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THE INVESTIGATION OF AN EFFICIENT SYNTHESIS OF BICYCLOBUTANE AND CYCLOBUTENE MONOMERS

by

Keith Fox Johnston

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1999
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DEDICATION

To my parents Marcia F. Ward and Dale W. Johnston, my wife Kristain L. Johnston, and my son Grant T. Johnston.
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ABSTRACT

The synthesis of bicyclobutane and cyclobutene monomers has been studied for the past 30 years. The polymers of these monomers have shown to possess superior properties in comparison to their linear analogs. The primary physical properties of interest are thermal stability and solvent resistance. Current synthetic methods used for the preparation of bicyclobutane and cyclobutene monomers require high temperature, high pressure, a large number of steps, and handling of toxic materials. Generally the synthetic methods employed have given very low yields.

Dipolar [2+2]-cycloaddition reactions between alkenes take place spontaneously when one alkene contains strong donor substituents and the other strong acceptor substituents. This cycloaddition provides an efficient method of producing large quantities of cyclobutanes. Our general synthetic scheme involved a [2+2]-cycloaddition to form cyclobutane derivatives containing an acidic proton at C3 or C2 and an electron donating substituent at C1. Following transformation of the donor substituent to a leaving group, bicyclobutanes or cyclobutenes were formed by 1,3- or 1,2-elimination. The scheme centered on the need for a donor substituent which was both electron-donating and easily converted to a leaving group. Phosphite, acetal, and amide as electron donor substituents in [2+2]-cycloaddition reactions with cyano- or ester-substituted electrophilic alkenes form a variety of cycloadducts. Difficulties with phosphites and acetals in [2+2]-cycloadditions were examined in detail. Our studies of phosphorus addition to electrophilic alkenes focused primarily on the equilibrium between the zwitterion and the
ylide. This study led us to a one-pot synthesis of cyclobutene involving an intramolecular Wittig reaction.

Ketene acetals as electron-donating alkene in our synthetic scheme led to a variety of cycloadducts, including 1:1 and 2:1 cycloadducts. The synthesis of cyclobutene and bicyclobutane monomer was attempted using diethyl 3,3-diethoxycyclobutane-1,2-dicarboxylate, the only viable cyclobutane obtained, however numerous problems were faced with the seemingly simple organic transformations.

A three-step synthesis of bicyclobutane using vinylamides was attempted based on our concept. High yields of cyclobutane were obtained from [2+2]-cycloadditions. Conversion to a leaving group followed by 1,3-elimination, led to oligomers of the desired bicyclobutanes, which in the past has been a promising indication. After 30 years this project is on the brink of major advances.
CHAPTER 1

INTRODUCTION

Polymer chemists have been interested in the opening of small carbon rings to form polymers for some time. The great deal of strain associated with such monomers offers a facile thermodynamic driving force for polymerization. The enthalpy of polymerization of bicyclobutanes, based on known thermodynamic chemical data, is approximately $-35$ kcal/mol.\(^1\) Ring strain in this small system causes a high enthalpy value and explains the polymerizability of this type of monomers. Cyclobutenes and bicyclobutanes are one class of these highly strained monomers. The cyclobutenes possess strained double bonds which upon addition polymerization yield polymers with 1,2-cyclobutylene units in the chain. Bicyclobutanes polymerize by opening the 1,3-bond to provide the corresponding 1,3-cyclobutylene unit. In this case, the central bond acts like a $\pi$-bond rather than a carbon-carbon single bond as demonstrated by the study of nucleophilic addition to this bond.\(^2\)^\(^3\)^\(^4\)^\(^5\)^\(^6\)

Wiberg in 1959 first synthesized a bicyclobutane ring and observed that ethyl bicyclobutane-1-carboxylate polymerized spontaneously when left at room temperature (Scheme 1).\(^7\) Unknown to polymer chemists, compounds containing a bicyclobutane ring remained a curiosity of organic chemists. Hall and co-workers, 10 years later, showed that bicyclobutanes carrying an electronegative substituent at the bridgehead position can
polymerize and copolymerize through anionic and free radical ring-opening mechanisms, resulting in the incorporation of cyclobutane rings into the polymer backbone.\(^8\)

**Scheme 1:** The first bicyclobutane

\[ \begin{align*}
\text{Br} & \quad \text{CO}_2\text{CH}_2\text{CH}_3 \\
\text{TrNa} & \rightarrow \\
& \quad \text{CO}_2\text{CH}_2\text{CH}_3
\end{align*} \]

Incorporation of rings into the polymer backbone often produces materials with desirable properties including high glass transition temperature, high melting point, and increased crystallinity, and therefore improved mechanical properties.\(^9\) Most polymers used commercially as films, fibers, and engineering plastics contain rings in the chain. The DuPont Co. set out to find a substitute for acrylonitrile in the preparation of textile fibers when they first investigated bicyclobutane monomers. Poly(l-cyanobicyclobutane) was found to have superior properties. Fibers from poly(l-cyanobicyclobutane) showed improved tensile properties and increased thermal and chemical stability.\(^1\) The high cost of the synthesis of the monomer prevented the commercial development of the polymer.

Our specific aim was the development of an efficient synthesis of bicyclobutane and cyclobutene monomers. The proposed synthetic scheme involved three steps (Scheme 2). The first step was a [2+2]-cycloaddition to form cyclobutane.
Scheme 2. Proposed synthetic scheme

[2+2]-Cycloadditions between electron-rich and electron-deficient alkenes generally give high yields of the corresponding cyclobutane. The cyclobutane formed is designed to possess an acidic proton at C3 or C2 and an electron-donating substituent at C1. Transformation of the donor substituent to a leaving group followed by 1,2- or 1,3-elimination generates cyclobutene or bicyclobutane, respectively. This synthetic scheme was first introduced by Brannock and co-workers in 1964 to generate 3,3-dimethylcyclobutene-1-carbonitrile (Scheme 3).\(^\text{10}\) N,N-Dimethylisobutenylamine as an electron-rich alkene undergoes [2+2]-cycloaddition with acrylonitrile to form the corresponding cyclobutane. Alkylation of the amine group to the quaternary ammonium salt followed by 1,2-elimination generated 3,3-dimethyl-1-cyanocyclobutene. The presence of the gem-dimethyl substituents rendered this cyclobutene nonpolymerizable.
Similarly, Hall later used N,N-dimethylisobutenylamine in a related synthetic scheme to produce bicyclobutane in good yields (Scheme 4).\textsuperscript{11} The bicyclobutane was not polymerizable because of the gem-dimethyl substituents.

**Scheme 3:** Synthesis of 3,3-dimethyl-1-cyanocyclobutene utilizing a [2+2]-cycloaddition.
Scheme 4: Synthesis of 3,3-dimethyl-1-bicyclobutanecarbonitrile utilizing a [2+2]-cycloaddition

In our work the electrophilic olefins studied, in order of increasing electrophilicity, were dimethyl(ethyl) fumarate, fumaronitrile, trimethyl ethylenetricarboxylate, dialkyl 2-cyanoethene-1,1-dicarboxylate, dimethyl cyanofumarate, tetraalkyl ethenetetracarboxylate, dimethyl dicyanofumarate, methyl 3,3-
dicyanoacrylate (MDA), dimethyl(ethyl) 1,1-dicyanoethene-2,2-dicarboxylate (DDED) and tetracyanoethylene (TCNE):

\[
\begin{align*}
\text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} \\
\text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} \\
\text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} \\
\text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} & \quad \text{E} & \quad \text{NC} \\
\end{align*}
\]

\[\text{E} = \text{CO}_2\text{Me, CO}_2\text{Et, CO}_2\text{fBu}\]

The nucleophilic olefins used were vinyloxy phosphorus derivatives, vinyl amide derivatives, and ketene acetals:

\[
\begin{align*}
\text{O} & \quad \text{PR}_2 \\
\text{N} & \quad \text{C} & \quad \text{R} \\
\text{O} & \quad \text{R} \\
\end{align*}
\]

\[\text{R} = \text{H, alkyl, phenyl}\]

This series of nucleophilic alkenes was chosen due to the ease with which the substituents could be converted to leaving groups. Vinly phosphites can be oxidized to phosphates or alkylated to phosphonium salts, both known leaving groups. Amides are
readily converted to iminium salts by O-alkylation or to Vilsmer salts by chlorination.\textsuperscript{12,13} Acetals or ketals can readily be converted to a more functional substituent, in the proposed synthetic scheme, through established organic transformations.

1,2- or 1,3-Elimination is then expected upon treatment of the cyclobutanes to give cyclobutenes or bicyclobutanes. In the past, these types of eliminations have been accomplished using non-nucleophilic bases such as sodium or potassium hydride, potassium tert-butoxide, or sodium amide.\textsuperscript{14}

The objective of this research was the investigation of a synthesis of bicyclobutane or cyclobutene monomers containing ester and/or cyano-substituents which had as few synthetic steps as possible but utilized a [2+2]-cycloaddition within the scheme.
CHAPTER 2

BACKGROUND

(2.1) Synthesis of Bicyclobutane and Cyclobutene Monomers

The literature describes many examples of the synthesis of polymerizable cyclobutene and bicyclobutane monomers. The first authentic bicyclo[1.1.0]butane derivative, ethyl bicyclo[1.1.0]butane-1-carboxylate, introduced by Wiberg and Ciula, stimulated interest in the chemistry and synthesis of highly strained structures. Several techniques for the synthesis of bicyclobutanes and cyclobutenes have been developed, including 1,3-dehydrohalogenation, intramolecular insertion or addition of carbene, intermolecular addition of carbene to cyclopropene or acetylene, the photolyis of dienes, 1,3-dehalogenation and cationic rearrangements. The roundabout classical synthesis based on malonic ester has been the most successful at producing polymerizable monomers, but requires many steps. A general method for producing bicyclobutane monomers (Scheme 5) begins with the cycloaddition of allene to acrylonitrile followed by ozonolysis, to generate 3-cyanocyclobutanone. The carbonyl group is then readily transformed to several leaving groups through a variety of organic transformations. Reduction to the
Scheme 5. General synthesis of bicyclobutane monomers

\[
\begin{align*}
H_2C&=C=CH_2 \ + \ \text{CN} & 200^\circ C & \text{Osmic acid} \ \text{5}^\circ C, \text{Et}_2\text{O} & \rightarrow \text{CN} \\
60\% & \text{CN} & 74\%
\end{align*}
\]

\[
\begin{align*}
\text{NaBH}_4 & \rightarrow \text{CN} & \text{SOCl}_2 & \rightarrow \text{Cl} & \text{KH} & \rightarrow \text{CN} \\
87\% & \text{CN} & 81\% & \text{CN} & 82\%
\end{align*}
\]

alcohol, replacement with chlorine, and dehydrochlorination formed 1-bicyclobutane carbonitrile. Alternatively, reaction of the carbonyl group with phosphorus pentachloride forms a dichloride. Dehydrohalogenation of the resulting 3,3-dichloronitrile gave 1-chlorobicyclobutane-3-carbonitrile. 3-Cyanocyclobutanone was proven to be a good and very versatile source of new bicyclobutane monomers. For example (see below), addition of nucleophiles to the carbonyl group, followed by replacement of the hydroxyl with a leaving group, gives rise to several monomers.\textsuperscript{33} Addition of hydrogen cyanide, replacement of the hydroxyl through the use of triphenylphosphine in carbon tetrachloride, and dehydrochlorination of the product gives 1,3-dicyanobicyclobutane. Addition of phenyl- or vinylmagnesium bromide followed by a similar reaction scheme led to 3-phenyl- or 3-vinylbicyclobutane-1-carbonitrile.\textsuperscript{34}
Another possible route involves reactions of 3-hydroxycyclobutanecarbonitrile with excess methylmagnesium bromide to yield 3-hydroxycyclobutylmethyl ketone (see below). Conversion of this to the tosylate and the iodide, followed by dehydrohalogenation, gave 1-acetylbicyclobutane. Similarly, using phenylmagnesium bromide in the same sequence led to 1-benzoylbicyclobutane. Acid hydrolysis of 3-chlorocyclobutanecarbonitrile leads to 3-chlorocyclobutanecarboxylic acid; esterification gave methyl, t-butyl, and neopentyl esters which were converted to the corresponding esters.\(^8\)
The carboxamide is generated from the treatment of bicyclobutane with hydrogen peroxide. Saponification of methyl 1-bicyclobutane carboxylate gave the crystalline acid. Lastly, 3-methylene cyclobutanecarbonitrile could be transformed into 1-methylbicyclobutane using a decarboxylative-chlorination route. Many organic transformations have been performed to produce bicyclobutane monomers from the cyclobutanone.\(^8\)

The cycloaddition of ketene to vinyl ethers (see below) was accomplished by Sieja in 1971. This general route led to bicyclobutane hydrocarbons. Either ethyl or \(\tau\)-butyl vinyl ether could be used in the synthesis. Reaction of nucleophiles with the carbonyl group, simultaneous conversion of the hydroxyl and alkoxy group to leaving groups such as chloro, followed by dehalogenation led to new bicyclobutanes. If the first nucleophile was hydride ion the procedure led to bicyclobutane itself. Other nucleophiles included phenyl-, methyl-, and vinylmagnesium bromide to generate the corresponding bicyclobutane.\(^{35}\)

\[\text{OR} + \text{O} = \text{O} \rightarrow \text{RO} - \text{O} \rightarrow \text{RO} - \text{OH} \]

\[\rightarrow X - \text{O} - X \rightarrow \text{O} \]

Other routes to bicyclobutanes involve readily available starting materials such as tetramethylcyclobutane-1,3-dione. This diketone reacts with phosphorus pentachloride to
form the tetrachloride. Reduction using tributyltin hydride gives the 1,3-dichloride, and sodium elimination gives the hydrocarbon. Attempts have also been made using a $\pi^2 + \pi^2$ cycloaddition of readily available olefins such as vinyl chloride with acrylonitrile.

Almost all of the reported literature procedures produce mono- or disubstituted bicyclobutanes. One example of a highly substituted bicyclobutane synthesis was reported by Hall and Fischer in 1977 (Scheme 6). Trimethyl bicyclobutane-1,2,2-tricarboxylate was synthesized in five steps beginning with the ferric chloride-catalyzed addition of chloroform to methyl acrylate to give methyl 2,4,4-trichlorobutyrate. Replacement of the 2-chloro group by iodide was followed by displacement with dimethyl malonate anion to

**Scheme 6. Synthesis of trimethyl bicyclobutane-1,2,2-tricarboxylate**

\[
\begin{align*}
\text{CHCl}_3 & \quad + \quad \text{CO}_2\text{CH}_3 \quad \xrightarrow{\text{FeCl}_3} \quad \text{Cl}_2\text{CHCH}_2\text{CHCO}_2\text{CH}_3 & \quad \xrightarrow{\text{NaI}} \quad \text{17\%}
\end{align*}
\]

\[
\begin{align*}
\text{Cl}_2\text{CHCH}_2\text{CHCO}_2\text{CH}_3 & \quad \xrightarrow{\text{CH}([\text{CO}_2\text{CH}_3])_2} \quad \text{Cl}_2\text{CHCH}_2\text{CHCO}_2\text{CH}_3 \quad \xrightarrow{\text{CH}_3\text{OH}} \quad \text{72\%}
\end{align*}
\]

\[
\begin{align*}
\text{X} & = \text{H}, \text{Na}
\end{align*}
\]
give trimethyl 4,4-dichlorobutane-1,1,2-tricarboxylate. Thermolysis of the corresponding sodium derivative gave trimethyl cis- and trans-3-chlorocyclobutane-1,2,2-tricarboxylates. Closure of the bicyclobutane ring was accomplished by potassium hydride with methanol catalyst.

Cyclobutene monomer synthesis has been accomplished using similar methods to those of bicyclobutane monomer synthesis.\textsuperscript{39,40} Cyclodimerization of acrylonitrile (see below) gives a mixture of cis- and trans-cyclobutane-1,2-dicarbonitriles followed by dehydrocyanation by base or catalytically to form cyclobutenecarbonitrile.\textsuperscript{41} Cycloaddition of acrylonitrile to vinyl chloride or 1-chloro-2,2-difluoroethylene gave cyclobutanecarbonitrile derivatives which could then be transformed to cyclobutenes.\textsuperscript{37-42}

\[
2 \overset{\text{CN}}{\longrightarrow} \text{CN} \quad \rightarrow \quad \overset{\text{CN}}{\text{CN}} \quad \rightarrow \quad \overset{\text{CN}}{\text{I}}
\]

Transformation of cyclobutanecarboxylic acid to aminocyclobutane, cyclobutyltrimethylammonium iodide, and Hofmann elimination gives cyclobutene (see below).\textsuperscript{43,44,45}
Photochemical rearrangements of butadienes also give mixtures of cyclobutene and bicyclobutane\(^{46,47}\). 1,3-Pentadiene and isoprene give, respectively, 3-methylcyclobutene and 1-methylcyclobutene under the same conditions.

Cyclobutene-1,2-dicarbonitrile is synthesized from cyclobutane-1,2-dicarbonitrile (see below). Dichlorination with phosphorus pentachloride gives a mixture of cis- and trans-1,2-dichloro-1,2-dicyanocyclobutanes which after dehalogenation with copper-zinc or Raney nickel gives the cyclobutene. Monochlorination to give 1-chloro-1,2-cyclobutane-1,2-dicarbonitrile followed by dehydrochlorination with tertiary amines produces the same cyclobutene.\(^48\)
Conversion of cyclobutanecarboxylic acid to the acid chloride, bromination, hydrolysis, and treatment with potassium hydroxide gives cyclobutene-1-carboxylic acid or treatment with methanol gives methyl cyclobutene-1-carboxylate.\textsuperscript{49}

The chemistry used to prepare bicyclobutanes from cyclobutanones can be applied to the preparation of cyclobutene monomers (see below). Reaction with phosphorus pentachloride gives a mixture of 1,1-dichlorocyclobutane and 1-chlorocyclobutene. Treatment of 1,1-dichlorocyclobutane with potassium t-butoxide gave 1-chlorocyclobutene.\textsuperscript{50}

![Chemical diagram]

The synthesis of cyclobutenes and bicyclobutanes has been under development for many years. An efficient method has not been designed for these desirable synthetic intermediates or monomers. The problems with the synthesis of these types of monomers has been their high sensitivity, low yields, large number of synthetic steps, and in some cases the non-polymerizability of the bicyclobutanes and cyclobutenes formed.

