Title: PART I. REACTIONS OF 2-ISOPROPOXYMETHYLENYECYCLO-
HEXANONE WITH ORGANOMETALLIC REAGENTS.
PART II. THERMAL REARRANGEMENTS OF ETHYL 3-(2-
VINYL CLOHEXEN-1-YL)PROPENOATE AND 1-VINYL-2-
PROPENYLIDENECYCLOHEXYL METHYL ETHER.

Abstract approved: ____________________________
Elliot N. Marvell

In a continuing study of the cyclization of cis 1,3,5-
hexatrienes, ethyl trans-3-(2-vinyl-1-cyclohexenyl)propenoate was synthesized and its rate of cyclization to 2-carb-ethoxy-2,3,4,6,7,8-hexahydronaphthalene via 2-carbethoxy-2,3,5,6,7,8-hexahydronaphthalene was determined over a temperature range of 125-150°C. The rate (k = 5.77 x
10^{-5} \text{ sec}^{-1} \text{ at } 130^\circ \text{C}) represented no change from that of the unsubstituted 1,2-divinylcyclohexane. The activation para-
meters, \Delta H^\dagger and \Delta S^\dagger (at 130^\circ \text{C}) were 26.2 kcal/mole and -14 cal/mole / ^\circ \text{K}^{-1}, respectively. Mechanistic implications,
including a transition-state geometry, are drawn in light of these and previous results.

Synthetic investigations directed toward cis-2-phenyl-1,3,5-hexatriene led to the discovery of an abnormal Wittig reaction between α-styryl-triphenylphosphonium methylide and acrolein to give 2-phenyl-1,3-cyclohexadiene. While a mechanism which involves a Michael addition of the Wittig reagent to the α,β-unsaturated carbonyl has been suggested for similar additions to esters and ketones, an alternative mechanism involving "normal" addition followed by a Cope rearrangement of the resultant betaine is proposed for the aldehyde.

Alkylation of hydroxymethylenecyclohexanone was found to give both 2-isopropoxymethylenecyclohexanone and 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde. Pure 2-isopropoxymethylenecyclohexanone was found to undergo conjugate additions with the following reagents (products in parentheses): lithium dimethylcopperate (2-isopropylcyclohexanone), ethylmagnesium bromide (2-(3-pentyl)cyclohexanone), vinylmagnesium bromide (2-propenylidene-1-vinylcyclohexanol) and 1-propynylmagnesium bromide (2-(2-butynylidene)-1-(1-propynyl)cyclohexanol). Reaction of 2-isopropoxymethylenecyclohexanone with sodium acetylide and vinylmagnesium gave 1,2-addition only.

Finally, 2-propenylidene-1-vinylcyclohexanol was found to rearrange to 1-(3-acetoxy-1-propenyl)-2-vinylcyclohexene in acetic acid. Pyrolysis of the methyl ether
of 2-propenylidene-1-vinylcyclohexanol at 350°C gave rise to loss of formaldehyde followed by rearrangement of the two resulting trienes to give 3-ethylidene-2-(1-propenyl)-cyclohexene and 2-methyl-1,2,3,5,6,7-hexahydronaphthalene.
Part I: Reactions of 2-Isopropoxymethylene cyclohexanone with Organometallic Reagents.

Part II: Thermal Rearrangements of Ethyl 3-(2-Vinylcyclohexen-1-yl)propenoate and 1-Vinyl-2-propenylidene-cyclohexyl Methyl Ether.

by

Michael Franklin Cleary

A THESIS

submitted to

Oregon State University

in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

Completed January 30, 1975

Commencement June 1975
APPROVED:

Redacted for privacy

Professor of Chemistry, in charge of major

Redacted for privacy

Head of Chemistry

Redacted for privacy

Dean of Graduate School

Date thesis is presented January 20, 1975

Typed by Kathleen C. Cleary for Michael Franklin Cleary
TABLE OF CONTENTS

INTRODUCTION

HISTORICAL
I. Thermal reactions of the cis-1,3,5-Hexatriene series.
   A. Synthesis
   B. Thermal Chemistry
      1. General Considerations
      2. Rate Data
      3. Mechanistic Interpretations
      4. Calculated Transition State Geometry
II. Competitive 1,2 and 1,4 Addition to 2-Isopropoxymethylene cyclohexanone.
   A. Conjugate Addition of Organometallic Reagents to \( \alpha,\beta \)-Unsaturated Carbonyls.
   B. Nature of the \( \alpha,\beta \)-Unsaturated Substrate.

