cyclopropanation
reactions because it can be reduced to copper(I) by the diazoacetate (in situ) or an equimolar equivalent of hydrazine.

The next major advancement was by Nozaki and co-workers\textsuperscript{27}, who demonstrated the first enantioselective intermolecular cyclopropanation to be catalyzed by a homogenous transition metal-complex (Scheme 13)\textsuperscript{28}, chiral copper(II) salicylaldimine. Their work also demonstrated the first example of a chiral catalyst being used as a means of enantiocontrol.\textsuperscript{29}

\[
\begin{align*}
& \text{Ph} \quad + \quad \text{N}_2 \quad \text{CO}_2\text{Et} \quad \text{Ph} \quad \text{CO}_2\text{Et} \\
& \text{cat.} \quad 72\% \\
& \text{cis} \quad \text{trans} \quad \text{minor product} \\
& \text{(1R,2R)} \quad \text{from (R)-1} \\
& 6\% \text{ ee} \\
& \text{(1:2:3)} \\
& \text{R} = \text{[NH}_2\text{]} \\
& \text{catalyst}
\end{align*}
\]

\textbf{Scheme 15: First Enantioselective Cyclopropanation Reaction with a Homogeneous Copper Catalyst}

The reactions of Nozaki involved the decomposition of ethyl diazoacetate with styrene in the presence of a copper(II) salicylaldimine catalyst to produce both \textit{cis} and \textit{trans}-2-phenyl-cyclopropanecarboxylates (Scheme 12), which were found to be optically active. The results of this work supported the combination of the carbene (from diazo decomposition) with the transition metal-complex to form a metal-carbenoid. It is generally believed that the transition metal-carbenoid complex stays intact and controls the asymmetry induction observed in the cyclopropane product. Despite the low enantiomeric excess (<10\% ee) resulting from Nozaki's method, it did provide a new way to prepare optically active cyclopropane derivatives in a single step.
As a branch off of Nozaki’s work, the next major advancement of the field was by Aratani.\textsuperscript{28} Aratani’s work, as with Nozaki’s, dealt with asymmetric cyclopropanation using copper catalysts; however, Aratani expanded the transformation for use in industrial production. His work involved the decomposition of an acceptor-only substituted diazoacetate with an alkene in the presence of a chiral copper catalyst to give optically active cyclopropanecarboxylate compounds (Scheme 14).

\begin{equation}
\begin{array}{c}
\text{CH}_3 \\
\text{H}_2\text{C} \\
\text{N}_2 \\
\text{H}_2\text{CO}_2\text{Et} \\
\text{cat.} \\
\text{H}_3\text{C} \\
\end{array}
\rightarrow
\begin{array}{c}
\text{H}_3\text{C} \\
\text{CO}_2\text{R} \\
\text{N}_2 \\
\text{H}_2\text{CO}_2\text{Et} \\
\text{cat.} \\
\text{H}_3\text{C} \\
\end{array}
\end{equation}

\textit{Scheme 16: Aratani’s Synthesis of Optically Active Cyclopropanecarboxylates}\textsuperscript{29}

The usefulness of this transformation to industry was illustrated by the synthesis of various cyclopropanecarboxylic acid derivatives to serve as building blocks for major industrial syntheses. Aratani’s cyclopropane transformation has a wide scope as it is useful in synthesizing a wide range of fine chemical products. It also has improved stereoselectivity compared to Nozaki’s transformation. Aratani also proposed a mechanism of how chirality is transferred from the copper carbene-complex to the product. Strong support is also provided of the structure of the original copper complex not being maintained throughout the catalytic process. The catalyst goes into the reaction as one species and then must be activated before undergoing cyclopropanation.

After Aratai, Pfaltz introduced a copper catalyst with chiral semicorrin ligands (Scheme 15).\textsuperscript{30}
The results of Pfaltz’s work improved enantiocontrol for copper-catalyzed cyclopropanations when monosubstituted alkenes were employed. The effectiveness of these processes were diminished, however, when 1,2- or tri-substituted alkenes were employed.

**RHODIUM(II)-CATALYZED CYCLOPROPENATION**

Today, dirhodium(II) catalysts have been demonstrated to be the most powerful, efficient, and versatile transition metals for catalytic decomposition of diazoacetates. Although rhodium(II) is 2500 times more expensive than copper metal, it has been proven to be more selective and it has been particularly useful for the catalytic asymmetric [2+1] cyclopropenations of acetylenic compounds.