Our proposed synthesis involved simple organic chemistry with very few steps. In theory each step should give high yields. The bicyclobutanes or cyclobutenes would contain cyano and ester substituents, enhancing the compounds' polymerizability.
(2.2) Tetramethylene Intermediate Concept

According to Woodward-Hoffman rules,\(^{51}\) concerted supra, supra [2+2]-cycloadditions between donor alkenes and acceptor alkenes leading to cyclobutanes are thermally forbidden. Therefore, they are required to be stepwise reactions. Initially a bond is formed between the two alkenes giving a tetramethylene intermediate, followed by the formation of the second bond to generate cycloadduct. In recent years, these tetramethylene intermediates have been extensively studied on a theoretical basis.

The unsubstituted tetramethylene intermediate was first theoretically studied by Hoffman et al.\(^ {52}\) in 1970. Later studies showed the existence of two energy minima on the potential energy surface, corresponding to the gauche and trans conformers:\(^ {53}\)

\[
\begin{array}{c}
\text{gauche} \\
\end{array} \quad \begin{array}{c}
\text{trans} \\
\end{array}
\]

Donor-acceptor substituted tetramethylenes were studied by Huisgen\(^ {54}\) who concluded that 1,4-diradical (DR) and 1,4-zwitterion (ZI) forms of the tetramethylenes are not different entities, but rather are the extremes of a continuum. These tetramethylenes can be regarded as resonance hybrids of the DR and ZI forms:
The predominant nature of this tetramethylene is determined by the substituents at the terminals as follows:\textsuperscript{54,55}

The diradical character of the tetramethylene is dominant when vinyl or aryl is the donor substituent and diester, cyano-ester, anhydride or chloride is the acceptor substituent at the terminals. The zwitterion tetramethylene is formed when hard donors such as nitrogen or oxygen and strong acceptors such as dicyano are at the terminals. This zwitterion can proceed to products in a variety of ways\textsuperscript{11} and demonstrates many of the complications that occur in attempted [2+2]-cycloadditions.

The cyclobutane is the kinetically favored product, but not the thermodynamically favored product due to ring strain and substituent effects. Therefore the cyclobutane may revert to the zwitterion intermediate.

The rate of reversion to the zwitterion is greatly increased by heat and strong polar solvents which can solvate the zwitterion. The zwitterion can then proceed to more thermodynamically favored products (Scheme 7). If β-hydrogens are present, a hydrogen
shift in the zwitterion can lead to an open chain linear unsaturated adduct (reaction 1). In protolytic solvents, the zwitterion may be trapped (reaction 2). Finally, the structurally stabilized zwitterion intermediates can add an additional molecule of either electron-rich or electron-poor olefin affording the cyclohexane derivatives (reaction 3). Hall et al.\textsuperscript{11} observed this reaction with the former and Brannock et al.\textsuperscript{10} reported the latter:

**Scheme 7.** The variety of products from zwitterion tetramethylene intermediates
β-Substituents may have no influence on the ZI or DR nature of a tetramethylene, but they can determine the conformation of a tetramethylene: they favor the gauche conformation over the trans-conformation through the "gem dimethyl" effect. The gauche conformer favors the formation of small molecules due to the proximity of the terminals. Moreover, steric hindrance of the β-substituent will retard bond formation at that position.

Solvent plays an important role in [2+2]-cycloadditions:

For the diradical tetramethylene intermediate, solvent has little effect, resulting in approximately the same rates of [2+2]-cycloadditions in a variety of solvents.

For the zwitterion tetramethylene intermediate, the rate of [2+2]-cycloaddition increases with the solvent polarity. Huisgen et al. have reported that solvent polarity has a very marked effect on rate of the [2+2]-cycloaddition reaction of TCNE and enol ether. The formation of cyclobutane is approximately 104 times faster in acetonitrile than
in carbon tetrachloride. This is attributed to the stabilization of the zwitterion intermediate.

Due to the high reactivities of these tetramethylene intermediates isolation or detection has never been accomplished even in the case of highly stabilized tetramethylene intermediates. There is much indirect evidence for these tetramethylenes: trapping of intermediates, stereochemical effects, substituent effects and orientation phenomena, kinetic effects, effects of solvents or pressure on the reaction rate, and rearrangement of donor substituents. Detection or trapping is the most decisive evidence for the existence of an intermediate, according to Gompper.
(2.3) Transformation to a Leaving Group and 1,3-Elimination

The electron-rich alkene must have a substituent that can readily be converted to a leaving group to set the stage for 1,3-elimination. Leaving groups often seen in elimination reactions include the following: NR₃⁺, PR₃⁺, SR₂⁺, OHR⁺, SO₂R, OSO₂R, OCOR, NO₂, F, Cl, Br, I, and CN.²²

In the past the most successful leaving groups for the formation of cyclobutene or bicyclobutane monomers through 1,2- or 1,3-elimination have been I, Br, Cl, CN, and quaternary ammonium salts.¹¹

Transformation to a leaving group can be accomplished using a variety of methods. As described previously by Hall and Brannock in separate publications, alkylation of a tertiary amine to the quaternary ammonium salt provided a very good leaving group which could undergo either 1,2- or 1,3-elimination to form cyclobutene or bicyclobutane respectively.¹⁰,¹¹

Sirrisi found that the oxidation to sulfones or sulfoxides or the alkylation to form sulfonium salts created an acidic proton at the 3 position therefore creating sulfur ylides rather than bicyclobutanes.⁷³

The 1,3-elimination is influenced by the nature of the leaving group and the attacking base. The formation of cyclobutene and bicyclobutane have been accomplished using strong, non-nucleophilic bases such as sodium hydride, potassium hydride, and potassium t-butoxide.
(2.4) Synthesis and Reactions of Electrophilic Olefins

1. Tetraeyanoethylene as Electrophilic Olefin

Using TCNE as electrophilic olefin for spontaneous [2+2]-cycloadditions has been extensively studied: Huisgen et al.\textsuperscript{56} investigated the spontaneous [2+2]-cycloadditions of TCNE and a variety of electron-rich olefins (see below). These reactions occur through zwitterion tetramethylene intermediates. The intermediate can be trapped by methanol and the rate is enhanced in polar solvents, indicating a zwitterion tetramethylene intermediate.

\[ \text{Do} \quad \text{NC} \quad \text{CN} \quad \text{Do} \quad \text{NC} \quad \text{CN} \quad \text{NC} \quad \text{CN} \quad \text{Do} \quad \text{NC} \quad \text{CN} \quad \text{Do} \]

Do = donor substituent

McKusick\textsuperscript{74} reported a 2:1 cycloadduct from the reaction of TCNE with styrene in refluxing toluene in 18% yield. He concluded that this was a cyclohexane adduct:
2. Dialkyl 1,1-Dicyanoethene-2,2-dicarboxylates (DDED's) as Electrophilic Olefin

DDED's are synthesized from the reaction between diethyl ketomalonate and malononitrile as shown:

\[
\begin{align*}
\text{RO}_2\text{C}_2\text{C}_2\text{O} + \text{CH}_2\text{C}_2\text{CN} & \rightarrow \text{RO}_2\text{C}_2\text{C}_2\text{C}_2\text{CN} \\
\text{RO}_2\text{C}_2\text{C}_2\text{C}_2\text{CN} + \text{CH}_2\text{C}_2\text{C}_2\text{CN} & \rightarrow \text{RO}_2\text{C}_2\text{C}_2\text{C}_2\text{CN} \text{ (monomers)}
\end{align*}
\]

The spontaneous [2+2]-cycloadditions of electrophilic DDED olefins and various nucleophilic olefins were studied by Hall and Sentman. DDED’s are tetrasubstituted electrophilic olefins capable of both [2+2]-cycloaddition to electron-rich olefins and copolymerizing with electron-rich comonomers (see below). Then initially form charge-
transfer complexes with the electron-rich olefin, as witnessed by the intense color formed, and then give tetramethylene intermediates which can collapse to cyclobutanes or initiate copolymerization depending on the reaction conditions.

In the case of DDED's two reasonable tetramethylene intermediates can be postulated: one with two cyano groups at the electrophilic end and one with two ester groups at the electrophilic end. The orientation of the [2+2]-cycloadduct to date has been confirmed to be as shown. The tetramethylene intermediate with terminal cyano groups is the electronically favored intermediate due to the greater stabilization provided by the two cyano groups. However, the copolymer has the opposite orientation of the gem-cyano groups.

3. Methyl 2,2-Dicyanoacrylate (MDA) as Electrophilic Olefin.

MDA is synthesized by the Knoevenagel reaction between poly(methyl glyoxylate) and malononitrile in the presence of a catalytic amount of acetic acid:

\[
\begin{align*}
\text{CH}_2\text{O} & \quad + \quad \text{CH}_2\text{CN} \quad \rightarrow \quad \text{H}_3\text{CO}_2\text{C} \quad = \quad \text{HCN} \\
\text{CO}_2\text{CH}_3 & \quad \text{CN} & \quad \text{CN} & \quad \text{CN}
\end{align*}
\]

Padias and Hall\textsuperscript{76} reported that MDA undergoes reaction with electron-rich alkenes to generate various products depending on the reaction conditions used (see below).
Alternating copolymerization was favored in non-polar solvents, while cycloaddition was favored in polar solvents. The modes of cycloaddition depended on the polarity of the solvent. Double Diels-Alder adducts were obtained in dipolar aprotic solvents, while cyclobutanes were favored in protic solvents. Methanol as solvent gave only the [2+2]-cycloadduct.
4. Dimethyl Dicyanofumarate (DDCF) as Electrophilic Olefin

DDCF is synthesized by the reaction between methyl cyanoacetate and thionyl chloride in tetrahydrofuran.\textsuperscript{77}

\[
2 \text{CH}_2\text{CO}_2\text{CH}_3 + \text{SOCl}_2 \rightarrow \text{H}_3\text{CO}_2\text{C} = \text{C} = \text{CO}_2\text{CH}_3
\]

DDCF is one of the electrophilic alkenes having at least one ester at the olefin end that were reported by Hall et al.\textsuperscript{78,79} to undergo inverse electron-demand Diels-Alder reactions with nucleophilic olefins (see below). This type of electrophilic alkene possesses at least one ester substituent at the electrophilic end of the tetramethylene intermediate.

\[
\text{H}_3\text{CO} = \text{O} + \text{Do} \rightarrow \text{H}_3\text{CO} = \text{O}_{\text{Do}}\text{Do}
\]

Do = OR, p-methoxystyrene, p-methylstyrene, styrene
5. Dimethyl Cyanofumarate as Electrophilic Olefin

This electron-poor olefin is synthesized by the Knoevenagel reaction between poly(methyl glyoxylate) and methyl cyanoacetate:

\[
\begin{align*}
\text{CH}_2\text{O} & + \text{CH}_2\text{CN} \rightarrow \text{H}_3\text{CO}_2\text{C} \equiv \text{CN} \\
\text{CO}_2\text{CH}_3 & \quad \text{CO}_2\text{CH}_3
\end{align*}
\]

Inverse electron-demand Diels-Alder reaction can take place with electron-rich alkenes giving the corresponding 3,4-dihydro-2H-pyrans. Due to the presence of one ester at the electron-poor alkene end Hall et al.\textsuperscript{78, 79} found that the reaction with electron-rich alkenes such as vinyl ether and styrenes gave pyrans exclusively.

\[
\begin{align*}
\text{H}_3\text{CO}_2\text{C} & \text{O} \\
\text{NC} & \quad \text{H} \\
\text{CO}_2\text{CH}_3 & \quad \text{CO}_2\text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{Do} = \text{OR, styrene}
\end{align*}
\]

6. Dialkyl 2-Cyanoethylene-1,1-dicarboxylates (DCD’s) as Electrophilic Olefins

DCD’s are synthesized by the Wittig reaction between cyanoethylenetriphenylphosphorane and diethyl ketomalonate:

\[
\begin{align*}
\text{C} & \text{CH}_2\text{Cl} + \text{PPh}_3 \rightarrow \text{NC} \text{CH}=\text{PPh}_3
\end{align*}
\]

\[
\begin{align*}
\text{RO}_2\text{C} & \text{O} \\
\text{NC} & \quad \text{H} \\
\text{CO}_2\text{R} & \quad \text{CO}_2\text{R}
\end{align*}
\]
DCDD's can undergo inverse electron-demand Diels-Alder reactions with electron-rich alkenes as reported by Hall,\textsuperscript{78,79} again owing to the fact that there is at least one ester substituent at the terminal end of the alkene.

\[ \text{Do} = \text{OR, styrene} \]

7. Trimethyl Ethylenetricarboxylate as Electrophilic Alkene

This electron-poor olefin is synthesized by the Knoevenagel reaction between dimethyl malonate and poly(methyl glyoxylate):

\[ [\text{CH-O}]_n + \text{CH}_2\text{CO}_2\text{CH}_3 \rightarrow \text{H}_3\text{CO}_2\text{C}-\text{CO}_2\text{CH}_3 \]
Hall et al.\textsuperscript{78,79} reported the inverse electron-demand Diels-Alder reaction of this electron-poor alkene with ethers and styrenes:

\[
\begin{align*}
\text{H}_3\text{CO}_2\text{C} & \quad \text{H}_3\text{CO} \quad \text{O} \\
\text{H}_3\text{CO}_2\text{C} & \quad \text{H}_3\text{CO} \quad \text{O} \\
\text{Do} & \quad \text{Do} \\
\text{Do} = \text{OR}, \text{styrene}
\end{align*}
\]

Hall and Glogowski found that in the reaction of N,N-dimethylvinylamine with trimethyl ethylenetricarboxylate, a [2+2]-cycloadduct was not isolable. However, attempts at trapping the cyclobutane product led to the isolation of a 2:1 cyclohexane adduct formed by reaction of the zwitterion intermediate with a second N,N-dimethylvinylamine molecule.
CHAPTER 3
RESULTS AND DISCUSSION

SECTION 1: VINYL PHOSPHITES

3.1.0 Monomer Synthesis Concept: Vinyl Phosphorus Compounds

The focus of this research project, past and present, has centered on the need for an efficient synthesis of bicyclobutane or cyclobutene monomers. Our synthetic scheme involves three steps with the fundamental requirement of the electron-rich alkene in our synthetic scheme contain an electron-donating substituent that must meet two requirements. First, the substituent must be readily converted to a leaving group and second, it must not stabilize the zwitterion tetramethylene intermediate to such an extent that the kinetically favored cyclobutane is not stable.

In the lifetime of this project many alkenes bearing electron-donating substituents have been examined. These substituents have been based on different elements from the Periodic Table, including chlorine, oxygen, nitrogen, sulfur, and phosphorus.

The first part of our research extends what has previously been studied to the element phosphorus. Phosphorus in phosphines is nucleophilic and therefore electron-donating. Phosphines are readily oxidized to good leaving groups, making them excellent candidates for the proposed synthetic strategy (Scheme 8).

Phosphites and phosphates as electron-donating substituents have previously been used in Diels-Alder cycloadditions. Bis(2,6-di-methoxyphenyl) 1-methylene-2-propenyl
phosphate displays reactivity and regioselectivity comparable to the analogous (trimethylsilyl)oxy diene in reactions with dienophiles. 

Scheme 8. Proposed synthesis using vinyl phosphites.

![Scheme 8](image)

In theory, vinyl phosphites should undergo [2+2]-cycloadditions with electrophilic alkenes to form cyclobutanes. To date there are no literature examples which demonstrate a [2+2]-cycloaddition of vinyl phosphites.

Following a successful [2+2]-cycloaddition, the phosphite substituent at the 3-position on the cyclobutane ring could readily be converted to a leaving group. Transformation to a leaving group can be accomplished either by alkylation to phosphonium salts or oxidation to phosphates. In the previous syntheses of cyclobutene and bicyclobutanes by Brannock or Hall, an amine was converted to a quaternary
ammonium salt. A phosphonium salt should act as a leaving group similar to the ammonium salt. Phosphates are seen quite commonly as leaving groups in such reactions as Wittig reactions. Phosphates can also be reacted with trimethylsilyl iodide to provide the corresponding cyclobutyl iodide along with bis(trimethylsilyl) phosphonate. Halogens such as iodide have been used to prepare bicyclobutanes in the past.

The final step, 1,3-elimination, must be carried out under very anhydrous conditions using bases which are non-nucleophilic. Bicyclobutanes have been shown to be extremely sensitive to nucleophiles.

### 3.1.1 Synthesis of Vinyl Phosphites and Phosphates

Vinyl phosphites and phosphates are of interest for the formation of flame-retardant polymers, insecticides, and many pharmaceuticals. Inspection of the literature yields many synthetic routes to these compounds, such as the Perkow reaction, the use of mercurials, chloroacetaldehyde, dehydrochlorination of the corresponding 2-chloro ethyl esters, and chloroethylene carbonate.

The established synthetic methods generally produce substituted phosphates. The most commonly used, the Perkow reaction (see below), involves addition of a trivalent phosphorus containing at least one alkoxy group to an α-haloketone. It is desirable to
avoid the Perkow method since it involves the use of anhydrous chloroacetaldehyde, which presents problems due to its hazardous nature and lack of availability.

In the specific case of unsubstituted vinyloxy phosphorus compounds, which are most desirable as monomers, chloroacetaldehyde was generally required. Other methods which produce substituted vinyloxy phosphorus compounds include the use of mercury salts. Mercury salts present a definite economical barrier, particularly for large scale synthesis, and pose environmental and toxicity problems. Ireland and Pfister have reported the formation of diethyl vinyl phosphate utilizing the work of Stork and co-workers who introduced the reduction of $\alpha,\beta$-unsaturated ketones by lithium in ammonia, as an excellent source of enolate anions. Gross and Costisella report average yields from the conversion of chloroethylene carbonate, in the presence of a catalytic amount of triethylamine, to chloroacetaldehyde followed by addition of triethyl phosphite (see below).