RESULTS AND DISCUSSION

INTRODUCTION

I. The Synthesis and Thermolysis of Ethyl 3-(2-Vinyl-1-cyclohexenyl)propanoate.
   A. Synthesis
   B. Thermolysis
      Kinetics
      Mechanistic Implications
II. Synthetic Approach Directed Toward cis 2-Phenyl-1,3,5-hexatriene.
III. Reactions of 2-Isopropoxymethylene cyclohexanone with Organometallic Reagents.
IV. Further Reactions of the Derivatives of 2-Isopropoxymethylene cyclohexanone.

EXPERIMENTAL

INTRODUCTION

2-Hydroxymethylene cyclohexanone (9) & 2-Isopropoxymethylene cyclohexanone (10) &
2-Isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (12)
3-Ethynyl-3,4,5,6-tetrahydrobenzaldehyde (19)
2-Vinyl-3,4,5,6-tetrahydrobenzaldehyde (17)
Triethyl Phosphonoacetate
Ethyl 3-(2-vinyl-1-cyclohexenyl)propanoate (16)
Thermolysis of 16
\( \alpha \)-(Bromomethyl)styrene (21)
2-Phenyl-2-propenyltriphenyolphosphonium bromide
<table>
<thead>
<tr>
<th>Reaction of acrolein with α-styryl triphenylphosphonium methylide</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogenation of 2-phenyl-1,3-cyclohexadiene (36)</td>
<td>105</td>
</tr>
<tr>
<td>1-Phenylcyclohexene (26)</td>
<td>106</td>
</tr>
<tr>
<td>Phenylcyclohexane (27)</td>
<td>107</td>
</tr>
<tr>
<td>4-Benzyloxy cyclohexanol (30)</td>
<td>108</td>
</tr>
<tr>
<td>4-Benzyloxy cyclohexanone (31)</td>
<td>108</td>
</tr>
<tr>
<td>4-Benzyloxy-1-phenylcyclohexene (32)</td>
<td>109</td>
</tr>
<tr>
<td>4-Phenyl-3-cyclohexanol (33)</td>
<td>110</td>
</tr>
<tr>
<td>S-Methyl xanthate ester of 4-phenyl-3-cyclohexenol (34)</td>
<td>110</td>
</tr>
<tr>
<td>1-Phenyl-1,3-cyclohexadiene (28) and 1-phenyl-1,4-cyclohexadiene (35)</td>
<td>111</td>
</tr>
<tr>
<td>Vinyl bromide</td>
<td>112</td>
</tr>
<tr>
<td>2-(2-propenylidene)-1-vinylcyclohexanol (37)</td>
<td>112</td>
</tr>
<tr>
<td>2-Allylcyclohexanone (39)</td>
<td>113</td>
</tr>
<tr>
<td>2-Propylcyclohexanone (40)</td>
<td>114</td>
</tr>
<tr>
<td>1-Ethyl-2-propylcyclohexanol (38)</td>
<td>114</td>
</tr>
<tr>
<td>Hydrogenation of 37</td>
<td>115</td>
</tr>
<tr>
<td>Reaction of 10 with ethylmagnesium bromide</td>
<td>115</td>
</tr>
<tr>
<td>A. Excess Grignard Reagent</td>
<td>115</td>
</tr>
<tr>
<td>B. Inverse Addition of Grignard Reagent</td>
<td>116</td>
</tr>
<tr>
<td>3-(2-Butynylidene)-2-(1-propynyl)cyclohexene (44)</td>
<td>116</td>
</tr>
<tr>
<td>Reaction of 10 with lithium dimethylcuprate</td>
<td>117</td>
</tr>
<tr>
<td>1-(3-Acetoxy-1-propenyl)-2-vinylcyclohexene (46)</td>
<td>118</td>
</tr>
<tr>
<td>Methyl 2-propenylidene-1-vinyl-1-cyclohexyl ether (47)</td>
<td>119</td>
</tr>
<tr>
<td>Pyrolysis of 47</td>
<td>120</td>
</tr>
<tr>
<td>1-Ethyl-2-propylcyclohexene (50)</td>
<td>123</td>
</tr>
<tr>
<td>1-Ethyl-2-propylcyclohexane (49)</td>
<td>124</td>
</tr>
<tr>
<td>Photolysis of 47</td>
<td>124</td>
</tr>
</tbody>
</table>