The first reported asymmetric synthesis of a chiral cyclopropene compound was reported by Doyle, Müller, and co-workers in 1992. The catalysts used by Doyle were the dirhodium(II) tetrakis[methyl 2-oxopyrrolidine-5(R or S)-carboxylates, or Rh₂(5R or 5S-MEPY)₄. In Doyle’s work, diazoesters were decomposed with dirhodium(II) catalyst in the presence of terminal alkynes to form the cyclopropene products in moderate yield (Scheme 16).
Rh(5R-MEPY)_4 + R_2 \rightarrow R_1 - 70\% \text{ yield} \\
70 - 98\% \text{ ee}

\[
\begin{align*}
R_1 &= \text{CH}_2\text{OR, CH}_2\text{OCOR, CH(OR)}_2, \text{CH}_2\text{NR}_2 \\
R_2 &= \text{OMe, OEt, OtBu, O-D-Menthyl, O-L-Menthyl, NMe}_2
\end{align*}
\]

Scheme 18: Doyle's Cyclopropanation

Doyle's catalyst presented an effective enantioselective method for the synthesis of chiral cyclopropene compounds in moderate yields and enantioselectivities from terminal alkynes. One major drawback was that cyclopropanation of 1,2-disubstituted alkynes was less effective which resulted in low overall yields and enantioselectivities (< 20\% ee).

The second advancement in dirhodium(II)-catalyzed cyclopropanation methodology was reported by Corey. The dirhodium(II) catalyst designed by Corey and co-workers is Rh_2(OAc)(DPTI)_3. It was found to be an efficient method for the enantioselective cyclopropanation of terminal alkynes that gives high yields and excellent enantioselectivities (> 90\% ee) (Scheme 17).

\[
\begin{align*}
R_1 &= \text{CH}_2\text{OR, CH}_2\text{OCOR, CH(OR)}_2, \text{CH}_2\text{Br, n-Alk, }^1\text{Bu} \\
R_2 &= \text{OMe, OEt, OtBu, O-D-Menthyl, O-L-Menthyl, NMe}_2
\end{align*}
\]

Scheme 19: Corey's Cyclopropanation

A wide range of terminal alkynes were investigated which indicated that the [2+1] cyclopropanation methodology is extremely functional group tolerant. Alkenes were also tested and found to yield cyclopropane compounds with satisfactory efficiency for cyclopropanation. The research
of Corey and co-workers also provided mechanistic insight into the structure of the dirhodium carbenoid complex during the cyclopropenation reaction. The overall advantages of Corey's catalyst is that it widen the scope of reactive terminal alkynes towards the synthesis of cyclopropene compounds in high overall yields and enantiomeric excesses. However, one common disadvantage is the catalysts are only reactive with terminal alkynes.

The most recent advancement in the methodology for dirhodium(II)-catalyzed cyclopropenation was reported by Davies and co-workers involving the cyclopropenation of terminal alkynes and methyl aryl diazoacetates in the presence of a dirhodium tetrakis((S)-N-(dodecylbenzensulfonyl)prolinate) \( \text{Rh}_2(S\text{-DOSP})_4 \) catalyst (Scheme 18).  

![Scheme 20: Davies' Cyclopropenation](image)

The major advantage of Davies' published \([2+1]\) cyclopropenation methodology is the utilization of a donor/acceptor-substituted diazoacetate compound. The work of Davies offered insight into the approach of the alkyne toward the carbenoid, and therefore insight into the cyclopropenation mechanism that is understood the least. This methodology produces cyclopropenes containing a quaternary center in an enantioselective fashion. Yet again, the major disadvantage of this strategy is the lack of reactivity of the internal alkyne compounds (Scheme 19).
Scheme 21: Davies’ Methodology Applied to the Synthesis of a Tetrasubstituted Cyclopropene

Consistent among all the results reported in the literature for the dirhodium(II) catalyzed [2+1] cyclopropenation reaction is the apparent poor reactivity of 1,2-disubstituted alkynes. This observation opens up an opportunity to advance the transition metal catalyzed [2+1] cyclopropenation methodologies for the synthesis of highly functionalized cyclopropene compounds.
HYPOTHESIS