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\end{align*}
\quad \xrightarrow{\text{NEt}_{3}} \quad (\text{CH}_{2}\text{CHCHO}) \quad \xrightarrow{\text{P(OCH}_{2}\text{CH}_{3})_{3}} \quad \begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\end{align*}
\text{OP(OCH}_{2}\text{CH}_{3})_{2}
\]

In our search for a versatile and straightforward synthesis of a large variety of vinyloxy phosphorus compounds we considered the lithium salt of vinyl alcohol as a viable intermediate. Bates and co-workers generated this lithium enolate of acetaldehyde from the cycloreversion of tetrahydrofuran in the presence of $n$-butyllithium (Scheme 9). The versatility of the acetaldehyde enolate using Bates’ method has been well documented. Jung and Blum demonstrated that the lithium enolate of acetaldehyde could
be O-acylated, O-silylated or C-alkylated. Duggan and Roberts found that acylation of the enolate with diphenyl thiocarbonate afforded vinyl phenyl thiocarbonate in reasonable yields. Using diethyl phosphorochloridate, Widlanski and co-workers generated phosphate diesters which could not be synthesized using standard phosphoramidite methodology, again demonstrating the versatility of the method employed.

To determine the utility of the lithium enolate of acetaldehyde in the synthesis of phosphorus derivatives, its reaction with a series of chlorophosphates and chlorophosphites was investigated yielding the corresponding vinyl phosphates and vinyl phosphites respectively, as shown in Scheme 9 and Table 1. High yields were obtained for all reactions and these yields remained high upon scale-up. Isolation and purification were extremely simple, namely evaporation of the excess THF followed by vacuum distillation. Elemental analysis and NMR confirmed the structure of these compounds and their purity.

**Scheme 9.** Synthesis of vinyloxy phosphorus compounds

\[
\begin{align*}
\text{O} \quad \text{OPR}_2 \\
\text{O} \quad \text{Li}^+ \\
\text{H}_2\text{C} \equiv \text{CH}_2 + \quad \text{O} \quad \text{Li}^+ \\
\text{OPR}_2
\end{align*}
\]
Table 1. Synthesis of vinyloxy phosphorus compounds.

<table>
<thead>
<tr>
<th>Phosphorylating agent</th>
<th>Vinyloxy phosphorus compound</th>
<th>Yield,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl–P(OCH₃)₂</td>
<td>O–P(OCH₃)₂</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cl–P(OCH₂CH₃)₂</td>
<td>O–P(OCH₂CH₃)₂</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cl–P(OCH₂CH₃)₂</td>
<td>O–P(OCH₂CH₃)₂</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cl–P(N(CH₃)₂)₂</td>
<td>O–P[N(CH₃)₂]₂</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Cl–P(aryl)</td>
<td>O–P(aryl)</td>
<td>71</td>
</tr>
</tbody>
</table>
Cl-P'[N(CH₂CH₃)₂]₂

Cl-P[O][N(CH₂CH₃)₂]₂

Cl-PPh₂

Cl-PPh₂

Cl-P' \[O\]

\[\text{unstable.}\]
Vinyl phosphite and phosphate derivatives 11-16 (see below) were prepared in approximately 60% yield. Upon isolation these underwent either polymerization or autoxidation. Compounds 1-11 were isolated in high yields except for compound 7 which polymerized upon attempted isolation.

Trivalent phosphorus compounds are normally oxidized to the corresponding phosphoryl derivatives by molecular oxygen even in the absence of catalyst. The ease of reaction depends on the nucleophilicity of the phosphorus compound, increasing in the order \( P_4, \text{PCl}_3 < (\text{RO})_3\text{P} < \text{R}_3\text{P} \). White phosphorus and phosphorus trichloride are
oxidized slowly in the absence of hydrocarbons; tributyl phosphite is converted to the phosphate in 50% yield in 20 hours at 55 °C.

Many of the vinyl phosphorus compounds were prepared using readily available chlorophosphites or phosphorochloridates, but in several cases preparation of the chlorophosphorus compound was required. These types of compounds can be prepared from literature procedures. The reaction involves the use of the appropriate alcohol with pyridine at reflux followed by the addition of phosphorus oxychloride. This procedure generally gives in excess of 75% yield with relatively few byproducts.

In summary, enol phosphites and phosphates result from the interaction of acetaldehyde enolate and a phosphorylating agent with very little required in terms of purification to obtain high yields. By this method vinyl phosphites, vinyl phosphates, and vinyl thiophosphates with varying substituents have been prepared. These studies have given facile access to a sufficient variety of structures so that attention can be focused on applications of vinyloxy phosphorus compounds.

3.1.2 Attempted [2+2]-Cycloadditions of Vinyl Phosphites

[2+2]-Cycloaddition of electron rich vinyl phosphites with electron poor alkenes in theory should be straightforward; however, phosphorus can be both electrophilic and nucleophilic.

Our initial attempts at [2+2]-cycloadditions were focused on diethyl vinyl phosphite as electron-rich alkene. Reaction of diethyl vinyl phosphite with a series of electrophilic alkenes produced no cyclobutanes. A variety of reaction conditions were
examined, but lowering temperature, increasing solvent polarity, or changing the concentration of the reaction did not lead to any cyclobutane adducts. The observed product, a phosphorus ylide, came from the addition of nucleophilic trivalent phosphorus to electrophilic alkenes. The addition of phosphorus to electrophilic alkenes will be discussed below.

The nucleophilicity of phosphorus can be altered in three ways. First, increased steric hindrance of the substituents on phosphorus should decrease its nucleophilicity. Compounds such as diphenyl vinyl phosphite, di-t-butyl vinyl phosphite, and bis(2,4-substituted phenyl) vinyl phosphites were synthesized in order to increase the steric hindrance at phosphorus. In each of these cases no cyclobutane was produced upon reaction with electrophilic alkenes.

\[
\begin{align*}
\text{OP}(t\text{Bu})_2 \\
\text{OP} \quad \text{OP} \quad \text{OP} \\
\text{OP} \quad \text{OP} \quad \text{OP} \\
R = \text{CH}_3, \text{OCH}_3
\end{align*}
\]

Second, the steric hindrance at phosphorus and the electronic properties of the substituents can be used to decrease the nucleophilicity of phosphorus without hopefully affecting the reactivity of the carbon-carbon double bond. For example, substituents such as pentafluorophenoxy can be used to sterically crowd phosphorus and at the same time decrease the nucleophilicity of phosphorus by withdrawing electron density from phosphorus. Substituents such as N,N-dimethylamino sterically hinder phosphorus and
also add electron density to phosphorus and the carbon-carbon double bond. A few vinyl phosphites based on this assumption were synthesized, including:

Using these sterically hindered and electronically altered substituents on phosphorus did not give cyclobutane when reacted with electrophilic alkenes, but did produce the unwanted ylides.

Finally, phosphorus can be alkylated to the phosphonium salt or oxidized to the phosphate rendering it non-nucleophilic. Attempts at spontaneous [2+2]-cycloaddition of phosphates or phosphonium salts did not give any reaction. Increasing the electron-donating properties of the substituents on the phosphate or phosphonium salt, to increase the electron density at the carbon-carbon double bond, did not give spontaneous [2+2]-cycloadditions.

Increasing the electrophilicity of the electrophilic alkene by using Lewis acids,\textsuperscript{73} which complex to the electron-withdrawing substituent, at high temperatures did not produce cycloadduct in combination with any of the phosphates studied. The following
are the phosphates that were used in attempted spontaneous [2+2]-cycloadditions and Lewis acid-promoted [2+2]-cycloadditions:

\[
\begin{align*}
\text{O} & \quad \text{OP}[N(CH_3)_{2}]_2 \\
\text{S} & \quad \text{OP(OC\text{H}_2\text{CH}_3)}_2 \\
\text{CH}_3 & \quad \text{OP(OCH}_2\text{CH}_3)_2 \quad \text{OTf} \\
\text{OP(0CH}_2\text{CH}_3)_2 & \quad \text{OP(TBu)}_2 \\
\text{OPPh}_2 & \quad \text{OP} \quad \text{OP} \\
\end{align*}
\]

The failure of attempted [2+2]-cycloadditions of vinyl phosphites with electrophilic alkenes was not surprising. We had envisioned a cycloaddition occurring before the trivalent nucleophilic phosphorus could add to the carbon-carbon double bond.
but the undesired addition of phosphorus to the activated carbon-carbon double bond was unavoidable.

3.1.3 Phosphorus Addition to Carbon-Carbon Double Bonds

The addition of trivalent phosphines and phosphites to activated carbon-carbon double bonds results in the formation of a zwitterion product which is analogous to the first intermediate in other nucleophilic attacks by neutral molecules. Interest in the addition of trivalent phosphorus compounds to activated alkenes stems from the versatility of phosphorus chemistry. Various applications such as the dimerization of alkenes, the initiation of polymerization, and the formation of ylides for Wittig reactions have been developed in the past.

Early investigations on the addition of phosphorus to activated alkenes focused on the formation of stable zwitterions.\textsuperscript{97,98,99} Electron-donating substituents at the β-position, especially in aromatic systems, inhibit the reaction; no reaction takes place between \textit{p}-dimethylaminobenzylidenemalononitrile and triethylphosphine, while the \textit{p}-nitro derivative yields an especially stabilized product. A \textit{p}-hydroxy group inhibits the reaction completely, while the same group in the \textit{m}-position yields adducts of low stability.\textsuperscript{100}
Triethylphosphine adds to less activated alkenes, in which the \( \alpha \)-position is substituted by two less efficient electron-attracting groups.\(^{100}\) With less extensively conjugated systems, such as acrolein, acrylonitrile or nitroolefins, in which stabilization of the adducts is diminished, nucleophilic polymerization takes place under the influence of phosphines.\(^{101}\)

\[
\text{PR}_3 + \underset{X}{\overset{\text{X}}{\text{X}}} \rightarrow \text{R}_3\text{P}^+\text{(CH}_2\text{CH}_2\text{X})_n\text{CH}_2\text{CH}_2\text{X} \rightarrow \text{R}_3\text{P}(\text{CH}_2\text{CH}_2\text{X})_n\text{CH}_2\text{CH}_2\text{X}
\]

Phosphonium salts may be obtained irrespectively of the order of the addition of the reagents, both by addition of HCl to the adduct or by addition of HCl to the ester followed by addition of the phosphine (see below).\(^{102}\)

Later the addition of trivalent phosphorus to activated alkenes was found to initially form a carbanion intermediate which undergoes prototropy to afford ylide, with
the effectiveness of the process being a function of the presence of an ylide-stabilizing group.

Oda\textsuperscript{103} initially investigated the reaction of acrylics with benzaldehyde and triphenylphosphine in equimolar portions and suggested the following mechanism for the reaction:

\[ \text{Ph}_3\text{P} + \overset{\text{CN}}{\text{C}} \rightarrow \text{[Ph}_3\text{P}—\text{CH}_2\text{CHCN} \rightleftharpoons \text{Ph}_3\text{P}—\text{CHCH}_2\text{CN}] \]

\[ \xrightarrow{\text{C}_4\text{H}_2\text{CHO}} \text{C}_6\text{H}_5\text{CH}—\text{CH}_2\text{CH}_2\text{CN} \]

This mechanism suggests initial nucleophilic addition of trivalent phosphorus to acrylonitrile to form an intermediate zwitterion which then undergoes a prototropic shift to form an ylide. The latter then reacts with the aldehyde. McClure\textsuperscript{104} followed this investigation and found that t-butyl alcohol as solvent gave high yields with good conversion of reactants.

In 1968 Morita,\textsuperscript{105} using the same reactants as Oda but only catalytic amounts of tricyclohexylphosphine (instead of triphenylphosphine), reported the isolation of 2-hydroxyalkyl derivatives of acrylate and related systems. Morita suggested that the name “carbinol reaction” should be used for the reaction scheme below.

\[ \overset{\text{H}}{\text{X}} + \overset{\text{RCHO}}{\overset{\text{R}}{\text{X}}} \rightleftharpoons \overset{\text{CHOH}}{\text{X}} \]

\( X = \text{CO}_2\text{R}, \text{CN} \)

\( R = \text{Alkyl, Ph, substituted Ph} \)
McClure,\textsuperscript{106} interested in the dimerization of acrylonitrile to 2-methyleneglutaronitrile using catalytic amounts of triarylphosphine, proposed the following mechanism which is similar to the mechanism proposed by Oda (Scheme 10).

\textbf{Scheme 10. Proposed mechanism of phosphorus addition to electrophilic alkenes}

\begin{align*}
\text{Ar}_3\text{P} + \text{CH}_2=\text{CHCN} & \xleftrightarrow{\text{AN}} \text{Ar}_3\text{PCH}_2\text{CHCN} & \xleftrightarrow{\text{AN}} \text{Ar}_3\text{PCHCH}_2\text{CN} \\
\text{Ar}_3\text{PCH}_2\text{CHCN} & \text{polymer} & \text{Ar}_3\text{PCHCH}_2\text{CN} & \xrightarrow{\text{AN}} \text{polymer} \\
\text{Ar}_3\text{PCH}_2\text{CCN} & \text{CH}_2\text{CH}_2\text{CN} & \text{Ar}_3\text{PCHCH}_2\text{CN} & \text{CH}_2\text{CH}_2\text{CN} \\
\text{Ar}_3\text{P} + \text{NCCCH}_2\text{CH}_2\text{CN} & \xleftrightarrow{\text{AN}} \text{Ar}_3\text{P} + \text{NCH}==\text{CHCH}_2\text{CH}_2\text{CN}
\end{align*}
Support for the presence of the phosphorus ylide intermediate has been demonstrated through the isolation of Wittig type reaction products when the dimerization of acrylonitrile is conducted in the presence of an aromatic or aliphatic aldehyde.

McClure\textsuperscript{104} observed improvements in the conversion to dimer when tritolylphosphine was used in place of triphenylphosphine as catalyst which can be attributed to the slightly greater nucleophilicity of the methyl-substituted phosphine. Improvements in yield were also observed when using triethylsilanol as a replacement for \(t\)-butyl alcohol. Triethylsilanol is a stronger protolytic source than \(t\)-butyl alcohol and better promotes the proton transfer steps. A proper balance between nucleophilicity of the phosphine catalyst and protolytic strength of the solvent is critical for high yields and good conversions.

The work of several investigators has led to the development of this extremely versatile chemistry. A crystalline hexamer from acrylonitrile was produced in the presence of a catalytic amount of triphenylphosphine in alcohol.\textsuperscript{107} Baizer found, under similar conditions in acetonitrile, a dimer and high oligomers of acrylonitrile were generated at high temperatures.\textsuperscript{108} Using a trialkylphosphine or the addition of small amounts of triethylaluminum resulted in the initially formed anion adding to aldehydes and expelling trialkylphosphine to afford a carbinol adduct.\textsuperscript{109,110,111,112} Ramirez\textsuperscript{113,114} studied the nucleophilic addition of trivalent phosphorus to such compounds as maleic anhydride, diethyl fumarate, and dibenzoylethylene in which a stable ylide was formed in
each case (see below). Trivalent phosphorus adds to the β-carbon of the α,β-unsaturated ketone of dibenzoylethylene to form an unstable phosphonium betaine which undergoes rapid proton shift to the moderately stable trimethoxybenzoylphenoxy methylene phosphorane.

Finally, Larpent and Patin\textsuperscript{115} found that triphenylphosphine m-trisulfonate and triphenylphosphine m-monosulfonate react in water with α,β-unsaturated acids to afford hydrosoluble phosphonium salts. The high polarity of the water and the acido-basic properties gave instant and qualitative reactions by displacement of equilibrium because reactive intermediates are instantaneously protonated.

\[ \text{NaO}_3\text{S} \quad + \quad \text{R}_1 \quad \text{R}_3 \quad \text{H} \quad \text{R}_2 \quad \text{CO}_2\text{H} \quad \text{H}_2\text{O} \quad \text{NaO}_3\text{S} \quad \text{P} \quad \text{C} \quad \text{C} \quad \text{CO}_2\text{H} \]

\( \text{R}_1 = \text{R}_2 = \text{R}_3 = \text{H} \)
\( \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{CH}_3 \)
\( \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{CH}_2\text{CO}_2\text{H} \)
\( \text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_3 = \text{H} \)
The majority of studies on phosphorus addition to activated carbon-carbon double bonds have focused on acrylates and acrylonitrile to produce dimers, carbon-carbon double bonds from one-pot Wittig reactions, and in the synthesis of interesting monomers such as “carbinols”.

We have found that reactive trivalent phosphorus with tri-substituted electrophilic alkenes, such as methyl 3,3-dicyanoacrylate, leads to a zwitterion in solution or in the presence of a protolytic source, stable ylides can be isolated in high yields. In attempted [2+2]-cycloaddition of diethyl vinyl phosphite (1) with methyl 3,3-dicyanoacrylate (2) in acetonitrile, the stable ylide 3 from phosphorus addition was recovered in high yields (see below). Column chromatography resulted in hydrolysis of the original phosphorane to generate a phosphate 4.

\[
\begin{align*}
\text{OP(OCH}_2\text{CH}_3)_2 + \text{H}_3\text{CO}_2\text{C} = \text{C(CN)}_2 & \rightarrow r.t. \quad \text{(CH}_3\text{CH}_2\text{O})_2\text{P} = \text{C-C(CN)}_2 \\
\text{OP(OCH}_2\text{CH}_3)_2 + \text{H}_3\text{CO}_2\text{C} = \text{C(CN)}_2 & \rightarrow r.t. \quad \text{(CH}_3\text{CH}_2\text{O})_2\text{P} = \text{C-C(CN)}_2 \\
\text{(CH}_3\text{CH}_2\text{O})_2\text{P} = \text{C-C(CN)}_2 & \rightarrow \text{OH} \quad \text{(CH}_3\text{CH}_2\text{O})_2\text{P} = \text{C-C(CN)}_2
\end{align*}
\]
Attempted [2+2]-cycloadditions of a variety of vinyl phosphite derivatives were examined. Many of the phosphites were sterically crowded or the substituents possessed varying electronic character. A non-nucleophilic trivalent vinyl phosphite suitable for a [2+2]-cycloaddition with electrophilic alkenes was not found, but a variety of highly substituted stable ylides were produced. Table 2 shows the variety of vinyl phosphites which were reacted with electrophilic alkenes. Although the substituents did not create conditions suitable for [2+2]-cycloaddition, they did play some role in the rate of the nucleophilic addition to the carbon-carbon double bond. Steric hindrance did not play a major role in decreasing the rate of the addition of phosphorus to the electrophilic alkenes, but the electronic properties of the substituent had a substantial effect on the reaction rate. Diethyl vinyl phosphite typically took approximately 3 hours to completely react in acetonitrile as indicated by the disappearance of the vinyl protons. Altering the substituents on phosphorus to a sterically hindered and electron-withdrawing substituent such as bis(pentafluorophenoxy) vinyl phosphite slowed the initial addition and reaction was not complete until after 24 hours. Di-\textit{t}-butoxy vinyl phosphite, although very sterically crowded, reacted in less than 30 minutes due to the \textit{t}-butoxy substituents' electron-donating properties which create a very nucleophilic phosphorus. The reactions were monitored using IR and $^{1}$H NMR and could also be followed by a change from colorless to yellow over time. Cyclic substituents were not suitable for the reaction due to the fact that after formation of the zwitterion intermediate a ring-opening reaction would occur creating a variety of uncharacterizable products.
The reaction of diethyl vinyl phosphite with the set of electrophilic alkenes was studied extensively and fully characterized. The remainder of the vinyl phosphites were reacted with each alkene, but only a select few were fully characterized due to instability of the products or value to the project.