BIBLIOGRAPHY | 126  |
LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Substituent effect on composition of 1,3,5-hexatrienes formed on elimination.</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Relative rates for electrocyclization of trienes using cis-hexatriene as a standard.</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>Enthalpies of formation of 2-butene and 2-pentenes ( \Delta H^O_T ) (kcal/mole).</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>Reaction of lithium dimethylcuprate with ( \beta )-acetoxy-( \alpha,\beta )-unsaturated carbonyls.</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>Kinetic results of the cyclization of ethyl trans-3-(2-vinyl-1-cyclohexenyl)propenoate.</td>
<td>52</td>
</tr>
<tr>
<td>6</td>
<td>Proton magnetic resonance spectral comparison of ( 16 ) and ( H_6 ).</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>Kinetic data.</td>
<td>103</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Production of cis-1,3,5-hexatrienes via semi-hydrogenation.</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Formation of 1- and 3-substituted cis-1,3,5-hexatrienes.</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Steric interaction between non-bonded hydrogens in 1-styryl-2-vinylcyclohexene.</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>Conformational equilibrium leading to the cyclization of cis-1,3,5-hexatrienes - C.W.Spangler.</td>
<td>17</td>
</tr>
<tr>
<td>5</td>
<td>An ORTEP II plot of the Cs symmetry transition state.</td>
<td>22</td>
</tr>
<tr>
<td>6</td>
<td>Alkylation of 2-hydroxymethylene cyclohexanone and its isopropyl ether - Dreiding and Nickel.</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>Formal 1,4 addition of an acetylenic organocopper reagent.</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>Synthesis of ethyl 3-(2-vinylcyclohexen-1-yl)propenoate.</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>Pmr spectrum of ethyl trans-3-(2-vinylcyclohexenyl)propenoate.</td>
<td>49</td>
</tr>
<tr>
<td>10</td>
<td>Thermolysis of ethyl trans-3-(2-vinyl-1-cyclohexenyl)propenoate.</td>
<td>53</td>
</tr>
<tr>
<td>11</td>
<td>Cyclization of cis-1,3,5-hexatrienes showing transition-state geometry and p-orbital utilization.</td>
<td>56</td>
</tr>
<tr>
<td>12</td>
<td>Synthesis of 1-phenyl-1,3-cyclohexadiene and 1-phenyl-1,4-cyclohexadiene.</td>
<td>60</td>
</tr>
<tr>
<td>13</td>
<td>Mechanistic proposal for the formation of the abnormal Wittig adduct - W.G.Dauben.</td>
<td>62</td>
</tr>
<tr>
<td>14</td>
<td>Production of abnormal Wittig product via a Cope rearrangement.</td>
<td>64</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>15</td>
<td>Pmr spectrum of 3-(2-butynylidene)-2-(1-propynyl)cyclohexene.</td>
<td>75</td>
</tr>
<tr>
<td>16</td>
<td>Reactions of 2-isopropoxymethylene cyclohexanone described in this work.</td>
<td>78</td>
</tr>
<tr>
<td>17</td>
<td>Proton magnetic resonance spectrum of 1-(3-acetoxy-1-propenyl)-2-vinylcyclohexene.</td>
<td>84</td>
</tr>
<tr>
<td>18</td>
<td>Proton magnetic resonance spectrum of the pyrolysis product of methyl 2-propenylidene-1-vinyl-cyclohexyl ether.</td>
<td>89</td>
</tr>
</tbody>
</table>
PART I. REACTIONS OF 2-ISOPROPXYMETHYLENECYCLOHEXANONE WITH ORGANOMETALLIC REAGENTS.

PART II. THERMAL REARRANGEMENTS OF ETHYL 3-(2-VINYLCYCLO-HEXEN-1-YL)PROPENOATE AND 1-VINYL-2-PROPENYLDENECYCLOHEXYL METHYL ETHER.