As illustrated previously, the dirhodium(II)-catalyzed [2+1] cycloaddition methodology has been applied to many alkenes, and to lesser extent, alkynes. Our current research goal will extend the dirhodium(II)-catalyzed [2+1] cycloaddition methodology using diazoacetate compounds to a variety of electronically and sterically diverse alkynes for the synthesis of [2+1] cyclopropenation compounds. We propose that increasing the electron density of the alkyne may have a measurable effect on its overall reactivity. It was hypothesized that during the cyclopropenation reaction, a partial positive charge builds in the transition state on one carbon of the triple bond. By increasing the electron density of the alkyne, this partial positive charge is stabilized, and the alkyne is therefore encouraged to undergo the cyclopropenation. The results of this study are presented herein.
RESULTS

The general dirhodium(II) tetraacetate catalyzed cyclopropenation methodology that will be used to study the substrate scope of [2+1] cyclopropenation reactivity is illustrated below (Scheme 20).

\[
\begin{align*}
\text{R} & \quad \text{Br} \\
\text{O} & \quad \text{N}_2 \\
\text{4-7} & \quad \text{3} \\
\end{align*}
\]

Scheme 22: General Dirhodium(II) Catalyzed Cyclopropenation of Electron-Rich 1,2-Disubstituted Alkynes

Dirhodium(II) tetraacetate is a benchmark catalyst widely used for the discovery of alternative transition metal catalysts, mechanistic insight, and computational studies.

The research study began with the synthesis of the electron rich 1,2-disubstituted alkynes 4-6 (Figure 7).

\[
\begin{align*}
\text{4} & \\
\text{5} & \\
\text{6} & \\
\end{align*}
\]

Figure 7: Electron Rich 1,2-Disubstituted Alkynes

The project first started with the synthesis of 4-propynylanisole (4) (Figure 7) starting from commercially available, 4-ethynylanisole (8) (Scheme 20). Alkyne 8 was cooled in a dry-ice/acetone bath
to -78°C and was deprotonated by n-butyl lithium in THF. After an hour, methyl iodide was added and deprotonated 8 underwent an alkylation resulting in varying yields (69-99%) (Scheme 21).

Scheme 23: Synthesis of 4-Propynylanisole

The reaction conditions were further optimized with the goal to obtain complete conversion of starting material into product. It was thought that separation of the starting material and product would be rather difficult due to their similar physical properties. However, after varying the reaction conditions each attempt indicated unreacted starting material by crude 1H NMR. It was reasoned that all the reaction mixtures of starting material and product were combined and resubjected to the reaction conditions. Unfortunately, the crude 1H NMR of the bulk mixture indicated that there still remained incomplete conversion. Interestingly, an accidental contamination of the bulk mixture forced a column chromatographic purification, and ultimately, lead to the separation of starting material and product on silica in 100% hexanes and the collection of greater than 100 fractions. When the reaction was attempted again at a later date, complete conversion (99% yield) was observed.

With 4 in hand, it was subjected to the standard Rh2(OAc)4 catalyzed [2+1] cyclopropenation reaction conditions to yield 1-[1-(4-bromophenyl)-2-(4-methoxyphenyl)-3-methylcycloprop-2-en-1-yl] ethanone (9) (Scheme 22).
Scheme 24: Cyclopropenation of 4-Propynylanisole

The second alkyne that was synthesized was 3-(4-methoxyphenyl)prop-2-yn-1-yl acetate (5) (Figure 7) in a two step process starting again from commercially available 8 (Scheme 23).

Scheme 25: Synthesis of 3-(4-Methoxyphenyl)prop-2-yn-1-yl Acetate

Alkyne 8 was cooled to -78°C in THF and then treated with formaldehyde to afford 3-(4-methoxyphenyl)prop-2-yn-1-ol (10) (Figure 8) in 50% yield.

Figure 8: 3-(4-methoxyphenyl)prop-2-yn-1-ol

After several basic/acidic aqueous washings, 1H NMR of the crude solid indicated no further purification was required. Alkynyl alchohol 10 was then treated with acetic anhydride in pyridine at room temperature to produce 3-(4-methoxyphenyl)prop-2-yn-1-yl acetate (5) in 89% (overall 44%) yield.
Subsequently, alkynyl acetate 5 was subjected to our standard cyclopropenation conditions to produce [3-acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl acetate (11) in a suboptimal yield of >100% (Scheme 24).

Scheme 26: Cyclopropanation of 3-(4-Methoxyphenyl)Prop-2-yn-1-yl Acetate

Both $^1$H and $^{13}$C NMR data support that the product was, in fact, synthesized.