The results thus show that trivalent phosphorus is extremely nucleophilic within the series studied.

Table 2. Reactions of vinyl phosphites with electrophilic alkenes.
3.1.4 Intramolecular Wittig Reaction: Cyclobutene Formation

In order to utilize the results obtained in the study described previously, the feasibility of an intramolecular Wittig reaction to form cyclobutenes was examined.

The Wittig reaction is one of the most important methods of preparing alkenes. It involves the condensation of a phosphorus ylide with carbonyl compounds to produce an alkene, eliminating triphenylphosphorus oxide. Numerous reviews cover the Wittig reaction in great detail.

In the production of cycloalkenes in the laboratory, the Wittig reaction has been a favorite. Commonly 5-, 6-, and 7-membered ring cycloalkenes are produced fairly easily by intramolecular Wittig reactions. Formation of 4-membered ring cycloalkenes, cyclobutenes, had not been reported until very recently.

The theory proposed for an intramolecular Wittig reaction involves the zwitterion intermediate from the addition of trivalent phosphorus to electrophilic alkenes, followed by the addition of an α-haloketone to generate a phosphonium salt. The phosphonium salt in the presence of mild base should readily be converted to the cyclobutene precursor and then form cyclobutene through an intramolecular Wittig reaction (Scheme 11).
Scheme 11. Proposed intramolecular Wittig reaction to form cyclobutene

Formation of the cyclobutene precursor depends on the carbanion of the zwitterion intermediate displacing the halogen of the α-haloketone. The zwitterion intermediate must be stable enough so that proton shift does not occur to form the ylide. McClure\(^{106}\) demonstrated that the zwitterion intermediate carbanion can react before proton shift and subsequent formation of the ylide.

Reaction of a phosphorus ylide at the halo-carbon of an α-halocarbonyl compound was reported by Hatanaka et al.\(^{119}\) in the synthesis of cyclopentadiene via an intramolecular Wittig (Scheme 12).
Scheme 12. Intramolecular Wittig reaction forming cyclopentadiene

This reaction proceeds stepwise. The first step is a nucleophilic substitution of the halide by the carbanion of the 1,4-dipolar resonance to yield the phosphonium salt. Regeneration of the phosphorane causes an intramolecular Wittig reaction, to give cyclopentadiene.

An intramolecular Wittig reaction to form cyclobutene was very recently reported by Yavari et al. involving the reaction of triphenylphosphine with dimethylacetylene dicarboxylate in the presence of ethyl 4-aryl-2,4-dioxobutanoates (Scheme 13). The reaction proceeds from the initial addition of triphenylphosphine the acetylenic ester and protonation of the 1:1 adduct, followed by attack of the anion of the ethyl 4-aryl-2,4-
dioxobutanoates to vinyltriphenylphosphonium cation to form the phosphorane which undergoes an intramolecular Wittig to form the strained carbocyclic ring system.

**Scheme 13.** Cyclobutene from intramolecular Wittig reaction

\[
\text{Ph}_3\text{P} + \begin{array}{c} \text{CO}_2\text{CH}_3 \\ \text{CO}_2\text{CH}_3 \end{array} + \text{Ph}^- \cdots \text{CH}_2\cdots\text{CO}_2\text{CH}_3 \xrightarrow{\text{CH}_2\text{CH}_2} \text{Ph}^+ \cdots \text{H}_2\text{CO}_2\text{C}^- \cdots \text{C} = \text{PPh}_3 \cdots \text{CO}_2\text{CH}_3
\]

87%  

We made several attempts at the synthesis of cyclobutene in Scheme 11. The first attempt was done using MDA as the electrophilic alkene and tributylyphosphine. The addition of tributylyphosphine to MDA takes approximately 1 hour in methylene chloride and can be monitored by the disappearance of the carbon-carbon double bond in the IR and a change in the reaction mixture from colorless to yellow. Addition of chloroacetone and an additional 3-4 hours stirring at room temperature yields the phosphonium salt (see below). The phosphonium salt in this case was not isolated. Stirring for 12 hours in the presence of sodium bicarbonate, either anhydrous or a saturated solution, did not produce
the desired cyclobutene. From FAB/MS and IR the cyclobutene precursor, i.e. the phosphorane is present in the mixture. The intramolecular Wittig does not occur; instead, a conjugated phosphorane is generated from the loss of hydrogen cyanide indicated by the formation of vinyl protons in the $^1\text{H}$ NMR and the C=C absorption in the IR. The reaction mixture also turns very dark orange which indicates some type of conjugated system. The conjugated phosphorane is obtained in 68% yield after running the reaction for 12 hours at room temperature in methylene chloride.

Trimethyl ethylenetricarboxylate solves the problem of elimination of hydrogen cyanide (see below). The zwitterion from the reaction of trimethyl ethylenetricarboxylate
and tributylphosphine reacted with chloroacetone at room temperature in 4 hours, followed by the addition of sodium bicarbonate, either anhydrous or a saturated solution. After 12 hours stirring at room temperature only a 7% yield was observed. The yield of the cyclobutene was increased to 17%, as analyzed by GC/MS, after stirring at room temperature for two weeks. Changing the trivalent phosphorus to triphenylphosphine, a less nucleophilic phosphine, decreases the potential for a protropic shift of the zwitterion to ylide and enhances the Wittig reaction. Triphenylphosphine in the same reaction scheme gave a 15% yield after 12 hours of stirring and in two weeks generated a 47% yield of the cyclobutene. Heating either of the reaction mixtures caused ring opening of the highly strained cyclobutene to afford a highly substituted electrophilic butadiene in greater than 47% yield.
SECTION 2: KETENE ACETALS

3.2.0 Monomer Synthesis Concept: Ketene Acetal

Ketene acetals can be considered as electron-rich alkenes with intermediate nucleophilicity between that of enol ethers and enamines. The nucleophilicity of these types of compounds has provided an efficient component in cycloadditions. Enol ethers have been used successfully in many [2+2]-cycloadditions while enamines have been used with some difficulty. The literature presents several synthetic methods in which ketene acetals are used as starting materials in cycloadditions.\textsuperscript{121} The cycloaddition products of ketene acetals with electron-poor olefins have been used for the preparation of substituted cyclobutenes and butadienes,\textsuperscript{122} cyclobutanones,\textsuperscript{123} cyclobutenediones,\textsuperscript{124} and \(\gamma\)-functionalized esters.\textsuperscript{125,126} The intermediate nucleophilicity of ketene acetals is ideal for the synthesis of bicyclobutanes or cyclobutenes using our synthetic scheme which utilizes a [2+2]-cycloaddition.

Our interest in ketene acetals was to extend the [2+2]-cycloaddition reactions to the reaction of ketene acetals with di-, tri-, and tetrasubstituted electron-poor olefins. The [2+2]-cycloaddition of these types of compounds should generate electronegatively-substituted cyclobutane ketals. Hydrolysis of the ketal should produce cyclobutanones. Cyclobutanones represent excellent tools in organic synthesis and can be considered synthetic precursors to naturally occurring products and biologically active compounds.\textsuperscript{127,128} Reduction to the cyclobutanol, and finally formation of the leaving group using a variety of methods sets up for the elimination step (Scheme 14). The
addition of two synthetic steps to our synthetic scheme should pose no threat in the
efficiency of the overall synthesis. The two steps, hydrolysis of the ketal and reduction
of a ketone, are both well documented textbook procedures. Cycloadditions of ketene
acetal with di-, tri-, and tetrasubstituted electrophilic alkenes should provide a reasonable
method for generating cyclobutene and bicyclobutane monomers.

The two ketene acetals we investigated were diethyl ketene acetal and 2-
methylene-1,3-dioxepane. Both of these have become readily available in kilogram
quantities and had been used in [2+2]-cycloadditions with electron-poor alkenes in the
past.

Scheme 14. Proposed synthesis of bicyclobutane using ketene acetal as electron-rich
alkene

\[
\begin{align*}
OR & \quad OR \\
\text{Acc} & \quad \text{Acc} \\
\text{Acc} & \quad \text{Acc}
\end{align*}
\]

\[
\text{Acc} = \text{CO}_2 \text{CH}_3, \text{CN} \\
R = \text{CH}_2 \text{CH}_3, ...
\]
3.2.1 Cycloadditions of Ketene Acetals with Electrophilic Alkenes

Ketene acetals have been used as electron-rich alkenes in many [2+2]-cycloadditions with mono-, di-, tri-, and tetrasubstituted electrophilic alkenes. The [2+2]-cycloadditions which produce cyclobutanes generally give high yields and relatively pure or easily purified cyclobutanes. One complication of attempted [2+2]-cycloadditions of ketene acetals is the formation of 2:1 cycloadducts, cyclohexanes.

The [2+2]-cycloaddition of ketene acetals with mono-substituted electrophilic alkenes has been covered extensively in the literature. The monosubstituted electrophilic alkenes that have been studied such as methyl acrylate or acrylonitrile contain mainly ester or cyano substituents. For our purpose, highly substituted monomers, the [2+2]-cycloaddition of ketene acetals with these types of alkenes was not useful.

Our interest was mainly in the use of trisubstituted electrophilic alkenes with three electron-withdrawing substituents. The literature gives many examples of the reaction of ketene acetals with trisubstituted alkenes; some have given cyclobutanes while others have produced cyclohexanes from the addition of either a molecule of electron-rich alkene or a molecule of electron-poor alkene to the intermediate zwitterion. The question of 2:1 versus 1:1 cycloadducts will be addressed in the next section.

Polansky in 1980 reported the [2+2]-cycloaddition of diethyl ketene acetal with 1,1-dicyano-2-t-butylethylene and with 1,1-dicyano-2-isopropylethylene to give
cyclobutane in 50-70% yield (see below). The reaction of dicyanostyrene is listed with no experimental results, probably due to the formation of cyclohexane.

\[
\begin{array}{c}
\text{OCH}_3 \\
\text{OCH}_3 \\
\end{array}
+ \begin{array}{c}
\text{R-CN} \\
\text{CN} \\
\end{array}
\rightarrow \begin{array}{c}
\text{OCH}_3 \\
\text{OCH}_3 \\
\text{CN} \\
\text{CN} \\
\text{CN} \\
\end{array}
\]

\[ R = C(CH_3)_3, CH(CH_3)_2 \]

Scheeren investigated the reaction of ketene acetal with dicyanostyrene and \( p \)- or \( m \)-substituted dicyanostyrenes. The formation of both cyclobutanes and cyclohexanes were reported depending on the \( \pi \)-electron distribution in the ketene acetal and to a lesser extent on that in the electron-poor alkene.\(^{126}\)

The attempted [2+2]-cycloaddition of both diethyl ketene acetal and 2-methylene-1,3-dioxapane with our series of trisubstituted electrophilic alkenes gave exclusively cyclohexanes, the 2:1 cycloadduct (see below). In our case these cycloadducts contain two of the electron-poor alkenes and one ketene acetal. The conditions of the reactions were varied to facilitate cyclobutane formation with each of our electrophilic alkenes. The solvent polarity did not affect the outcome of the reaction. Polar solvents such as acetonitrile gave cyclohexane in high yield instantly, while non-polar solvents slowed the reaction to give approximately the same yields.
The temperature had no effect other than the formation of crystals at low temperature from the crystallization of the corresponding cyclohexanes. The triester-substituted electrophilic alkene did not react in non-polar solvents at low temperatures and in most cases required heat.

Order of addition had no effect on the outcome of the reaction. The concentration of the reaction mixture also had no effect. When ketene acetal was used as solvent, cyclohexanes were still generated exclusively, even at low temperature.

Scheeren reported that the dipolar intermediate in the reaction of dicyanostyrene with several ketene acetals could be trapped with water in tetrahydrofuran at 20 °C in tenfold excess of water (see below). The corresponding esters were isolated from the
trapping experiment.\textsuperscript{126}

Several attempts at trapping an intermediate in our synthesis using the same conditions as Scheeren did not succeed. In every case the cyclohexane (2:1 cycloadduct) was isolated. The addition of other electrophilic alkenes such as maleic anhydride and changes in temperature did not facilitate the trapping of an intermediate. The very best conditions for trapping should be the reaction of ketene acetal with trimethyl ethylenetricarboxylate in THF at very low temperatures, but at \(-50^\circ\text{C}\) there is no reaction between ketene acetal and the triester. Warming the reaction mixture very gradually with either an additional electrophilic alkene or water present did not give the trapped product.

The formation of cyclohexanes in attempted [2+2]-cycloadditions with trisubstituted electrophilic alkenes directed the study toward di- and tetrasubstituted electrophilic alkenes. These types of electron-poor alkenes in [2+2]-cycloadditions with ketene acetals gave cyclobutane adducts.

The tetrasubstituted electrophilic alkenes gave cyclobutanes with both diethyl ketene acetal and 2-methylene-1,3-dioxepane in high yield. In our synthetic scheme these highly substituted cyclobutanes would not produce the desired bicyclobutane or a cyclobutene that would be polymerizable. The tetrasubstituted alkenes were examined for comparison to the trisubstituted alkenes in attempted [2+2]-cycloadditions.
The [2+2]-cycloadditions of disubstituted electrophilic alkenes with ketene acetals have been previously thoroughly investigated. Brannock first reported the synthesis of 3,3-diethoxy-1,2-cyclobutanedicarboxylic acid diethyl ester in low yields from the reaction of diethyl fumarate with diethyl ketene acetal in refluxing acetonitrile (see below). Later, Bissachi reported the same [2+2]-cycloaddition in t-butyl alcohol to obtain the cyclobutane diester in higher yields as a starting material for cyclobutyl guanine nucleosides. Lewis acids have been utilized to increase the yield of two similar [2+2]-cycloadditions. Ahmed in 1990 used dialkylaluminum chloride as a Lewis acid catalyst in the cycloaddition of dimethyl ketene acetal and (-) dimethyl fumarate (see below).
Similarly, Yamamoto et al.\textsuperscript{133} used methyl aluminum bis(2,6-di-tert-butyl-4-methylphenoxide) (MAD) as Lewis acid in the [2+2]-cycloaddition of unsymmetrical fumarates with ketene acetals.

For our purposes the synthesis reported by Bissachi using \textit{t}-butyl alcohol was sufficient. The cyclobutane produced allowed us to further investigate the possibility of a synthesis of bicyclobutane or cyclobutene from the cyclobutyl ketal.
Attempts at using dimethyl fumarate in the [2+2]-cycloaddition with diethyl ketene acetal led to a mixture of products. The mixture was composed of diethyl ester, methyl ethyl ester, and dimethyl ester cyclobutyl ketal from the esterification of the dimethyl cyclobutane ketal from the presence of ethoxy groups on the ketene acetal.

One very important factor decreasing the yields of the cyclobutanes was the formation of the triethyl orthoester. We assumed that its formation was due to the removal of one molecule of ethyl alcohol of either a cyclic diene of the ketene acetal or the cycloadduct. This problem would not occur when using 2-methylene-1,3-dioxepane because of the cyclic structure of the ketene acetal unit.

The [2+2]-cycloaddition of fumaronitrile with more highly substituted ketene acetals has been reported in the literature. Scheeren in 1983 described two examples of the [2+2]-cycloaddition of fumaronitrile to substituted ketene acetals in good yields of around 80%:

Attempts at the cycloaddition of fumaronitrile with diethyl ketene acetal or 2-methylene-1,3-dioxepane did not produce the desired cyclobutane. Instead with diethyl ketene acetal a mixture of starting materials and oligomers were obtained. 2-Methylene-1,3-dioxepane underwent ring-opening polymerization at the temperatures required for a [2+2]-cycloaddition to give polymers and oligomers (see below).
3.2.2 2:1 Cycloadducts

Previously in Chapter 2 the reaction pathways of the 1,4-zwitterion were discussed in detail. One of the reaction pathways was the formation of cyclohexane from structurally stable zwitterions which add an additional molecule of either electron-rich or electron-poor alkene. Charge-transfer complexes form during many of these reactions as evidence from transient intense colors of the reaction mixture. The literature presents many examples of cyclohexanes that have been formed from the reaction of two electron-poor alkenes with one electron-rich alkene and from the reaction of two electron-rich alkenes with one electron-poor alkene. There are very few theories as to the preference of addition of electron-poor or electron-rich alkene, but the formation of cyclohexanes from electron-poor and electron-rich alkenes has been examined briefly.
A 2:1 cycloadduct which incorporated two electron-rich alkenes with one electron-poor alkene was observed as early as 1942 by McElvain and Cohen (see below). In ether, diethyl ketene acetal reacted with maleic anhydride to give the cyclohexane derivative which then lost alcohol to form 3,5-diethoxy-1,6-dihydrophthalic anhydride. The alcohol that was lost by the cyclohexane derivative converted an equivalent amount of ketene acetal into ethyl orthoformate. A reasonable explanation for this occurrence was not given.

\[\begin{align*}
2 \text{OCH}_2\text{CH}_3 + \text{OCH}_2\text{CH}_3 & \rightarrow \\
\text{H}_3\text{CCH}_2\text{O} + \text{H}_3\text{CCH}_2\text{O} & \rightarrow 2\text{EtOH}
\end{align*}\]

1,1,2,2-Tetracyano-3,5-diphenylcyclohexane (see below) was observed for the reaction of styrene with tetracyanoethylene by McKusick 20 years later. Again there is no mention of further investigations or a theory behind the formation of the 2:1 cycloadduct.
Hall finally touched on the fact that there was a zwitterion intermediate which could add an additional molecule of either electron-poor alkene or electron-rich alkene when he studied the reaction of N,N-dimethylvinylamine with trimethylethylene tricarboxylate (see below). The very effective stabilization of the charges in the zwitterion intermediate by the amine group (and the tri ester groups) accounts for the results.\textsuperscript{137}

\[ \text{N}(\text{CH}_3)_2 + \text{H}_3\text{CO}_2\text{C} \rightleftharpoons \text{H}_3\text{CO}_2\text{C} = \text{N}(\text{CH}_3)_2 \rightarrow \text{N}(\text{CH}_3)_2 \text{CO}_2\text{CH}_3 \]

Hall later observed that the reaction of N-vinylcarbazole with tetrasubstituted electron-poor alkenes resulted in the formation of 2:1 cycloadducts (see below). In this study the concentration of the N-vinylcarbazole was found to play an important role in the outcome of reaction products. In excess N-vinylcarbazole cationic homopolymerization occurs rather than cycloadduct formation.\textsuperscript{138}
It is interesting that in our studies on the reactions of ketene acetals with tri- and tetrarstitute electrophilic alkenes we did not observe the formation of a 2:1 cycloadduct that contained two electron-rich alkenes and one electron-poor alkene. Also the formation of cyclohexane was not seen when tetrarstitute electrophilic alkenes were used with ketene acetals.