INTRODUCTION

Our continuing interest in the ring closure of cis-1,3,5-hexatrienes led us to investigate the effect of an electron-withdrawing substituent on the terminal carbon. The synthetic investigations directed toward 16 involved the use of 10 as an intermediate. This compound provided such interesting chemistry that a major portion of this thesis is devoted to the reactions of 10 with various organometalllic reagents.

Another synthetic investigation directed toward 23 revealed an unexpected reaction of a Wittig reagent with an
Finally, two of the derivatives of 10, 37 and 47, produced some interesting chemistry of their own – the former an acid-catalyzed rearrangement and the latter a pyrolytic fragmentation and rearrangement.

Thus, the discussion is actually divided into four parts instead of the two indicated by the title.
I. Thermal Reactions of the cis-1,2,5-Hexatriene Series.

Over the past decade, some 20 man-years have been devoted to the study of the cyclization of 1,3,5-hexatrienes in this laboratory alone. An attempt by this writer to cover fully all of this work would be a disservice, both to those workers and to the reader. While parts of that work will be presented, we would refer the interested reader to the doctoral thesis of James L. Platt for a more complete compilation of data and historical background up to 1969.

A. Synthesis.

Two special objectives dominate our triene syntheses: first, the development of the proper double bond stereochemistry and, second, the attainment of the desired substitution pattern. In almost all cases, formation of the middle cis double bond is the crucial step.

In our laboratory, two routes have been devised for the synthesis of that cis double bond. The first route, shown in Figure 1, involves hydrogenation of a triple bond to produce, stereoselectively, the appropriate cis double bond. The fact that the enyne rather than the dienyne is chosen for hydrogenation is a result of careful study of the semi-hydrogenation of these conjugated
systems.

\[
\begin{align*}
R_1-\text{CH}=&\text{CR}_2-\text{C}=&\text{H} &\xrightarrow{1.\text{LiNH}_2} &R_1\text{CH}=&\text{CR}_2-\text{C}=&\text{CH}_2-\text{CHR}_3 \\
2.\text{R}_3\text{CH}=&\text{CH}_2 & &\xrightarrow{1.})\text{TsCl/py} &R_1\text{CH}=&\text{CR}_2-\text{CH}=&\text{CH}=&\text{CH}_2-\text{CHR}_3 \\
&\xrightarrow{2.})\text{Me}_3\text{CO}^{-}, & &\xrightarrow{\text{DMSO}} &R_1\text{CH}=&\text{CR}_2-\text{CH}=&\text{CH}=&\text{CHR}_3
\end{align*}
\]

Figure 1. Production of cis 1,3,5-hexatrienes via semi-hydrogenation.

The other route used in this laboratory makes use of the cis-geometry required of the cyclohexene double bond. The starting material, 1,2-cyclohexanedione (1) is twice alkylated with vinyllic Grignard reagents and the resulting diol eliminated with diphosphorus tetraiodide.
This approach has little value if one wishes to vary the substitution pattern on the central double bond, but it is well suited to the formation of trienes with substitution at the other positions. Yields are modest\(^3\),\(^5\) but only one isomer is obtained.

For the preparation of trienes with substitution patterns about the central double bond, C.W. Spangler\(^6\),\(^7\),\(^8\) used the method shown in Figure 2, which he adopted from previous workers\(^9\).

![Chemical Reaction Equation]

\[ \begin{align*}
\text{OH} & \quad \text{R}_1\text{CH} = \text{CH}\text{CCH}_2\text{CH} = \text{CH} \quad \text{R}_2
\begin{array}{c}
\text{1.)PBr}_3 \\
\rightarrow \\
\text{2.)Me}_2\text{NCH}_2\text{Ph}, \\
\text{MePh}
\end{array}
\rightarrow \\
\text{(CH}_3\text{)}_2\text{NCH}_2\text{Ph Br}^-
\rightarrow \\
\text{R}_1\text{CH} = \text{CH}\text{CCH}_2\text{CH} = \text{CH}_2
\end{align*} \]

\[ \begin{align*}
\text{NaOH} & \quad \Delta, \text{H}_2\text{O} \\
\rightarrow \\
\text{R}_1\text{CH} = \text{CH}\text{CH} = \text{CHCH} = \text{CH}_2
\end{align*} \]

Figure 2. Formation of 1- and 3-substituted \textit{cis}-1,3,5-hexatrienes.