We then set out to make the third alkyne 3-(4-methoxyphenyl)prop-2-yn-1-ylmethyl carbonate (6) (Figure 7). Again, 8 was cooled to -78°C in THF and treated with formaldehyde. In this instance, the crude reaction mixture was purified via column chromatography before continuing. Alkynyl alcohol 10 was then treated with commercially available methyl chloroformate in pyridine at room temperature to produce 3-(4-methoxyphenyl)prop-2-yn-1-ylmethyl carbonate (6) in 25% yield (Scheme 25).

Scheme 27: Synthesis of 3-(4-Methoxyphenyl)Prop-2-yn-1-ylmethyl Carbonate

Next, alkynyl carbonate 6 was subjected to standard cyclopropanation conditions to afford [3-acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl methyl carbonate (12) in 14% yield (Scheme 26).
Scheme 28: Cyclopropenation of 3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate

The fourth cyclopropenation was performed on commercially available diphenylacetylene (7) (Figure 7). Unactivated internal alkyne 7 was subjected to the standard cyclopropenation conditions; however, no cyclopropene product was observed via crude $^1$H NMR (Scheme 27).

Scheme 29: Attempted Cyclopropenation of Diphenylacetylene

Column chromatography of the reaction mixture produced several inseparable uncharacterizable substances. It is believed that the absence of the methoxy group in conjugation with the alkyne does not permit a productive reaction.
CONCLUSIONS

Functionalized cyclopropane and cyclopropene compounds have been shown to be useful synthetic intermediates. Although there is significant interest in the field, previous work has not succeeded in expanding the current [2+1] cycloaddition methodology of cyclopropene formation to include 1,2-substituted cyclopropene products.

The focus of this M.S. thesis was to expand the current methodology to include 1,2-substituted cyclopropene products. A few different electron-rich internal alkynes were synthesized and treated with p-bromophenyl methyl diazoacetate 3 in the presence of a catalytic amount of Rh2(OAc)4 in the attempt to produce the corresponding 1,2-substituted cyclopropene products.

It has been shown that the electron-donating nature of the methoxy group increases the reactivity of the previously thought unreactive 1,2-disubstituted alkyne. It was thought that 7 was not sufficiently electron-rich and was not able to successfully undergo the [2+1] cyclopropenation reaction.

Finally, this work demonstrated the proof of principle, that the Rh2(OAc)4-catalyzed [2+1] cycloaddition of internal alkynes and diazoacetate compounds is successful for the production of 1,2-disubstituted cyclopropenes. Future directions of this project include extending the methodology for use with chiral copper catalysts and also broadening the range of internal alkynes tested.
EXPERIMENTAL PROCEDURES

CHEMICALS AND INSTRUMENTATION

All chemicals were ordered from Sigma-Aldrich and proper storage and handling was followed when they were not in use. Bulk chemicals were obtained from the Chemical Stockroom of the College of Science at RIT. All chemicals and solvents were used from the storage vessel as is, unless otherwise indicated. All reactions were conducted under dry argon gas. Infrared spectroscopic analyses were performed neat on a Shimadzu IRPrestige-21 Fourier Transform Infrared Spectrometer. Samples for liquid chromatography mass spectroscopic data were dissolved in a solution of 1% acetic acid in methanol then filtered prior to injection. LCMS analyses were performed on an Applied Biosystems MDS SCIES 3200 Q Trap LC/MS/MS System. High resolution mass spectral (HRMS) samples (< 1mg) were dissolved in dichloromethane and sent for analysis on the Thermo Finnigan MAT 95XL Mass Spectrometer at State University of New York at Buffalo’s Mass Spectrometry Facility. We gratefully acknowledge the NSF Grant CHE0091977 awarded to the University at Buffalo for their support. Nuclear Magnetic Resonance Spectroscopic data was collected on RIT’s Bruker Avance DRX-300 MHz NMR spectrometer. All samples were dissolved in CDCl₃ with a TMS internal standard prior to analysis. We are indebted to the University of Rochester Chemistry Department NMR facilities for access when the RIT NMR spectrometer was under repair for the summer of 2009.
SYNTHESES

3-(4-Methoxyphenyl)prop-2-yn-1-ol (10): To a solution of 4-ethynylanisole (8) (5 g, 37.8 mmol) and THF (18 mL) was added n-BuLi (19.86 mL, 39.72 mmol) dropwise via syringe. The mixture was stirred at -78 °C. After 2 h paraformaldehyde (4.77 g, 158.8 mmol) was added. The mixture was allowed to stir at room temperature for 2.5 h, then diluted with ethyl acetate and extracted with water (x3) and brine (x3). The combined organic extracts were washed with ethyl acetate, dried over magnesium sulfate, and filtered then concentrated under vacuum. The product was purified on silica and eluted with a 30% solution of DCM in hexanes. The product was isolated as yellow oil in 50% yield. $^1$H NMR (CDCl$_3$, 300 MHz):  $\delta$ 7.37 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 4.47 (s, 2H), 3.80 (s, 3H).