The following literature examples which involve the formation of 2:1 cycloadducts from two electron-poor alkenes with one electron-rich alkene are more closely related to our research. These studies also provide some insight as to the reasons for 2:1 cycloadduct formation.

Hasek and Martin\textsuperscript{139} studied the reaction of ketene and dialkylketene with enamines (see below). They found that the order of addition of the reactants was important to obtain optimal yields. Best results were obtained by addition of the dialkylketene to a solution of enamine. Highly polar solvents increased the rate of the reaction and generated 1:1 adduct, large quantities of 2:1 adduct, and 3:1 dialkylketene
Enamine adducts. This was attributed to the stabilization of the charge separation in the ionic intermediate to facilitate further addition of ketene and the subsequent formation of the higher adducts.

\[
\begin{align*}
\text{H}_3\text{C} & \equiv \text{C} = \text{O} \\
\text{H}_3\text{C} & + \text{H}_3\text{C} \equiv \text{N} (\text{CH}_3)_2 \\
\text{Brannock (see below) reinforced the theory of sufficient stabilization of the anionic center and the electrophilic alkene being sufficiently free of steric hindrance allowing reaction with another mole of electrophilic alkene rather than collapsing to form}
\end{align*}
\]

\[
\begin{align*}
\text{CO}_2\text{CH}_2\text{CH}_3 & \equiv \text{CO}_2\text{CH}_2\text{CH}_3 \\
\text{H}_3\text{C} & + \text{H}_3\text{C} \equiv \text{N} (\text{CH}_3)_2 \\
\text{Brannock (see below) reinforced the theory of sufficient stabilization of the anionic center and the electrophilic alkene being sufficiently free of steric hindrance allowing reaction with another mole of electrophilic alkene rather than collapsing to form}
\end{align*}
\]
cyclobutane. The reaction of dimethyl malonate with N,N-dimethylisobutenylamine produced a 2:1 cycloadduct which contained 2 molecules of dimethyl malonate and 1 molecule of N,N-dimethylisobutenylamine.\textsuperscript{10}

Polansky also found that the reaction of N-vinylmorpholine with dicyanostyrene generated a 2:1 cycloadduct containing two molecules of dicyanostyrene and one molecule of N-vinylmorpholine. Polansky was also able to produce a 1:1 cycloadduct from N-isobutenylmorpholine probably due to a less stable zwitterion intermediate.\textsuperscript{140}

In the copolymerization of vinylidene cyanide with styrene (see below), Stille found 1,1,3,5-tetracyano-4-phenylcyclohexane, composed of one molecule of styrene and two molecules of vinylidene cyanide and the copolymer.\textsuperscript{141} The closest intermediate to both the cycloadduct and the copolymer is the donor-acceptor complex since the cycloadduct is a product of head-to-head addition of styrene and vinylidene cyanide while the copolymer is head-to-tail.

\begin{center}
\begin{tikzpicture}
\node[draw,circle] (A) at (0,0) {+} ;
\node[draw,circle] (B) at (1,0) {$\text{CN}$} ;
\node[draw,circle] (C) at (2,0) {$\text{CN}$} ;
\node[draw,circle] (D) at (3,0) {$\equiv$} ;
\node[draw,circle] (E) at (0,-1) {$\equiv$} ;
\node[draw,circle] (F) at (1,-1) {$\text{CN}$} ;
\node[draw,circle] (G) at (2,-1) {$\text{CN}$} ;
\node[draw,circle] (H) at (3,-1) {$\equiv$} ;
\node[draw,circle] (I) at (4,-1) {$\equiv$} ;
\node[draw,circle] (J) at (5,-1) {$\text{NC}$} ;
\node[draw,circle] (K) at (6,-1) {$\text{CN}$} ;
\node[draw,circle] (L) at (4,0) {$\text{CN}$} ;
\node[draw,circle] (M) at (5,0) {$\text{CN}$} ;
\node[draw,circle] (N) at (6,0) {$\equiv$} ;
\node[draw,circle] (O) at (7,0) {$\equiv$} ;
\node[draw,circle] (P) at (8,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (Q) at (9,0) {$\text{CN}$} ;
\node[draw,circle] (R) at (10,0) {$\text{CN}$} ;
\node[draw,circle] (S) at (11,0) {$\equiv$} ;
\node[draw,circle] (T) at (12,0) {$\equiv$} ;
\node[draw,circle] (U) at (13,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (V) at (14,0) {$\text{CN}$} ;
\node[draw,circle] (W) at (15,0) {$\text{CN}$} ;
\node[draw,circle] (X) at (16,0) {$\equiv$} ;
\node[draw,circle] (Y) at (17,0) {$\equiv$} ;
\node[draw,circle] (Z) at (18,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (AA) at (19,0) {$\text{CN}$} ;
\node[draw,circle] (BB) at (20,0) {$\text{CN}$} ;
\node[draw,circle] (CC) at (21,0) {$\equiv$} ;
\node[draw,circle] (DD) at (22,0) {$\equiv$} ;
\node[draw,circle] (EE) at (23,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (FF) at (24,0) {$\text{CN}$} ;
\node[draw,circle] (GG) at (25,0) {$\text{CN}$} ;
\node[draw,circle] (HH) at (26,0) {$\equiv$} ;
\node[draw,circle] (II) at (27,0) {$\equiv$} ;
\node[draw,circle] (JJ) at (28,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (KK) at (29,0) {$\text{CN}$} ;
\node[draw,circle] (LL) at (30,0) {$\text{CN}$} ;
\node[draw,circle] (MM) at (31,0) {$\equiv$} ;
\node[draw,circle] (NN) at (32,0) {$\equiv$} ;
\node[draw,circle] (OO) at (33,0) {$\text{C}_6\text{H}_5$} ;
\node[draw,circle] (PP) at (34,0) {$\text{CN}$} ;
\node[draw,circle] (QQ) at (35,0) {$\text{CN}$} ;\end{tikzpicture}
\end{center}

Stille again saw the formation of a cyclohexane, 1,1-diethoxy-2,2,4,4-tetracyanocyclohexane, from the reaction of diethyl ketene acetal with vinylidene
Cyanide (see below). Higher yields were produced in more polar solvents and regardless of the mole ratio of the donor or acceptor the yield remained constant.$^{142}$

\[
\begin{align*}
\text{H}_2\text{CCH}_2\text{O} & \quad \text{OCH}_2\text{CH}_3 \\
\text{CN} & \quad \text{CN} \\
\text{OCH}_2\text{CH}_3 & \quad \text{OCH}_2\text{CH}_3 \\
\end{align*}
\]

The explanation given was as follows: Whether a four- or six-membered cycloaddition product is obtained may depend either on steric factors which prevent closure to a four-membered ring or on the ability of the cation to be sufficiently delocalized thus allowing insertion of a second vinylidene cyanide before closure. When the vinyl ether is diethyl ketene acetal, severe eclipsing takes place in the formation of the cyclobutane ring, whereas this can be relieved in the formation of the cyclohexane (Figure 1). This same behavior can be seen in previous examples.

\[
\begin{align*}
\text{H}_3\text{CCH}_2\text{O} & \quad \text{OCH}_2\text{CH}_3 \\
\text{CN} & \quad \text{CN} \\
\text{NC} & \quad \text{CN} \\
\end{align*}
\]

**Figure 1.** Eclipsing in cyclobutane and cyclohexane ring closure

Hall and Ykman got a 2:1 cycloadduct when N,N-dimethylisobutenylamine was reacted with tricyanoethylene. The product from two molecules of tricyanoethylene and one molecule of N,N-dimethylisobutenylamine loses hydrogen cyanide to form a cyclohexene.$^{11}$
Lastly, Scheeren, whose work most closely relates to ours, studied in detail the effects of the π-electron distribution on 1:1 versus 2:1 cycloadduct formation. The theory is that the nature of the products for the reaction of ketene acetals is strongly determined by the π-electron distribution in the ketene acetal and to a lesser extent by that in the electrophilic alkene. The symmetrically-substituted ketene acetals in reactions with electron-poor olefins always yielded cyclobutanes. The unsymmetrically-substituted ketene acetals have been reported to yield cyclohexanes.\textsuperscript{122}

According to frontier orbital theory, two limiting geometries of addend approach are possible in reactions of electron-rich with electron-poor alkenes, having higher LUMO-coefficients on the \(\beta\)-C atom. The \(1S^D + 1S^A\) approach is preferred by ketene acetals, having a much larger HOMO-coefficient on \(C(\beta)\) than on \(C(\alpha)\) (Figure 2). The \(2S^D + 1S^A\) approach becomes more probable as the difference between the HOMO-coefficients decreases and finally vanishes.

![Figure 2. Limiting geometries of addend approach](image)

Scheeren supposed that in the \(1S^D + 1S^A\) approach unsymmetrically substituted reactants start their interaction in a \emph{trans} arrangement. The developing charges are far
apart and rotation around the primary formed C-C bond into cisoid gauche conformation is necessary for the completion of cyclobutane formation. This allows for trapping by one of the reactants of the long-living dipolar intermediate.

Stille and Scheeren have developed two theories which fit the results of our attempted [2+2]-cycloadditions of ketene acetals with electrophilic alkenes. According to Stille's theory the 2:1 cycloadducts produced in our investigations with tri-substituted electrophilic alkenes can be attributed to the severe eclipsing in the formation of a cyclobutane ring therefore the formation of a cyclohexane ring relieves eclipsing. In the [2+2]-cycloaddition of tetra-substituted electrophilic alkenes with ketene acetals the amount of eclipsing in the formation of both the cyclobutane and the cyclohexane is substantial and possibly greater in the formation of the cyclohexane, therefore a 1:1 cycloadduct, cyclobutane is formed.

According to Scheeren, the 1:1 versus 2:1 cycloadduct outcome is dependent on the \( \pi \)-electron distribution in the electron-rich or electron-poor alkene. The trisubstituted electron-poor alkenes are unsymmetrical and therefore form cyclohexanes, whereas the tetrasubstituted electron-poor alkenes are symmetrical and form cyclobutanes in [2+2]-cycloaddition reactions with ketene acetals.
3.2.3 Attempted Synthesis of Cyclobutene and Bicyclobutane Monomers from 3,3-Diethoxy-1,2-Cyclobutane Dicarboxylic Acid, Diethyl Ester

The synthesis of a cyclobutene or bicyclobutane monomer depended on the formation of a viable cyclobutane from the first step, the [2+2]-cycloaddition. The cyclobutanones obtained from the reaction of tetrasubstituted electrophilic alkenes with ketene acetals were believed to be too highly substituted for the synthesis of a polymerizable bicyclobutane or cyclobutene. The only viable cyclobutane ketal generated was from the reaction of diethyl ketene acetal with diethyl fumarate. 3,3-diethoxy-1,2-cyclobutanedicarboxylic acid, diethyl ester see below).

The successful synthesis of a cyclobutene or bicyclobutane monomer following the formation of a cyclobutane ketal depended on two seemingly simple steps. First, the hydrolysis of the cyclobutyl ketal to the cyclobutanone and then the reduction of the ketal to the cyclobutanol. The steps following these had been demonstrated in past cyclobutene monomer and bicyclobutane monomer syntheses by many researchers.

The hydrolysis of a similar cyclobutane ketal had been reported by Conia et al. using strong acids such as 33% hydrochloric acid or 33% sulfuric acid to give reasonable yields. In our attempts using the conditions previously reported, the linear triester from acid-catalyzed ring opening was obtained quantitatively. Several methods were examined for the transformation of the ketal such as elimination, halogenation, reduction, cleavage, oxidation, alkylation, and addition. Cyclobutanone was finally obtained using 88% formic acid at room temperature for 30 minutes in a 75% yield. Heating the
The second step, reduction of the cyclobutanone containing electron-withdrawing substituents, had not been reported in the literature. Attempts at reducing the cyclobutanone were futile. Methods of reducing ketones such as using complex metal hydrides, alkoxyaluminates, bis-methoxyethoxyaluminum hydride, borohydrides, metal borohydrides, alkoxy- and alkylborohydrides, and catalytic hydrogenation failed to produce any quantity of cyclobutanol. Work-up of each reaction gave none of the starting cyclobutanone but did give the original diethyl fumarate from cycloreversion in varying quantities. This problem was believed to be caused by the presence of an acidic α-hydrogen on the cyclobutanone ring.
The $\alpha$-hydrogen theory was later proven by Hall and Kniep by alkylating the cyclobutyl ketal from the [2+2]-cycloaddition of diethyl ketene acetal with methyl acrylate. Alkylation replaced the $\alpha$-hydrogen with a methyl group which allowed hydrolysis to the cyclobutanone and reduction of the cyclobutanone to the cyclobutanol in good yield with no cycloreversion.

Alkylation of 3,3-diethoxy-1,2-cyclobutanedicarboxylic acid, diethyl ester had previously been attempted in hopes of a bicyclobutane synthesis, but the alkylation occurred in the 3-position, not the desired 2-position (see below). Attempted alkylation of the cyclobutanone, a $\beta$-ketoester, again appeared to be textbook, but even very mild conditions such as potassium carbonate and methyl iodide at low temperature resulted in cycloreversion or decomposition of the cyclobutanone.
SECTION 3: VINYL AMIDES

3.3.0 Monomer Synthesis Concept: Vinyl Amides

Vinyl amides do not appear to be good electron-donating substituents or good candidates for the synthesis of cyclobutenes or bicyclobutanes using our synthetic scheme. Typically amides are thought of as electron-withdrawing substituents when considering the main resonance structures of an amide, as follows:

\[
\begin{align*}
R & \quad O \\
\text{N} & \quad \text{C} \quad \text{R} \\
\text{N} & \quad = \quad \text{C} \quad \text{R}
\end{align*}
\]

The successful synthesis of a bicyclobutane using N,N-dimethylisobutenylamine by Hall and the failed attempts at a [2+2]-cycloaddition of N,N-dimethylvinylamine made vinylamides as electron-rich alkenes in [2+2]-cycloadditions seem somewhat attractive. The nucleophilicity of the carbon-carbon double bond of a vinylamide is less than that of N,N-dimethylvinylamine due to the electron-withdrawing carbonyl and the zwitterion resonance structure. The problem with N,N-dimethylvinylamine in past attempts at [2+2]-cycloadditions was in the stabilizing ability of the N,N-dimethylamine substituent on the zwitterion intermediate. The zwitterion intermediate was highly stabilized and therefore able to proceed to products other than the desired cyclobutane. Vinylamides, if able to undergo the initial formation of a zwitterion intermediate in a [2+2]-cycloaddition, should form a less-stabilized zwitterion intermediate and therefore more readily close to form cyclobutanes.
The [2+2]-cycloaddition of vinylamides to trisubstituted electrophilic alkenes to form cyclobutanes followed by the conversion of the amide to a leaving group and 1,3-elimination should produce the corresponding bicyclobutane (Scheme 15).

Scheme 15. Proposed synthesis of bicyclobutane using a vinylamide as the electron-rich alkene

\[ \ldots \]

R = H, CH₃
R₁ = H, CH₃
Acc = CN, CO₂CH₃
3.3.1 [2+2]-Cycloadditions of Vinyl Amides with Electrophilic Alkenes

The investigation of [2+2]-cycloaddition reactions of vinyl amides with trisubstituted electrophilic alkenes was initially carried out using vinyl formamide and vinyl acetamide as electron-rich alkenes which were readily available in our laboratory (see below). These were not useful for the continued synthesis of cyclobutane due to the hydrogen on the nitrogen that would be deprotonated by the base used in the elimination step. The first attempted reactions of these compounds with trisubstituted electrophilic alkenes were conducted in acetonitrile using equimolar amounts of the alkenes at room temperature. The initial formation of the zwitterion normally indicated by an intense color from a charge transfer complex was not observed upon mixing the reactants. Cyclobutane was not obtained due to stability problems which gave uncharacterizable products at room temperature. Altering the reaction conditions such as using tetrahydrofuran and lowering the temperature to around −20 °C followed by swift
removal of the solvent under reduced pressure at −20 °C produced cyclobutane in greater than 70% yield using both vinyl formamide and vinylacetamide as the electron-rich alkene.

The successful syntheses of cyclobutanes from [2+2]-cycloadditions of these vinylamides were very encouraging. 1-Vinyl-2-pyrridinone as an electron rich alkene in our synthetic scheme seemed a good choice since the amide had no troublesome hydrogen substituent. The [2+2]-cycloaddition of 1-vinyl-2-pyrolidinone with trisubstituted electrophilic alkenes was run at room temperature in acetonitrile and depending on the electrophilic alkene took 4 to 12 hours to form cyclobutane (see below). The white crystalline cyclobutanes were readily purified by recrystallization from 5% methylene chloride/95% ether. The cyclobutanes are believed to be trans based on the 
\(^1\)H NMR spectrum and comparison to previously isolated cis and trans cyclobutanes having similar absorptions. The cyclobutanes below were generated under the above-mentioned conditions. In the case of trimethylethylene tricarboxylate, heating the reaction decreased the required time substantially.

\[
\begin{align*}
\text{cis} & : \text{H}_3\text{CO}_2\text{C} & \text{CO}_2\text{CH}_3 \\
\text{trans} & : \text{H}_3\text{CO}_2\text{C} & \text{CO}_2\text{CH}_3 \\
\end{align*}
\]
3.3.2 Transformation of Amides to Leaving Groups and 1,3 Elimination

Following the formation of cyclobutanes from the [2+2]-cycloadditions with trisubstituted electrophilic alkenes, conversion of the amide to a good leaving group is required. By analogy to the successful bicyclobutane synthesis by Hall involving the alkylation of N,N-dimethylamine to the quaternary ammonium salt, alklylation at nitrogen would be desirable. Amides are known to be alkylated at oxygen rather than nitrogen to form iminium salts.