Table 1. Substituent effect on composition of 1,3,5-hexatrienes formed on elimination.

<table>
<thead>
<tr>
<th>Substituents</th>
<th>Composition, %\textit{cis} (central double bond)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R(_1)=H; R(_2)=Me</td>
<td>45</td>
</tr>
<tr>
<td>R(_1)=H; R(_2)=Et</td>
<td>65</td>
</tr>
<tr>
<td>R(_1)=H; R(_2)=iPr</td>
<td>75</td>
</tr>
</tbody>
</table>
Table 1, cont.

<table>
<thead>
<tr>
<th>Substituents</th>
<th>Composition, %\textsubscript{cis} (central double bond)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( R_1=H; R_2=tBu )</td>
<td>100</td>
</tr>
<tr>
<td>( R_1=\text{trans Me}; R_2=H )</td>
<td>44</td>
</tr>
<tr>
<td>( R_1=\text{trans Et}; R_2=H )</td>
<td>32</td>
</tr>
<tr>
<td>( R_1=\text{trans iPr}; R_2=H )</td>
<td>0</td>
</tr>
<tr>
<td>( R_1=\text{trans t-Bu}; R_2=H )</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1 reveals the main problem of this approach - the competitive, and sometimes preponderant, formation of the \textit{trans} isomer.

A. Padwa\textsuperscript{10,11} has used a Wittig reaction in the formation of the four isomeric 1,2,6-triphenyl-1,3,5-hexatrienes whose central double bonds are in a \textit{cis}-geometry.

![Wittig reaction diagram]

The Wittig reaction has been reviewed in depth by M. Schlosser\textsuperscript{12} and, for our purposes, he may be summarized as saying that resonance stabilized ylides (such as \( \Phi_3\text{P-CHCO}_2\text{Et} \)) react with aldehydes to give almost exclusively \textit{trans} olefins, while non-stabilized ylides react to give
cis olefins, particularly in salt-free non-polar solvents (Schlosser modification\textsuperscript{13}). Although somewhat at variance with Schlosser's mechanistic interpretations, W. Schneider, in a contemporary work\textsuperscript{14} reiterates those principles. The fact that Padwa's Wittig ylide, \(\overset{\text{O}}{\overset{\text{O}}{\text{CH=CHCHP\textsubscript{3}}}}\), seems to be an unlikely candidate for a nonstabilized ylide, coupled with the observation that he used neither a salt-free environment nor a non-polar solvent, makes the production of the cis olefin a fortuitous happenstance. This suggests that these systems show more of a tendency to give the cis isomer (in a Wittig reaction) than we had suspected.

This then gives four routes by which cis-1,3,5-hexatrienes have been synthesized. In any given synthesis, the method of choice depends largely upon the desired substitution pattern - e.g., one would not consider semi-hydrogenation as a route to 3- or 4-substituted hexatrienes. One last consideration is that 2- and 5-substituted hexatrienes may cyclize so readily that the latter stages of their syntheses and purification must take this into account. For instance, 2,5-dicarbethoxy-1,3,5-hexatriene (2) has a half life of ten minutes at 20\(^{\circ}\)\textsuperscript{15}.

B. Thermal Chemistry

1. General Considerations. The thermal cyclization of cis-1,3,5-hexatriene is the classic textbook example of
a Woodward-Hoffmann concerted, disrotary electrocyclic reaction. The experimental results bear out the theory perfectly.

\[ \text{The trans, cis, trans-octatriene (2) gives only cis-dimethylcyclohexadiene (4); trans, cis, cis-octatriene (5) gives the trans dimethyl isomer (6) but at a rate about two orders of magnitude slower, owing to steric interactions of the cis methyl group. In fact, the cis-methyl interaction is so severe that the cyclization reaction of all cis 2,4,6-octatriene is supplanted by a 1,7 hydrogen shift.} \]

The experimental value for the energy difference between 1,3,5-hexatriene (7) and 1,3-cyclohexadiene is -14.5 kcal, which is mentioned only to assure the reader that the reverse reaction (ring opening) need not be considered when discussing rate data. Activation parameters
vary with substituent effects, but $\Delta H^\ddagger$ values (not including 2- or 5-substituted trienes) range from 25 to 30 kcal/mole while $\Delta S^\ddagger$ is predictably negative - generally on the order of -5 to -10 eu. More will be said of these numbers and their implications about transition-state geometry in the next section.