3-(4-Methoxyphenyl)prop-2-yn-1-yl Acetate (5): To a solution of 3-(4-methoxyphenyl)prop-2-yn-1-ol (3.05 g, 18.8 mmol) and pyridine (27.66 mL, 0.951 mol) was added acetic anhydride (3.56 mL) dropwise via syringe. The mixture was stirred at room temperature overnight, then diluted with ethyl acetate and extracted with water (x3) and saturated NH$_4$Cl (x3). The combined organic extracts were washed with ethyl acetate, dried over magnesium sulfate, and filtered then concentrated under vacuum. The product was purified on silica and eluted with a solution gradient of 10%-40% ether in hexanes. The product was isolated in 70% yield. $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 7.39 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 4.89 (s, 2H), 3.80 (s, 3H), 2.12 (s, 3H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 170.3, 159.9, 133.4, 114.1, 113.9, 86.4, 81.5, 55.2, 52.9, 20.7; HRMS m/z (M + H)$^+$ calcd for C$_{13}$H$_{12}$O$_3$ 204.0786, found 204.2.

3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl)methyl Acetate (11): To a stirring solution of 3-(4-methoxyphenyl)prop-2-yn-1-yl acetate (0.90 g, 4.41 mmol), Rh$_2$(OAc)$_4$ (1.9
mg, 0.004 mmol) and DCM (2.6 mL) was added a solution of 1-(4-bromophenyl)-1-diazoacetone (1.12 g, 4.98 mmol) and DCM (2 mL) dropwise via syringe pump over 6 h. The mixture was passed through a silica plug and eluted with DCM (20 mL). The mixture was concentrated under vacuum. The product was first purified by kugelrohr, then purified on silica and eluted with a solution gradient from 10-30% ether in hexanes. The product was isolated as a white solid. The product was obtained in a suboptimal yield of >100%; IR (film) \( \nu = \) 1744, 1711, 1213 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) 7.94 (d, \( J = 8.8 \) Hz, 2H), 7.57 (d, \( J = 8.4 \) Hz, 2H), 7.30 (d, \( J = 8.4 \) Hz, 2H), 6.98 (d, \( J = 8.9 \) Hz, 2H), 4.80 (s, 2H), 3.85 (s, 3H), 3.42 (s, 3H), 1.76 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) 194.1, 170.0, 165.7, 163.9, 145.9, 134.0, 132.7, 131.4, 131.0, 130.9, 129.3, 123.1, 114.1, 63.0, 55.3, 53.3, 20.4; HRMS \( m/z \) (M + H)\(^+\) calcd for C\(_{21}\)H\(_{19}\)BrO\(_5\) 430.0415, found 446.03571.

4-Propynylanisole\(^3\) (4): To a stirring solution of 4-ethynylanisole (2.5 g, 18.92 mmol) and THF (47 mL) was added n-BuLi (23.5 mL, 47 mmol) dropwise via syringe. The mixture was warmed to room temperature. After 1 h, iodomethane (3 ml, 48.2 mmol) was added dropwise via syringe. The mixture was allowed to stir overnight. The crude reaction mixture was not purified. The product was isolated as yellow oil in 99% yield. \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) 7.32 (d, \( J = 8.8 \) Hz, 2H), 6.81 (d, \( J = 8.8 \) Hz, 2H), 3.79 (s, 3H), 2.03 (s, 3H).

1-[1-(4-Bromophenyl)-2-(4-methoxyphenyl)-3-methylcycloprop-2-en-1-yl] Ethanone (9): To a stirring solution of 4-propynylanisole (0.54 g, 3.69 mmol), Rh\(_2\)(OAc)\(_4\) (27 mg, 0.061 mmol), and DCM (24.4 mL) was added a solution of 1-(4-bromophenyl)-1-diazoacetone (0.31 g, 1.22 mmol) in DCM (12.2 mL) dropwise via syringe pump over 6 h. The mixture was passed through a silica plug and eluted with DCM (70 mL). The product was purified on silica eluting with a solution gradient from 3-10% ether in hexanes to isolate the product. IR (film) \( \nu = \# \), \( \# \) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) 7.45 (d, \( J = 8.7 \) Hz,
2H), 7.37 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.68 (s, 3H), 2.33 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 174.9, 160.1, 140.3, 131.0, 130.6, 129.8, 119.9, 118.6, 114.4, 107.8, 107.2, 55.3, 51.9, 34.6, 9.3.