As shown below, conversion of the amide to a good leaving group can be
accomplished in a number of ways. Amides can be reduced to amines followed by alkylation to the quaternary ammonium salt, directly alkylated at oxygen to the iminium salt,\textsuperscript{149} converted to the Vilsmer complex by reaction with phosphorus oxychloride,\textsuperscript{150} or oxidized to the imide.\textsuperscript{151}

The best methods for conversion to a leaving group in our case appeared to be the alkylation to the iminium salt and the formation of the Vilsmer complex. Reduction of the amide to the amine would most likely lead to ring opening of the cyclobutane to afford the unsaturated linear butene similar to the $N,N$-dimethylamine substituents:

\[
\begin{array}{c}
\text{O} \\
\text{Acc}
\end{array}
\quad \xrightarrow{\text{Acc}} \quad
\begin{array}{c}
\text{Acc} \\
\text{Acc}
\end{array}
\quad \xrightarrow{\text{H}} \quad
\begin{array}{c}
\text{Acc} \\
\text{Acc}
\end{array}
\]

Oxidation of the amide to the imide seemed risky since imides are not very good leaving groups. The conditions for the elimination of an imide would be unsuitable in the presence of the bicyclobutane product.
Alkylation of the amide at oxygen was accomplished, after several attempts using various reaction conditions, with triethyloxonium tetrafluoroborate. The ideal conditions were methylene chloride as solvent at \(-5^\circ C\) for 3.5 to 4 hours after which a white precipitate had formed. Isolation of the material was difficult due to the hygroscopic nature of the iminium salt formed. In most cases the product was used directly in the 1,3-elimination step. The structure of the iminium salt was confirmed by IR (1655 cm\(^{-1}\), \(^1\)N=C) and by \(^1\)H and \(^{13}\)C NMR.

Attempts at forming a Vilsmer complex with any of the cyclobutane derivatives was unsuccessful and resulted in a brown decomposed product mixture which was unidentifiable by NMR.
The 1,3-elimination of these compounds to form bicyclobutane (see below) was attempted under conditions that had previously given bicyclobutanes from 1,3-eliminations successfully. Most promising was the method used by Hall and Fischer to form a trisubstituted bicyclobutane using potassium hydride in ether at room temperature. These conditions using our cyclobutane iminium salts were not sufficient. Extended reaction times produced no bicyclobutane and the original cyclobutane iminium salt was recovered. A more hindered base, potassium t-butoxide, at lower temperatures gave similar results. It was decided that the leaving group in this case was not very good and would require harsher conditions.

Using potassium t-butoxide at room temperature in ether gave dimers and higher oligomers of the corresponding bicyclobutanes and the lactim ether leaving group. It has been well-documented that bicyclobutanes are very susceptible to free radical and anionic media. The addition of an inhibitor to the reaction mixture caused decomposition when potassium t-butoxide was used as base. but using potassium hydride in tetrahydrofuran at reflux in the presence of inhibitor again led to the formation of oligomers. The most promising observations in this synthesis were the isolation of the lactim ether and the bicyclobutane oligomers, indicating that the bicyclobutane formed but then oligomerized.
CHAPTER 4

CONCLUSIONS AND FUTURE RESEARCH

In this study, three electron-rich alkenes bearing different electron-donating substituents were investigated in the synthesis of cyclobutene and bicyclobutane monomers utilizing a [2+2]-cycloaddition step. The three electron-rich alkenes were studied systematically with a general set of electrophilic alkenes substituted with combinations of cyano- and ester-substituents.

An efficient synthesis of polymerizable vinyl phosphorus compounds was developed. This synthesis allowed the production of a wide variety of electron-rich vinyl phosphites for the first step in our synthetic scheme. Vinyl phosphites did not give any cycloadduct in the attempted [2+2]-cycloadditions. This lack of cycloadduct did not depend on reaction conditions, the steric hindrance on phosphorus, or the electronic properties of either the electron-rich or the electron-poor alkene. The addition of trivalent phosphorus led to the formation of 1,3-zwitterions which eventually underwent protolytic shifts to give stable ylides. The formation of the zwitterion intermediate and control over the protolytic shift was examined in detail. The 1,3-zwitterion was used to demonstrate its usefulness in such applications as intramolecular Wittig reactions to form cyclobutenes.

Ketene acetals became very attractive electron-rich alkenes due to their availability in large quantities. The attempted [2+2]-cycloadditions of ketene acetals with trisubstituted electrophilic alkenes generated 2:1 cycloadducts. This investigation was in agreement with the theories proposed by Stille and Scheeren which involve the eclipsing
which occurs in the formation of cyclobutane versus cyclohexane and the π-electron distribution in the alkenes, respectively. Formation of [2+2]-cycloadducts from tetrastituted electrophilic alkenes with ketene acetals also supported the above proposed theories. A seemingly simple synthesis of bicyclobutane or cyclobutene from the easily formed cycloadduct of diethyl ketene acetal with diethyl fumarate proved to be quite challenging. Alkylation of the cyclobutyl ketal gave the wrong isomer and alkylation of the cyclobutanone was unsuccessful. The chemistry of ketene acetals proved to be somewhat more complex than had been expected.

Vinyl amides, although at first glance not appearing to be electron-rich, have given very desirable results with electrophilic alkenes in [2+2]-cycloadditions. Conversion of the amide substituent was accomplished in high yield by alkylation at oxygen forming the iminium salt. 1,3-Elimination of iminium salts was examined under several different reaction conditions including solvent, temperature, and base. The formation of oligomers and the isolation of the lactim ether leaving group showed that the bicyclobutane must have formed, and therefore demonstrated the great potential in this approach.

The encouraging results with amide as the donor group deserve further examination in particular, acylation of the N-vinylacetamide cycloadducts using trifluoroacetic or triflic anhydrides might five better leaving groups.

In another departure enolates might act as electron-rich olefins and give [2+2]-cycloadducts. Literature examples already exist. In particular aluminum or tin enolates look promising.
CHAPTER 5

EXPERIMENTAL

Instrumentation

$^1$H and $^{13}$C NMR spectra were recorded with a Varian Gemini 200 magnetic resonance spectrometer at 200 and 50 MHz respectively. Infrared spectra were obtained on a Nicolet 410 spectrometer. Melting points were measured using a Thomas-Hoover capillary melting point apparatus. GC/MS analyses were obtained using a Hewlett-Packard GC/MS system. Gas chromatograms were obtained using a Varian 3300 GC with an OV-17 or an OV-101 column. Elemental analyses were determined by Desert Analytics, Tucson, AZ.

Chemicals

Solvents: All solvents were refluxed over CaH$_2$, distilled under argon and then stored over molecular sieves. Tetrahydrofuran was refluxed with metallic sodium/benzophenone until the blue color of benzophenone ketyl was well established, then distilled under argon prior to use. Anhydrous diethyl ether and absolute ethanol were used directly.
Olefins: Tetracyanoethylene (TCNE) was purified by sublimation (120-130 °C/0.5 mmHg) through an activated carbon layer (mp = 198-200 °C). Poly(methyl glyoxylate) was obtained from E. I. Du Pont de Nemours. Malononitrile was distilled before use and stored at −50 °C. Methyl cyanoacetate and dimethyl malonate were distilled before use. Ketene diethyl acetal and 2-methylene-1,3-dioxepane were obtained from Wacker Corporation and used directly. Vinyl pyrrolidinone and vinyl imidazole were purchased from Aldrich Chemical Co. and distilled before use. Diethyl fumarate, dimethyl fumarate and fumaronitrile were distilled over CaH₂ before use.

**Synthesis of Electron-Poor Olefins**

**Dimethyl 2,2-Dicyanoethylene-1,1-dicarboxylate (DDED)**

Dimethyl oxomalonate,¹⁵² 46.8 g (0.32 mol), 5.28 g (0.08 mol) of malononitrile, 3.00 g of glacial acetic acid, 0.75 g of β-alanine, and 70 mL of toluene were refluxed with a Dean-Stark trap for 24 h. The toluene was removed under vacuum and the remaining solution was vacuum distilled twice to give 82% yield of product. bp.: 65-70 °C, 0.5 mmHg. ¹H NMR (CDCl₃): δ 3.9 (s). IR (NaCl, neat) 2230 (CN); 1740 (CO); 1610 (C=C) cm⁻¹
Methyl 3,3-Dicyanoacylate (MDA)

By modification of the method of Sentman and Hall, 8.8 g (0.01 mol) of poly(methyl glyoxylate), 3.3 g (0.05 mol) of malononitrile, 70 mL distilled acetonitrile and 2 drops of acetic anhydride were mixed. The reflux apparatus was outfitted with a Soxhlet extractor containing 4Å molecular sieves. The solution was refluxed for 3 h. The solvent and unreacted starting material were removed under aspirator vacuum, and the remaining liquid was distilled under vacuum twice (60% yield). Bp.: 87 °C, 1.4 mmHg. \(^1\)H NMR (CDCl\(_3\)): 7.2 (s, 1H); 3.9 (s, 3H). IR (NaCl, neat): 2225 (CN); 1740 (CO); 1600 (C=C) cm\(^{-1}\).

Dialkyl Dicyanofumarate\(^77\)

Tetrahydrofuran (10 mL) was carefully added to thionyl chloride (12 mL, 0.168 mol), and alkyl cyanoacetate (0.1 mol) was slowly added over 10 min. The reaction mixture was refluxed for 3 h and stirred at room temperature overnight. The red semi-solid product was filtered and washed with ice-cold ethanol. The crude alkene was recrystallized from ethanol (60% yield). mp.: 115-116 °C for ethyl. \(^1\)H NMR (CDCl\(_3\)): 6.57 (s, 1H); 4.47-4.38 (q, J=7.06 Hz, 2H); 4.38-4.30 (q, J= 7.19 Hz, 2H); 1.42-1.37 (t, J=7.06 Hz, 3H); 1.37-1.31 (t, J=7.19 Hz, 3H).

Tetramethyl Ethylenetetracarboxylate

The tetramethyl ester was prepared analogously to the tetraethyl ester listed in Organic Syntheses. The white crystalline solid was recrystallized from an ether-ethyl
acetate mixture. mp 118-119 °C. $^1$H NMR (CDCl$_3$): $\delta$ 3.83 (s, 12H). IR (NaCl, neat): 2960 (C-H); 1750 (CO); 1645 (C=C) cm$^{-1}$.

**Dimethyl Cyanofumarate (CNF)$^{78,79}$**

Dimethyl cyanofumarate was synthesized using the method described above for the synthesis of methyl 3,3-dicyanoacrylate. Poly(methyl glyoxylate) (15.48 g, 0.18 mol) and methyl cyanoacetate (9.0 g, 0.09 mol) were dissolved in acetonitrile and refluxed for 8 h. The reflux apparatus was outfitted with a Soxhlet extractor filled with freshly activated 4 Å molecular sieves. Acetonitrile and unreacted methyl glyoxylate were removed using a rotary evaporator. The resulting reddish brown liquid was distilled at 0.5 mmHg and then recrystallized from ether giving the pure product in 63% yield. mp 60-61 °C. $^1$H NMR (CDCl$_3$): $\delta$ 7.43 (s, 1H); 3.95 (s, 3H); 3.91 (s, 3H). IR (NaCl, neat): 2226 (CN); 1730 (CO); 1630 (C=C) cm$^{-1}$.

**Dialkyl 2-Cyanoethylene-1,1-dicarboxylate$^{78,79}$**

Cyanomethylenetriphenylphosphorane (30.1 g, 100 mmol) was added to a solution of dialkyl oxomalonate (100 mmol) in 200 mL benzene cooled in an ice bath over 1 min. After 20 min., the benzene was evaporated and ether was added to crystallize the triphenylphosphine oxide side product. The ether was evaporated and the crude product was vacuum distilled (50% yield). bp.: 97-100 °C, 1.4 mmHg. $^1$H NMR (CDCl$_3$): $\delta$ 6.55 (s, 1H); 3.92 (s, 3H); 3.87 (s, 3H). IR (NaCl, neat): 2200 (CN); 1725 (CO); 1625 (C=C) cm$^{-1}$. 
Trimethyl Ethylenetricarboxylate\textsuperscript{78,79}

Equivalent amounts of poly(methyl glyoxylate), dimethyl malonate, and acetic anhydride were mixed and refluxed overnight at 125-130 °C. Excess acetic anhydride, acetic acid, and dialkyl malonate were removed under vacuum, and the olefin was obtained by vacuum distillation (53% yield). bp: 100-110 °C, 0.2 mmHg. \textsuperscript{1}H NMR (CDCl\textsubscript{3}): 6.90 (s, 1H); 3.90 (s, 3H); 3.86 (s, 3H); 3.81 (s, 3H). IR (NaCl, neat): 1731 (CO); 1655 (C=C) cm\textsuperscript{-1}.

\textbf{Synthesis of Electron-Rich Olefins}

\textbf{Typical Procedure for Vinyl Phosphorus Derivative Synthesis:} Dry tetrahydrofuran (50 mL, 0.61 mole) was placed in a dry three-neck, round-bottomed flask under nitrogen. \textit{n}-Butyllithium in \textit{n}-hexane solution (2.5M, 32.4 mL, 0.08 mole) was added using a syringe. After 3 hours stirring at room temperature under nitrogen the mixture was cooled to \textit{-}50 °C followed by dropwise addition of the chlorophosphorus compound over 20 min. After an additional 3 h the reaction mixture was concentrated \textit{in vacuo} and distilled under reduced pressure using a Kugelrohr apparatus.

\textbf{Dimethyl Vinyl Phosphate (1).} 80% yield, 80-82 °C/10 mmHg. IR (NaCl, neat) 3075, 2986, 1640, 1376 cm\textsuperscript{-1}. \textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}) \textdelta 6.62 (m, 1H), 4.89 (m, 1H), 4.59 (m, 1H), 3.80 (d, J= 11.5 Hz).
**Diethyl Vinyl Phosphite (2).** 87% yield, 105-107 °C/20 mmHg. IR (NaCl, neat) 3118, 2997, 1636, 1388, 1045 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 6.61 (ddd, J=6.15, 6.88, 12.67 Hz, 1H), 4.61 (dd, J=0.87, 1.10, 12.67 Hz, 1H), 4.32 (ddd, J=1.10, 2.82, 6.15 Hz, 1H), 3.91 (q, 4H), 1.22 (t, 6H). ¹³C NMR (50 MHz, CDCl₃) δ 143.0 (J_CP = 5.6 Hz), 96.2 (J_CP = 10.1 Hz), 58.9 (J_CP = 6.0 Hz), 17.3 (J_CP = 6.3 Hz). Anal. Calcd. for C₇H₁₂O₃P: C, 43.90; H, 7.98; P, 18.87. Found: C, 43.50; H, 8.12; P, 18.76.

**Diethyl Vinyl Phosphate (3).**¹⁶,¹⁷ 85% yield, 94-95 °C/11 mmHg. IR (NaCl, neat) 3077, 2986, 1645, 1282 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 6.39 (ddd, J=5.95, 6.57, 13.46 Hz, 1H), 4.71 (ddd, J=1.01, 1.75, 13.46 Hz, 1H), 4.39 (ddd, J=1.75, 2.90, 5.95 Hz, 1H), 3.95 (q, 4H), 1.17 (t, 6H). ¹³C NMR (50 MHz, CDCl₃) δ 141.8 (J_CP = 5.7 Hz), 99.2 (J_CP = 10.3 Hz), 63.9 (J_CP = 6.1 Hz), 15.6 (J_CP = 6.5 Hz).

**Diethyl Vinyl Phosphorothioate (4).** 85% yield, 82-84 °C/7.5 mmHg. IR (NaCl, neat) 3095, 2984, 1643, 1137 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 1.31 (t, 3H), 4.16 (q, 4H), 4.60 (ddd, J=1.83, 2.76, 5.89 Hz, 1H), 4.87 (ddd, J=1.05, 1.83, 13.55 Hz, 1H), 6.70 (ddd, J=5.89, 6.27, 13.55 Hz, 1H). ¹³C NMR (50 MHz, Acetone-d₆) δ 142.2 (J_CP = 4.9 Hz), 99.3 (J_CP = 11.6 Hz), 64.6 (J_CP = 5.6 Hz), 15.7 (J_CP = 7.3 Hz). Anal. Calcd for C₆H₁₃O₃PS: C, 36.73; H, 6.68; S, 16.34. Found: C, 36.86; H, 6.70; S, 16.72.
**O-Ethenyl-N,N,N',N'-Tetramethyl Phosphoric Diamide (5).** 87% yield, 125-127 °C/20 mmHg. IR (NaCl, neat) 3069, 2929, 1640, 1303 cm⁻¹. ¹H NMR (200 MHz, Acetone-d₆) δ 6.61 (ddd, J=5.94, 6.92, 13.72 Hz, 1H), 4.72 (ddd, J=0.98, 1.83, 13.72 Hz, 1H), 4.41 (ddd, J=1.83, 2.91, 5.94 Hz, 1H), 2.88 (s, 3H), 2.64 (s, 3H), 2.62 (s, 3H), 2.57 (s, 3H). ¹³C NMR (50 MHz, acetone-d₆) δ 144.1 (JCP=4.9 Hz), 97.7 (JCP=10.0 Hz), 37.20, 36.76, 36.70. Anal. Calcd for C₁₀H₁₃N₂O₂P: C, 40.4; H, 8.5; N, 15.7. Found: C, 40.3; H 8.2; N 15.7.

**O-Phenylenedi Vinyl Phosphate (6).** 71% yield, 132-134 °C/20 mmHg. IR (NaCl, neat) 3097, 2994, 1640, 1383 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 7.15-7.35 (m, 4H), 6.74 (ddd, J=5.70, 6.39, 13.21 Hz, 1H), 5.10 (ddd, J=1.06, 1.51, 13.21 Hz, 1H), 4.84 (ddd, J=1.51, 2.57, 5.70 Hz, 1H). ¹³C NMR (50 MHz, acetone-d₆) δ 144.6, 142.3 (JCP=7.2 Hz), 125.2, 124.2, 113.4 (JCP=13.4 Hz), 112.9 (JCP=12.7 Hz), 102.8 (JCP=10.5 Hz). HRMS (matrix, NBA): calcd. for C₈H₇O₄P•H⁺ 199.0082, found 199.0160.