2. Rate data. The following table, taken largely from Reference 2, gives a listing of reaction rates.

Table 2. Relative rates for electrocyclization of trienes using cis-hexatriene as a standard.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rel. Rate</th>
<th>$\Delta H^\ddagger$ kcal/mole</th>
<th>$\Delta S^\ddagger$ eu</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.0</td>
<td>29.0</td>
<td>-5</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>29.0</td>
<td>-7</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>0.01</td>
<td>32.0</td>
<td>-5</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>0.03</td>
<td>32.0</td>
<td>-14</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>3.0</td>
<td>29.0</td>
<td>-6</td>
<td>2</td>
</tr>
</tbody>
</table>
Table 2 cont.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rel. Rate</th>
<th>$\Delta H^\ddagger$ kcal/mole</th>
<th>$\Delta S^\ddagger$ eu</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>3.0</td>
<td>29.0</td>
<td>-1</td>
<td>2</td>
</tr>
<tr>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>0.02</td>
<td>33.0</td>
<td>-5</td>
<td>2</td>
</tr>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
<td>1.3</td>
<td>25.0</td>
<td>-15</td>
<td>2</td>
</tr>
<tr>
<td><img src="image4" alt="Chemical Structure" /></td>
<td>1.2</td>
<td>28.0</td>
<td>-8</td>
<td>2</td>
</tr>
<tr>
<td><img src="image5" alt="Chemical Structure" /></td>
<td>0.005</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><img src="image6" alt="Chemical Structure" /></td>
<td>1.5</td>
<td>27.4</td>
<td>-18</td>
<td>5</td>
</tr>
<tr>
<td><img src="image7" alt="Chemical Structure" /></td>
<td>1.2</td>
<td>25.0</td>
<td>-18</td>
<td>2</td>
</tr>
<tr>
<td><img src="image8" alt="Chemical Structure" /></td>
<td>0.03</td>
<td></td>
<td></td>
<td>23</td>
</tr>
</tbody>
</table>
Table 2 cont.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rel. Rate</th>
<th>$\Delta H^\ddagger$ kcal/mole</th>
<th>$\Delta S^\ddagger_{\text{eu}}$</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ca $2 \times 10^3$</td>
<td></td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>C</td>
<td>1.2</td>
<td></td>
<td></td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>ca $2 \times 10^6$</td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>ca $3 \times 10^5$</td>
<td></td>
<td></td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>1.4$ \times 10^3$</td>
<td>20.0</td>
<td>-17.5</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>0.02</td>
<td>27.4</td>
<td>-19.0</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>28.9</td>
<td>-5</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>26.1</td>
<td>-12</td>
<td>6</td>
</tr>
</tbody>
</table>
Table 2 cont.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Rel. Rate</th>
<th>$\Delta H^\circ\text{ kcal/mole}$</th>
<th>$\Delta S^\circ\text{ eu}$</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="structure1" /></td>
<td>1.9</td>
<td>27.8</td>
<td>-6.2</td>
<td>6</td>
</tr>
<tr>
<td><img src="image2" alt="structure2" /></td>
<td>5.0</td>
<td>26.0</td>
<td>-11.3</td>
<td>6</td>
</tr>
<tr>
<td><img src="image3" alt="structure3" /></td>
<td>25</td>
<td>26.7</td>
<td>-11.3</td>
<td>6</td>
</tr>
</tbody>
</table>

3. Mechanistic Interpretations. The above data may be summarized by the following statements about substituent effects:

1. Weakly electron-donating groups on the terminal carbons in a trans position have a negligible effect upon the reaction rate.

2. The same groups in a cis position on the terminal carbons tend to retard the rate at least two orders of magnitude, depending largely upon the steric bulk of the substituent.

3. Radical stabilizing groups on C-2 or C-5 show a marked rate enhancement with the exception of compound 8.

4. Alkyl substituents at C-3 or C-4 display a modest rate enhancement.

These observations, respectively, have been interpreted
in the following manner:

1. In the transition state, C-1 and C-6 do not possess appreciable residual p-orbital character which would be stabilized by electron-donating groups.