3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate (6): To a solution of 3-(4-methoxyphenyl)prop-2-yn-1-ol (1.92 g, 11.85 mmol) and pyridine (23.7 mL) was added methyl chloroformate (1.84 mL, 23.7 mmol) dropwise via syringe. The solution was allowed to stir for 5 min, followed by extraction with water. The combined organic extracts were washed with ethyl acetate, dried over magnesium sulfate, and filtered, then concentrated under vacuum. The product was purified on silica and eluted with a solution gradient of 10-35% ether in hexanes. Product was isolated as clear oil in 25% yield. IR (film) \(\nu\) = 1751, 1244 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 7.39 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.71 Hz, 2H), 4.95 (s, 2H), 3.82 (s, 3H), 3.79 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 160.4, 155.7, 133.9, 114.4, 114.3, 87.6, 81.4, 56.8, 55.7, 55.5; HRMS m/z (M + Na)\(^+\) calcd for C\(_{17}\)H\(_{14}\)O\(_4\)Na 220.0735, found 243.06306.

[3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Methyl Carbonate (12): To a stirring solution of 3-(4-methoxyphenyl)prop-2-yn-1-ylmethyl carbonate (0.95 g, 4.31 mmol), Rh\(_2\)(OAc)\(_4\) (31.8 mg, 0.072 mmol), and DCM (28.7 mL) was added a solution of 1-(4-bromophenyl)-1-diazoacetone (0.37 g, 1.44 mmol) and DCM (14.4 mL) dropwise via syringe pump over 6 h. The mixture was passed through a silica plug and eluted with DCM (70 mL). The product was purified on silica eluting with a solution gradient of 20-30% ether in hexanes. The product was isolated in 14% yield. IR (film) \(\nu\) = 1753, 1717, 1248 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 7.52 (d, J = 8.5 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 5.30 (d, J = 4.4 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 3.69 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 174.2, 161.5, 155.8, 139.6, 132.0, 131.6, 130.4, 120.9,
117.6, 115.0, 112.5, 105.5, 61.1, 55.8, 55.6, 52.7, 36.2; HRMS m/z (H + Na)^+ calcd for C_{21}H_{19}BrO_6Na
446.0364, found 469.02643.
Figure 9: $^1$H NMR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-ol (10)
Figure 10: \(^1\)H NMR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-yl Acetate (5)
Figure 11: $^{13}$C NMR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-yl Acetate (5)
Figure 12: HRMS Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-yl Acetate (S)
Figure 13: $^1$H NMR Spectrum of [3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Acetate (11)
Figure 14: $^{13}$C NMR Spectrum of [3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Acetate (11)
Figure 15: HRMS Spectrum of [3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Acetate (11)
Figure 17: $^1$H NMR Spectrum of 4-Propynylanisole (4)
Figure 18: $^1$H NMR Spectrum of 1-[1-(4-Bromophenyl)-2-(4-methoxyphenyl)-3-methylcycloprop-2-en-1-yl] Ethanone (9)
Figure 19: $^{13}$C NMR Spectrum of 1-(1-(4-Bromophenyl)-2-(4-methoxyphenyl)-3-methylcycloprop-2-en-1-yl) Ethanone (9)
Figure 20: $^1$H NMR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate (6)
Figure 21: $^{13}$C NMR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate (6)
Figure 22: HRMS Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate (6)
Figure 23: IR Spectrum of 3-(4-Methoxyphenyl)prop-2-yn-1-ylmethyl Carbonate (6)
Figure 24: $^1$H NMR Spectrum of [3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Methyl Carbonate (12)
Figure 25: $^{13}$C NMR Spectrum of [3-Acetyl-3-(4-bromophenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl)methyl Methyl Carbonate (12)
Figure 26: HRMS Spectrum of [3-Acetyl-3-(4-bromo phenyl)-2-(4-methoxyphenyl)cycloprop-1-en-1-yl]methyl Methyl Carbonate (12)
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