**O-Phenylenedi Vinyl Phosphite (7).** 72% yield, 117-119 °C/15 mmHg. IR (NaCl, neat) 3067, 1634, 1331 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 7.01-7.36 (m, 4H), 6.33 (ddd, J=5.82, 6.94, 13.59 Hz, 1H), 4.70 (ddd, J=1.10, 1.54, 13.57 Hz, 1H), 4.40 (ddd, J=1.54, 2.97, 5.82 Hz, 1H). ¹³C NMR (50 MHz, acetone-d₆) δ 145.7, 142.0 (JCP=3.9 Hz), 125.4, 124.1, 114.8, 113.2, 100.8 (JCP=7.2 Hz). HRMS (matrix, NBA): calcd. for C₈H₇O₃P•H⁺ 183.0133, found 183.0211.
O-Ethynyl-N,N,N',N'-tetraethyl Phosphite Diamine (8). 78% yield, 110-114 °C/18 mmHg. IR (NaCl, neat) 3091, 2098, 1642, 1330. $^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 6.46 (ddd, J=5.95, 6.31, 13.7 Hz, 1H), 4.44 (dd, J=1.50, 13.71 Hz, 1H), 4.11 (dd, J=1.50, 2.93, 5.95 Hz, 1H), 2.88-3.17 (m, 8H), 1.04 (t, 12H). $^{13}$C NMR (50 MHz, acetone-$d_6$) $\delta$ 147.7 ($J_{CP}$=18.6 Hz), 93.5 ($J_{CP}$=10.7 Hz), 40.2, 39.8, 15.3 ($J_{CP}$=2.8 Hz). Anal. Calcd for C$_{10}$H$_{22}$N$_2$OP: C, 55.0; H, 10.6; N, 12.8. Found: C, 54.6; H, 10.6; N, 12.8.

Diphenyl Vinyl Phosphite (9). 82% yield from gas chromatography. Attempted isolation of this product resulted in the formation of oligomers.

Diphenyl Vinyl Phosphine Ester (10). 66% yield, 147-149 °C/15 mmHg. IR (NaCl, neat) 3058, 1639, 1235. $^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 7.88-7.99 (m, 4H), 7.51-7.59 (m, 6H), 6.76 (ddd, J=5.94, 7.97, 13.60 Hz, 1H), 5.05 (dd, J=1.83, 13.60 Hz, 1H), 4.63 (dd, J=1.83, 5.94 Hz, 1H). $^{13}$C NMR (50 MHz, acetone-$d_6$) $\delta$ 142.1 ($J_{CP}$=6.3 Hz), 133.2 ($J_{CP}$=7.0 Hz), 132.1

Vinyl-1,3,2-dioxaphosphite. 57% yield, 110-112 °C/20 mmHg. IR (NaCl, neat) 3060, 2904, 1639, 1313 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 6.45 (ddd, J=5.58, 6.22, 13.56 Hz, 1H), 4.63 (dd, J=1.42, 13.56), 4.33 (dd, J=1.42, 5.58 Hz, 1H), 4.25 (m, 2H), 4.05 (m,
$^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 142.7 ($J_{CP}$=12.7 Hz), 97.5 ($J_{CP}$=9.4 Hz), 64.0 ($J_{CP}$=8.7 Hz).

**Di-t-butyl Vinyl Phosphite.** >15% yield. This compound was never isolated, but $^1$H NMR indicated a low yield of a mixture of the phosphate from autoxidation of the phosphite and the phosphite.

**Bis(pentafluorophenyl) Vinyl Phosphite.**

a.) Bis(pentafluorophenyl)phosphorus chloride. Dry benzene was placed in a dry three-neck, round-bottom flask under nitrogen. Phosphorus trichloride was added using a syringe. The mixture was cooled to -5 °C followed by the dropwise addition of pentafluorophenyl iodide at a rate which kept the temperature at 0 °C. After an additional 4 hours at room temperature, the reaction mixture was concentrated in vacuo and the crude product used directly in the next step.

b.) Bis(pentafluorophenyl)phosphorus chloride was added dropwise to the acetaldehyde enolate followed by removal of solvent at reduced pressure. $^1$H NMR indicated >5% of the desired product. $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 6.58 (ddd, $J$=5.41, 6.43, 13.59 Hz, 1H), 4.90 (dd, $J$=1.8, 13.59 Hz, 1H), 4.55 (ddd, $J$=1.80, 2.81, 5.41 Hz, 1H).
2,2-Dimethyl-1,3-isobutyl Vinyl Phosphite.

a.) Phosphite. Dry toluene was placed in a dry three-neck, round-bottom flask under nitrogen. Phosphorus trichloride and neopentyl glycol were added. The reaction mixture was cooled to -5 °C followed by the dropwise addition of triethylamine. The reaction was stirred under nitrogen overnight. Excess solvent and triethylamine were removed under reduced pressure and the crude product distilled to produce the alkyl chlorophosphite. $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 4.29 (m, 4H), 1.25 (s, 6H).

b.) The chlorophosphite was added to the enolate of acetaldehyde and allowed to stir at room temperature for 3 hours. Removal of solvent afforded a crude yellow product which was distilled using a Kugelrohr apparatus. 64% yield, 121-123 °C/mmHg. $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 6.62 (m, 1H), 4.71 (m, 1H), 4.41 (m, 1H), 4.15 (m, 4H), 1.30 (s, 3H), 1.25 (s, 3H).

Typical Procedure for Attempted [2+2]-Cycloadditions

One molar equivalent of electron-rich olefin and one molar equivalent of electron-poor olefin were mixed in acetonitrile at room temperature and stirred until the reaction was complete. The end of the reaction was indicated by the disappearance of the color of the charge complex, or monitored by $^1$H NMR spectroscopy. The solvent was evaporated and the crude product was purified.
Typical Procedure for Attempted Lewis Acid-Promoted [2+2]-Cycloaddition

One molar equivalent of Lewis acid was placed in a reaction flask and dried under vacuum at 300 °C. Under dry nitrogen one molar equivalent of electron-poor olefin and solvent were added and stirred vigorously for a minimum of 30 min. One molar equivalent of electron-rich olefin was added. The reaction was followed by $^1$H-NMR spectroscopy. When the reaction was finished, the mixture was extracted with chloroform and 6N hydrochloric acid. The chloroform layer was washed with water and dried over anhydrous magnesium sulfate. After evaporation of the solvent using a rotary evaporator, the crude product was purified.

Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Tetracyanoethylene

The reaction was conducted at room temperature in ether and finished within 5 min. The crude dark brown product separated into a solid layer and a liquid layer. The solid was unreacted tetracyanoethylene. The liquid layer was washed with pentane several times followed by analysis. 52% yield. IR (NaCl, neat) 3027, 2987, 2224, 1640, 1318 cm$^{-1}$. $^1$H NMR (200 MHz, acetone-d$_6$) δ 6.60 (m, 1H), 4.88 (d, J=13.33 Hz, 1H), 4.62 (d, J=5.62 Hz, 1H), 4.13 (m, 4H), 3.81 (s, 1H), 1.30 (m, 1H).
Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Diethyl 2,2-Dicyanoethylene-1,1-dicarboxylate (DDED)

The reaction was conducted at room temperature in acetonitrile and finished in 3 hours. The crude product was washed several times with pentane to yield 73% of the addition product. IR (NaCl, neat) 3029, 2998, 2224, 1735, 1632, 1318 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 6.62 (m, 1H), 4.64 (dd, J=13.54 Hz, 1H), 4.55 (m, 1H), 4.12 (m, 8H), 2.85 (s, 1H), 1.29 (m, 9H).

Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Dialkyl Dicyanofumarate

The reaction was carried out at room temperature in acetonitrile and finished in 8 hours. The crude yellow liquid was washed several times with pentane to afford 62% yield of the product from phosphorus addition. IR (NaCl, neat) 3092, 2987, 2223, 1744, 1645, 1328 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 6.72 (m, 1H), 4.82 (d, J=13.44 Hz, 1H), 4.56 (m, 1H), 4.10 (m, 4H), 3.89 (s, 3H), 3.87 (s, 3H), 2.80 (s, 1H), 1.25 (m 6H).
Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Methyl Dicyanoacrylate (MDA)

The reaction was conducted at room temperature in acetonitrile and finished in 4 hours. The crude yellow product was washed with pentane several times to give 92% yield of yellow oil.

Spectra on crude. IR (NaCl, neat) 3185, 2987, 2214, 1696, 1754, 1373 cm$^{-1}$. $^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 6.62 (m, 1H), 4.83 (dd, $J=1.22$, 13.46 Hz, 1H), 4.54 (m, 1H), 4.12 (m, 4H), 3.87 (s, 3H), 2.27 (d, $J=10.7$ Hz, 1H), 1.30 (m, 6H).

Spectra after column (Basic Al$_2$O$_3$, 3:1 hexane/ethyl acetate). IR (NaCl, neat) 2983, 2220, 1732, 1334 cm$^{-1}$. $^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 4.99 (dd, $J=4.88$, 10.90 Hz, 1H), 4.23 (m, 4H), 4.05 (m, 2H), 3.88 (s, 3H), 3.08 (d, $J=15.9$ Hz, 1H), 1.31 (m, 6H). $^{13}$C NMR (50 MHz, acetone-$d_6$) $\delta$ 166.4, 112.8, 64.4 (d, $J=6.9$ Hz), 53.5, 45.4 (d, $J=130.2$ Hz), 22.4, 16.2 (d, $J=5.7$ Hz).

Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with 2-Phenyl-1,1-dicyanoethylene

The reaction was conducted at room temperature in acetonitrile and finished in 5 hours. The crude dark orange product was washed with pentane to afford 66% yield of the addition product. IR (NaCl, neat) 3183, 2987, 2217, 1663, 1388 cm$^{-1}$. $^1$H NMR $\delta$ 7.90-7.41 (m, 5H), 6.61 (m, 1H), 4.59 (d, $J=13.77$ Hz, 1H), 4.35 (d, $J=6.21$ Hz, 1H), 4.15 (m, 4H), 2.20 (m, 1H), 1.33 (m, 6H).
Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Dimethyl Cyanofumarate

The reaction was conducted at 110 °C in toluene and finished in 8 hours. The crude yellow product was washed several times with pentane to afford 57% yield of the addition product. IR (NaCl, neat) 2973, 2224, 1733, 1318 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 6.61 (m, 1H), 4.95 (d, J=13.28 Hz, 1H), 4.66 (m, 1H), 4.19 (m 4H), 3.79 (s, 3H), 3.60 (s, 3H), 1.88 (s, 1H), 1.33 (s, 6H).

Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with 1-Cyanoacrylate

The reaction was conducted at reflux in acetonitrile and finished in 3 days. The crude product was washed with pentane several times to give a white solid and a yellow liquid. Filtration gave a 34% yield of the crude yellow addition product. IR 2988, 2215, 1735, 1324 cm⁻¹. ¹H NMR (200 MHz, acetone-d₆) δ 6.60 (m, 1H), 4.85 (m, 1H), 4.55 (m, 1H), 3.83 (m, 2H), 2.94-2.52 (m, 3H), 1.35 (m, 9H).
Attempted [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with \( \text{t-Butyl Dicyanoacrylate} \)

The reaction was conducted at room temperature in acetonitrile and was finished overnight. The crude product was washed several times with pentane to yield 58% of a yellow oil. IR (NaCl, neat) 3075, 2998, 1738, 1640, 1381 cm\(^{-1}\). \(^1\)H NMR (200 MHz, acetone-\(d_6\)) \(\delta\) 6.61 (m, 1H), 4.89 (dd, \(J=1.02, 13.67\) Hz, 1H), 4.56 (m, 1H), 4.15 (m, 4H), 2.95 (d, \(J=7.23\) Hz, 1H), 1.52 (s, 9H), 1.31 (m, 6H).

Attempted \(\text{ZnCl}_2\)-Catalyzed [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Methyl Dicyanoacrylate

The reaction was conducted in 2,5-dimethyltetrahydrofuran at room temperature and finished in less than 30 min. The IR and \(^1\)H NMR were the same as in the uncatalyzed reaction of diethyl vinyl phosphite with methyl dicyanoacrylate, indicating the addition product.

Attempted \(\text{LiClO}_4\)-Catalyzed [2+2]-Cycloaddition of Diethyl Vinyl Phosphite with Trimethyl Ethylenetricarboxylate

The reaction was carried out in 2,5-dimethyltetrahydrofuran at reflux and was finished in 3 hours. The crude product was washed with pentane to give a 66% yield of yellow oil. IR and \(^1\)H NMR spectra were identical to those in the uncatalyzed reaction.
Attempted \([2+2]\)-Cycloaddition of O-Phenylene Vinyl Phosphite with Methyl Dicyanoacrylate

The reaction was conducted in acetonitrile at room temperature and finished overnight. The crude product was washed with pentane to give a yellow oil in 52% yield. IR (NaCl, neat) 2980, 2220, 1738, 1383 cm\(^{-1}\). \(^1\)H NMR (200 MHz, acetone-\(d_6\)) \(\delta\) 7.31-6.70 (m, 4H), 5.19 (dd, \(J= 1.1, 12.2\) Hz, 1H) 3.81 (s, 3H), 3.33 (d, \(J= 7.5\) Hz, 1H).

Attempted Lewis Acid-Promoted \([2+2]\)-Cycloaddition of Non-nucleophilic Vinyl Phosphorus Compounds with Electron-Poor Olefins

One molar equivalent of Lewis acid was placed in a reaction flask and dried under vacuum at 300 °C. Under dry nitrogen one molar equivalent of electron-poor olefin and solvent were added and stirred vigorously for at least 30 min. One molar equivalent of electron-rich olefin was added using a syringe. The reaction was followed by \(^1\)H NMR. After refluxing for up to 1 month, solvent was removed under reduced pressure. \(^1\)H NMR indicated starting material only.

Addition of Triethyl Phosphite to Methyl 2,2-Dicyanoacrylate

One molar equivalent of methyl dicyanoacrylate was added to dry acetonitrile at room temperature under nitrogen. One molar equivalent of triethyl phosphite was added via syringe all at once. The reaction was stirred overnight followed by removal of excess solvent under reduced pressure. IR (NaCl, neat) 2979, 2243, 1745, 1666, 1387 cm\(^{-1}\). \(^1\)H
NMR (200 MHz, CDCl₃) δ 5.30 (d, J=24.17 Hz, 1H), 4.23 (m, 6H), 3.65 (s, 3H), 1.44 (m, 9H).

**Addition of Tri-n-butylphosphine to Trimethyl Ethylenetricarboxylate**

One molar equivalent of trimethyl ethylenetricarboxylate was added to dry acetonitrile at room temperature under nitrogen. One molar equivalent of tri-n-butylphosphine was added via syringe all at once. The reaction was stirred overnight followed by removal of excess solvent under reduced pressure. IR (NaCl, neat) ¹H NMR (200 MHz, CDCl₃) 4.85 (d, J= 5.7 Hz, 1H), 3.42 (s, 3H), 3.51 (s, 3H), 3.55 (s, 3H), 2.01-1.50 (m, 6H), 1.41-0.95 (m, 12H), 0.65-0.49 (m, 9H).

**Intramolecular Wittig Reactions: Cyclobutene Synthesis**

**Tri-n-Butylphosphine with MDA and Chloroacetone**

To a magnetically-stirred solution of MDA (0.25g, 1.8 mmol) in 10 mL dichloromethane was added dropwise a solution of tributylphosphine (0.37g, 1.8 mmol) in 4 mL dichloromethane at room temperature over 10 minutes. The mixture was allowed to stir for 24 hours followed by the addition of 0.5 mL of a saturated sodium bicarbonate solution. After an additional 24 hours stirring at room temperature the solvent was removed at reduced pressure. The crude product was washed with ether (3x) and dried over magnesium sulfate. Removal of the ether under reduced pressure afforded a yellow oil in 68% yield. FAB/MS calcd. for C₂₀H₃₄NO₃P•H⁺ 368.46, found 368.34.
**Tributylphosphine and Trimethyl Ethylenetricarboxylate**

To a magnetically stirred solution of trimethyl ethylenetricarbocylate (0.25g, 1.8 mmol) in 10 mL dichloromethane was added dropwise a mixture of tributylphosphine (0.37g, 1.8 mmol) in 4 mL dichloromethane at room temperature over 10 min. The mixture was allowed to stir for 24 hours. FAB/MS calcd. for C_{20}H_{37}O_{6}P•H^+ 405.48, found 405.30.

A saturated solution of sodium bicarbonate was added dropwise and the solution allowed to stir for an additional 24 hours. The solvent was removed under reduced pressure to afford yellow oil in 67% yield. HRMS calcd. for C_{23}H_{41}O_{7}P•H^+ 461.2590. found 461.2659. The final product, cyclobutene, was obtained after stirring for 12 days at room temperature as a yellow residue in 17% yield. FAB/MS calcd. for C_{11}H_{14}O_{6}•H^+ 243.22, found 243.34.

**Ketene Acetals:**

**[2+2]-Cycloaddition of Diethyl Ketene Acetal with Diethyl Fumarate**

A mixture of diethyl ketene acetal (38.35 g, 0.331 mol) and diethyl fumarate (56.28 g, 0.327 mol) in 100 mL of tert-butyl alcohol was heated at 84 °C under argon for 72 h. The reaction mixture was distilled (bp 113-125 °C, 1 mmHg; lit. bp 103-109 °C, 0.2 mmHg) to afford 48.3 g, 50% yield. IR (NaCl, neat) 2979, 1733, 1445, 1307 cm\(^{-1}\). \(^1\)H NMR (200 MHz, CDCl\(_3\)) δ 4.16 (m, 4H), 3.30-3.81 (m, 6H), 2.58 (dd, J= 11.0, 12.1 Hz,
1H), 2.24 (ddd, J= 1.1, 8.8, 12.1 Hz, 1H), 1.20 (m, 12H). $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 174.1, 169.5, 99.9, 61.3, 61.1, 57.9, 57.2, 52.9, 34.8, 31.6, 15.4, 14.7, 14.6. High res MS cacld. 288.1573, found: 288.1662.