2. The effect of the cis terminally substituted olefins is mainly steric in nature.

3. The p-orbitals on C-2 and C-5 are isolated in the transition state and are readily stabilized by resonance interaction. The lack of enhancement in 1-(cis-styryl)-2-vinylcyclohexene (8) has been attributed to steric interaction between the phenyl group and two of the allylic hydrogens on the cyclohexene ring. See Figure 3.

![Figure 3. Steric interaction between non-bonded hydrogens in 1-styryl-2-vinylcyclohexene.](image)

A maximum stabilizing effect will occur when the p-orbital on C-2 is parallel with the p-orbital on the phenyl ring.
The two hydrogens shown prevent the phenyl group from rotating into a position of maximum stabilization.

Actually, Figure 3 represents a ground state conformation while the argument must refer to the transition state. The transition-state geometry which will be presented is similar to that shown in Figure 3 with similar non-bonded interactions of the phenyl hydrogens. In fact, models indicate that the o-hydrogens of the phenyl group may interact with the axial hydrogen on the carbon β to the double bond.

4. Substituent effects on C-3 and C-4 have been attributed to inductive effects of the alkyl substituents.

Of these four statements, the second and third do not lie within the scope of this thesis, and the first will be enlarged upon in the "Discussion" section. This, then, leaves the fourth statement, credited to C.W. Spangler, to be discussed at this point.

Spangler's observations, the last five entries in Table 2, were summarized as:

"...It appears that introduction of an electron-donating group in the 3-position, relatively remote from the reaction centers, increases the cyclization rate: 3-t-Bu > 3-Et > 3-Me. Similarly, introduction of the same group in the 1-position, a reaction site, has a much smaller effect on the overall rate: 1-Et > 1-Me-H...."

These results he interpreted as the manifestation of a
combination of three possible effects:

"(1) an increase in the polyene-π-electron density by introduction of a substituent electron-donating group remote from the reaction center will increase the rate of ring closure and lower the activation enthalpy;

(2) introduction of a group in the 3 position will alter the relative amounts of s-trans and s-cis conformations, thereby allowing an increase in cyclization rate as the relative percentage of s-cis conformations increase;

(3) introduction of a group in the 1 position leads only to a very slight increase in rate, and no meaningful reduction in the enthalpy owing to a competing steric retardation at the reaction sites. That this retardation is not more dramatic supports our contention that alkyl groups are acting as electron donors in this retardation."  

Actually, he alluded to a fourth explanation, that of differences in relative ground state energies, but discarded this as not being sufficient to explain the differences in activation enthalpies (3 kcal/mole).

The second point needs some elaboration. Spangler refers the reader to the work of D. Craig on the Diels
Alder reaction of 2-alkyl-1,3-butadienes with maleic anhydride.

As the steric bulk of the R group (on the 2-position of the butadiene) increases (H, Me, Et, iPr, t-Bu) so does the rate of the reaction. Thus the rate enhancement was attributed to the increasing stability of the s-cis conformation, required for the reaction.

Spangler concluded that a similar effect in the 3-alkylhexatrienes may be operative but affects only the 1,2 double bond and offers no such "assistance" to the 5,6 double bond. To this end, he drew the following diagram (Figure 4) in terms of required conformations:
s-trans, s-trans  \[\rightarrow C_n \rightarrow\]  s-cis, s-cis

\(C_n\) = other intermediate conformations.

Figure 4. Conformational equilibrium leading to the cyclization of cis 1,3,5-hexatrienes - C.W. Spangler.

Herein lies one of the common pitfalls in thinking about the hexatriene cyclization, the temptation to picture the reactive form of the triene system as an aromatic (benzene) ring with but a missing single bond. If one were to place the s-cis, s-cis conformation on the reaction potential surface, one would find it high on the slopes looking down upon both the valley of the ground state and the pass of the transition state. This is due to the fact that the "missing link" of the aromatic ring has been replaced by two carbon-hydrogen bonds. The planar s-cis, s-cis conformation, in order to keep these hydrogens from occupying the same space at the same time, must distort the normal \(sp^2\) bond angle of \(120^\circ\) considerably.
If we assign normal carbon-carbon and carbon-hydrogen bond lengths, keep the hydrogens separated by the sum of their van der Waals radii, and assume the six internal angles are equal, a little trigonometry gives a value of 137.2° for these angles. This amounts to a deformation of 17.2° from the expected angle of 120°. Angle deformation, \( \Delta \theta \), is related to strain energy by the following equation:\(^{30}\)

\[(17.5 \text{ cal/mole}) \ (\Delta \theta)^2 = \text{Strain Energy}\]