Attempted [2+2]-Cycloaddition of 2-Methylene-1,3-dioxepane with Diethyl Fumarate

A mixture of 2-methylene-1,3-dioxepane (37.78 g, 0.331 mol) and diethyl fumarate (56.28 g, 0.327 mol) in 100 mL of tert-butyl alcohol was heated at 84 °C under argon for 72 h.

Triethyl 1,2,3-propanetricarboxylate

A mixture of diethyl 3,3-diethoxycyclobutane 1,2-dicarboxylate (1 g, 3.5 mmol) and 3 mL of formic acid was stirred overnight at room temperature. The excess formic acid was removed at reduced pressure and the reaction mixture distilled (bp 105-110 °C, 1 mmHg) to afford 0.94 g (94% yield).

IR (NaCl, neat) 2979, 1734, 1405 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 4.13 (m, 6H), 3.20 (m, 1H), 2.50-2.91 (m, 4H), 1.22 (m, 9H). $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 177.2, 172.9, 171.3, 61.2, 60.8, 37.1, 35.2, 34.9, 14.0, 13.9. High Res. MS cacld. 260.1260. found: 260.1337.
Attempted [2+2]-Cycloaddition of Diethyl Ketene Acetal with Fumaronitrile

A mixture of diethyl ketene acetal (38.35 g, 0.331 mol) and fumaronitrile (25.50 g, 0.327 mol) in 100 mL of tert-butyl alcohol was heated at 84 °C under argon for 72 h.

Attempted [2+2]-Cycloaddition of 2-Methylene-1,3-Dioxepane Acetal with Fumaronitrile

A mixture of 2-methylene-1,3-dioxepane (37.78 g, 0.331 mol) and fumaronitrile (25.50 g, 0.327 mol) in 100 mL of tert-butyl alcohol was heated at 84 °C under argon for 72 h.

Reaction of Diethyl Ketene Acetal with Trimethyl Ethylenetricarboxylate

The reaction was conducted at room temperature in acetonitrile and finished overnight. After removing the solvent, the 2:1 cycloadduct was recrystallized from ether (89% yield).

IR (NaCl, neat) 2987, 1738, 1434 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 4.12 (q, 4H), 3.91 (m, 1H), 3.78 (s, 6H), 3.76 (s, 6H), 3.71 (s, 6H), 3.50-3.63 (m, X part of ABX, 1H), 2.60-2.89 (m, AB part of ABX, 2H), 1.25 (t, 6H).

Reaction of 2-Methylene-1,3-dioxepane with Trimethyl Ethylenetricarboxylate

The reaction was conducted at room temperature in acetonitrile and finished overnight. After removing the solvent, the 2:1 cycloadduct was recrystallized from ether.
**Reaction of Diethyl Ketene Acetal with MDA**

The reaction occurred spontaneously at room temperature in acetonitrile. After removal of the solvent, the 2:1 cycloadduct was washed with ether several times to give a quantitative yield.

IR (NaCl, neat) 2989, 2256, 1759, 1739, 1450 cm\(^{-1}\). \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 4.53 (d, \(J = 6.1\) Hz, 1H), 4.19 (m, 4H), 3.85 (s, 6H), 3.40-3.51 (m, X part of ABX, 1H), 2.35-3.10 (m, AB part of ABX, 2H), 1.25 (m, 6H). \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 169.6, 168.6, 111.3, 111.1, 61.8, 53.4, 41.7, 32.0, 23.8, 13.9. High Res. MS calcd. 388.1382, found: 388.1468.

**Reaction of 2-Methylene-1,3-dioxepane with MDA**

The reaction occurred spontaneously at room temperature in acetonitrile. After removal of the solvent, the 2:1 cycloadduct was washed with ether several times to give a quantitative yield.

IR (NaCl, neat) 2980, 2243, 1735, 1440 cm\(^{-1}\). \(^1\)H NMR (200 MHz. CDCl\(_3\)) \(\delta\) 3.85 (s, 6H), 3.30-3.49 (m, X part of ABX. 1H), 2.50-2.82 (m, AB part of ABX. 2H), 1.40-1.79 (m, 8H). High Res MS calcd. 386.1226, found: 387.1305.
[2+2]-Cycloaddition of Diethyl Ketene Acetal with Dimethyl 1,2-Dicyanoethylene-1,2-dicarboxylate

The [2+2]-cycloaddition occurred spontaneously at room temperature in acetonitrile. After removing the solvent, the cyclobutane was recrystallized from ether (88% yield).

IR (NaCl, neat) 2973, 2253, 1752, 1432 cm\(^{-1}\). \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 4.10 (m, 4H), 3.85 (m, 6H), 3.39-3.61 (m, 2H), 1.19 (m, 6H). \(^1^3\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 164.1, 162.0, 116.7, 113.5, 69.6, 66.3, 65.4, 57.8, 54.8, 44.5, 15.0. High Res FAB/MS calcd 310.1165 found 311.1243.

[2+2]-Cycloaddition of 2-Methylene-1,3-dioxepane with Dimethyl 1,2-Dicyanoethylene-1,2-dicarboxylate

The [2+2]-cycloaddition occurred spontaneously at room temperature in acetonitrile. After removing the solvent, the cyclobutane was recrystallized from ether (80% yield).

IR (NaCl, neat) 2985, 2257, 1745, 1450 cm\(^{-1}\). \(^1^3\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 166.7, 166.2, 117.1, 116.6, 66.3, 59.8, 56.2, 55.1, 42.5, 35.8, 29.1. High Res. FAB/MS calcd. 308.1008. found 309.1087.

Attempted [2+2]-Cycloaddition of Diethyl Ketene Acetal with Cyanoacrylate

The reaction was conducted at room temperature in acetonitrile and finished in 2 days. Removal of excess solvent and starting material under reduced pressure followed by several washings with ether yielded 65% of the 2:1 cycloadduct.
IR (NaCl, neat) 2989, 2257, 1736, 1444 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 4.10–4.40 (m, 4H), 3.89 (s, 6H), 3.50–3.85 (m, 2H), 3.05 (d, 1H), 2.82 (d, 1H), 2.01–2.43 (m, 2H), 1.12–1.40 (m, 6H). High Res. FAB/MS calcd. 338.1478 found 339.1556.

[2+2]-Cycloaddition of 2-Methylene-1,3-dioxepane with Tetracyanoethylene

The [2+2]-cycloaddition was run at −78 °C in ether and occurred spontaneously. The solvent was removed at −78 °C under reduced pressure to afford a white powder (35% yield).

IR (NaCl, neat) 2939, 1725, 1407 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 3.83–4.12 (m, 4H), 3.30 (s, 2H), 1.77–1.91 (m, 4H). High Res. FAB/MS calcd. 242.0804, found 243.0882.

Diethyl Methyfumarate

A mixture of redistilled citraconic acid (43 g, 0.3 mol), ethanol (75 g, 1.6 mol), and 3 mL concentrated sulfuric acid was refluxed for 12 hours. The mixture was poured into 250 mL water in a separatory funnel, the upper layer of crude ester was removed and washed with 100 mL of water, followed by 25 mL of saturated sodium bicarbonate and again with 50 mL of water. The crude ester was dried over anhydrous sodium sulfate. Distillation (120–127 °C, 2.0 mmHg) of the ester yielded 35.1 g (74% yield).

IR (NaCl, neat) 3088, 1640, 1735 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 6.72 (m, 1H), 4.21 (m, 4H), 2.23 (s, 3H), 1.29 (m, 6H). ¹³C NMR (50 MHz, CDCl₃) δ 167.6, 166.4.
144.2, 127.1, 62.0, 61.0, 14.6, 14.6, 14.5. High Res. MS calcd. 186.0892, found 186.0798.

Hydrolysis of Cyclobutane Ketal: 1,2-Diethylcyclobutanediacarboxylate

A mixture of diethyl 3,3-diethoxycyclobutane-1,2-dicarboxylate (1 g, 3.5 mmol) and 3 mL formic acid was stirred at room temperature for 30 min. Excess formic acid was removed under reduced pressure and the reaction mixture purified by vacuum distillation using a Kugelrohr apparatus (bp 108-112, 2 mmHg) to obtain a 75% yield.

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\text{IR (NaCl, neat) 2987, 1802, 1735, 1405 cm}^{-1}. \quad ^1\text{H NMR (200 MHz, CDCl}_3) \delta 4.50 \text{ (d, J=7.1 Hz, 1H), 4.15 \text{ (m, 4H), 3.62 \text{ (m, 1H), 3.41 \text{ (m, 2H), 3.22 \text{ (m, 1H), 2.50-2.89 \text{ (m, 2H), 1.25 \text{ (m, 6H).} \quad ^{13}\text{C NMR (50 MHz, CDCl}_3) \delta 195.5, 176.3, 172.9, 172.5, 165.0, 67.6, 61.9, 61.7, 60.8, 60.7, 50.5, 37.1, 35.3, 35.2, 34.8, 30.6, 14.1, 13.9. High Res. FAB/MS calcd. 214.0841, found 215.0912.}
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Alkylation of Cyclobutane Ketal: 3,3-Diethoxy-1-Methyl-1,2-Diethylcyclobutane Dicarboxylate

To a solution of diethyl 3,3-diethoxycyclobutane-1,2-dicarboxylate (1 g, 3.5 mmol) in 100 mL of dry tetrahydrofuran at -78 °C under argon was added 3.5 mL of 1.0 M sodium hexamethyldisilazane over a 5 min. period. After stirring for 20 min at -78 °C, methyl iodide (0.22 mL, 3.6 mmol) was added dropwise. The reaction mixture was stirred for an additional 30 min followed by stirring for 30 min. at room temperature. The mixture was washed with saturated NaCl and water (2x). The aqueous phase was back-extracted
with ether and the organic phases combined, dried over MgSO₄, and concentrated to a colorless oil. The oil was distilled at reduced pressure (bp 120-128.2 mmHg) using a Kugelrohr apparatus to afford 0.6 g (56.7% yield).

IR (NaCl, neat) 2991, 1737, 1439 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 4.15 (m, 8H), 3.31-3.62 (m, 2H), 2.32 (d, 1H), 1.20 (m, 15H). ¹³C NMR (50 MHz, CDCl₃) δ 172.1, 101.2, 60.6, 60.4, 58.2, 58.0, 57.3, 35.9, 29.9, 14.9, 14.8, 14.3, 14.1, 14.0. High Res. FAB/MS calcd. 228.1000, found 229.1076.

VINYL AMIDES

[2+2]-Cycloaddition of Vinyl Formamide with Tetracyanoethylene

The [2+2]-cycloaddition occurred spontaneously at -78 °C in ether. The solvent was removed under reduced pressure at -78 °C to avoid decomposition of the cyclobutane. A white powder was obtained in 55% yield.

¹H NMR (200 MHz, acetone-d₆) δ 8.37 (s, 1H), 5.59-5.40 (m, 1H), 3.90-3.78 (m, 1H), 3.64-3.50 (m, 1H), 2.90 (s, 1H).
[2+2]-Cycloaddition of Vinyl Acetamide with Tetracyanoethylene

The [2+2]-cycloaddition occurred spontaneously at —78 °C in ether. The solvent was removed at —78 °C and reduced pressure to avoid decomposition of the cyclobutane. The product, a white powder, was obtained in 63% yield.

$^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 8.50 (bs, 1H), 5.43-5.29 (m, 1H), 3.89-3.71 (m, 1H), 3.52-3.36 (m, 1H), 2.05 (s, 3H).

[2+2]-Cycloaddition of Vinyl Pyrrolidinone with Tetracyanoethylene

The [2+2]-cycloaddition occurred spontaneously at —78 °C in ether. The solvent was removed at —78 °C and reduced pressure to avoid decomposition of the cyclobutane. The product, a beige powder, was obtained in 72% yield.

$^1$H NMR (200 MHz, Acetone-$d_6$) $\delta$ 5.40 (t, 1H), 4.10-3.52 (m, 4H), 2.38 (t, 2H), 2.10 (m, 2H).

[2+2]-Cycloaddition of Vinyl Phthalimide with Tetracyanoethylene

The [2+2]-cycloaddition was conducted in acetonitrile and finished in 4 hours. The solvent was removed at reduced pressure at or below room temperature to avoid decomposition of the cyclobutane. The cyclobutane, an off-white powder, was obtained in 15% yield.

$^1$H NMR (200 MHz, acetone-$d_6$) $\delta$ 7.98 (s, 4H), 5.89 (t, 1H), 4.79-4.61 (dd, 1H), 4.02-3.79 (dd, 1H).
[2+2]-Cycloaddition of Vinyl Pyrrolidinone with Cyano fumarate

The reaction was carried out in acetonitrile at room temperature and finished in 8 hours. Removal of solvent under reduced pressure and recrystallization from ether/methylene chloride gave 88% yield of cyclobutane as white crystals.

IR (NaCl, neat) 2954, 2891, 2240, 1745, 1407 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 4.76-4.66 (dd, J= 8.50, 10.95 Hz, 1H), 3.88 (s, 3H), 3.68 (s, 3H), 3.69-3.55 (m, 1H), 3.49-3.31 (m, 2H), 2.64-2.53 (m, 2H), 2.52-2.31 (m, 2H), 2.20-2.01 (m, 2H). ¹³C NMR (50 MHz, CDCl₃) δ 175.9, 169.0, 166.5, 114.5, 54.1, 52.7, 52.2, 50.8, 44.9, 38.8, 30.7, 25.5, 18.7. High Res. FAB/MS calcd. 280.1059, found 281.1142.

[2+2]-Cycloaddition of Vinyl Pyrrolidinone with Methyl Dicyanoacrylate

The reaction was carried out in acetonitrile at room temperature and finished in 8 hours. Removal of solvent under reduced pressure and recrystallization from ether/methylene chloride gave 92% yield of cyclobutane as white crystals.

IR (NaCl, neat) 2954, 2246, 1745, 1407 cm⁻¹. ¹H NMR (200 MHz, CDCl₃) δ 5.07-4.97 (dd, J= 8.59, 11.03 Hz, 1H), 3.90 (s, 3H), 3.66-3.56 (m, 1H), 3.48-3.39 (m, 2H), 2.77-2.53 (m, 2H), 2.53-2.40 (m, 2H), 2.21-2.05 (m, 2H). ¹³C NMR (50 MHz, CDCl₃) δ 176.4, 167.6, 113.3, 111.8, 53.2, 51.6, 44.9, 41.0, 37.6, 30.7, 26.7, 18.6. High Res. FAB/MS calcd. 247.097, found 248.1029.
Alkylation of Cylcobutane Amides:

**MDA with Vinyl Pyrrolidinone**

Reaction of 2.0 g (8.1 mmol) of the cyclobutane with 1.5 g (8.5 mmol) triethyloxonium tetrafluoroborate in 5 mL of dry methylene chloride for 3.5 hours at -5 °C gave a quantitative yield of the pyrrolium tetrafluoroborate as a white solid.

IR (NaCl, neat) 1669 cm⁻¹. $^1$H NMR (200 MHz, CDCl₃) δ 5.09-4.95 (m, 1H), 4.30-4.01 (m, 2H), 3.88 (s, 3H), 3.57 (m, 1H), 3.49 (m, 2H), 3.21-2.81 (m, 3H), 2.59-2.48 (m, 1H), 2.41-2.22 (m, 1H), 1.61 (m, 3H).

**CNF with Vinyl Pyrrolidinone**

IR (NaCl, neat) 1655 cm⁻¹. $^1$H NMR (200 MHz, CDCl₃) δ 4.79-4.69 (m, 1H), 4.28-4.01 (m, 2H), 3.88 (s, 3H), 3.68 (s, 3H), 3.69-3.55 (m, 1H), 3.49-3.31 (m, 2H), 2.64-2.53 (m, 2H), 2.52-2.31 (m, 2H), 2.20-2.01 (m, 2H), 1.59 (m, 3H).

**Elimination**

To a solution of cyclobutane iminium salt in tetrahydrofuran, a solution of one molar equivalent of base in tetrahydrofuran was added. The reaction was followed by $^1$H NMR spectroscopy and after completion the mixture was concentrated. The residue was
diluted with ether, washed with saturated potassium chloride, and dried over magnesium sulfate. After, evaporation of the solvent, the oligomer of the bicyclobutane was obtained.

**5-Ethoxy-2H 3,4-dihydropyrrole (Lactim Ether)**

Bp, 139 °C/20 mmHg, IR (neat, NaCl) 1654 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) δ 1.28 (t, 3H), 1.60-2.20 (m, 2H), 2.15-2.56 (m, 2H), 3.53 (t, 2H), and 4.08 (q, 2H).

**MISCELLANEOUS COMPOUNDS**

**Vinyloxy p-Tolylsulfonate**

The enolate of acetaldehyde was prepared following the method described by Bates. To the enolate of acetaldehyde in tetrahydrofuran at room temperature was added p-toluenesulfonyl chloride at once. The reaction mixture was stirred for 2 hours and then poured over ice. The aqueous phase was extracted with methylene chloride and the combined organic layers dried over magnesium sulfate. The vinyl sulfonate was obtained in 78% yield.

¹H NMR (200 MHz, Acetone-d₆) δ 7.78 (d, 2H), 7.33 (d, 2H), 6.59 (dd, 1H), 4.91-4.82 (dd, 1H), 4.65 (m, 1H), 3.70 (s, 3H).
2-(Vinyloxy)tetrahydropyran

In an Erlenmeyer flask, 59 mL of benzene, 17 mL of a 50% NaOH solution, (2.9 g 0.014 mol), and tetra-n-butylammonium acid sulfate (TBAS, 4.80 g, 0.014 mol) were magnetically stirred for 6 h at 50 °C. The organic phase, recovered and washed with water, was dried (K$_2$CO$_3$). Distillation gave chemically pure product (1.70 g, 95%) having bp 105 °C (18 mmHg).

IR 2940, 2880, 2830, 1640, 1440, 1380, 1370 cm$^{-1}$, $^1$H NMR (CDCl$_3$, 50 MHz) $\delta$ 6.6-6.0 (dd, 1 H), 5.0-4.7 (m, 1H), 4.6-4.2 (dd, 1H), 4.1-3.8 (dd, 1H), 3.8-3.2 (m, 2H), 2.0-1.2 (m, 6H); $^{13}$C NMR (CDCl$_3$, 200 MHz) $\delta$ 148.98, 97.71, 90.88, 61.87, 29.63, 25.05, 18.61.
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