This gives a total strain energy of 31.1 kcal for the six angles, which would account for the entire enthalpy of activation without considering any of the other factors involved. The system can relieve some of the strain by rotating the hydrogens out of the plane of the six carbons, and the above value should be considered as a maximum.

A basic difference between this reaction and the Diels Alder reaction studied by Craig is that, in order for the cyclo-addition to occur, the diene must be in the s-cis
conformation when it encounters the dienophile and factors which promote the $s$-$cis$ conformation enhance the rate of reaction. For the electrocyclic reaction, factors which encourage an $s$-$cis$ conformation affect the rate only to the extent that they raise the ground state energy. Notwithstanding the fact that Spangler has chosen to compare a unimolecular process with a bimolecular one, it makes no more sense to write a planar (benzene-like) transition state for the hexatriene cyclization than it does to write one for the Diels Alder reaction, either in terms of steric hindrance or p-orbital utilization (Woodward-Hoffmann sense) to form new $\sigma$-bonds. We have chosen to think of the reaction pathway in terms of an $s$-$trans$, $s$-$trans$ conformation proceeding with simultaneous disrotation of the $C_2$-$C_3$ and $C_4$-$C_5$ bonds. Bulky groups attached to the 3 or 4 position may "urge" the ground state up this pathway.

Spangler's third possible explanation, that weakly electron-donating alkyl groups on the terminal carbons do exhibit a rate enhancement but that it is obscured by an opposing retardation due to steric effects, is at variance with our previously developed model. Since Spangler himself found that the 1-ethyl triene cyclization shows a twofold enhancement over the corresponding 1-methyl triene cyclization, one should then infer that either the methyl group is sterically less bulky or the ethyl group has more inductive stabilizing effect than the methyl group.
Interestingly, there is some evidence that the ethyl and methyl groups have comparable steric bulk. Table 3 presents enthalpies of formation of cis- and trans-2-butene and 2-pentene.

Table 3. Enthalpies of formation of 2-butenes and 2-pentenes

<table>
<thead>
<tr>
<th></th>
<th>cis</th>
<th>trans</th>
<th>ΔH_f^0 (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-butene</td>
<td>-1.86 ± .20</td>
<td>-2.99 ± .18</td>
<td>-1.13 ± .38</td>
</tr>
<tr>
<td>2-pentene</td>
<td>-7.00 ± .26</td>
<td>-7.93 ± .26</td>
<td>-0.93 ± .52</td>
</tr>
</tbody>
</table>

The difference between cis- and trans-2-butene represents steric interaction of two methyl groups, while the 2-pentenes correspond to a methyl-ethyl interaction. Thus, within experimental error, the cis methyl-methyl and methyl-ethyl interactions are the same.

Using Spangler's results, the 1-methyl triene cyclization rate is slightly slower (k_{rel} = 0.8) than the unsubstituted triene, while the 1-ethyl triene cyclizes about twice as fast (k_{rel} = 1.9). Since the steric bulk of these substituents is about the same, and if one subscribes to Spangler's interpretation, then an ethyl group must be significantly more of an electron-donor than a methyl group. Though the σ*(polar substituent effect from the Taft equation) of ethyl (-0.10) and methyl (0.00) substituents indicate that an ethyl group has more electron-donating character than a methyl group, it is doubtful whether this difference
in $\sigma^*$ is sufficient to explain the observed rates. The investigation of a triene with an electron-withdrawing group at the terminal position should clarify the electronic effects of C(1) substituents.

4. Calculated transition state geometry. W.C. Herndon has presented a comprehensive review\textsuperscript{33} entitled "The Theory of Cycloaddition Reactions", the purpose of which was to "review and summarize the applications of theoretical principles and calculations to cycloaddition reactions". (These also include electrocyclic reactions.) This article gives a background for the various methods of calculation. For further information on theoretical calculations, the reader is referred to this article.

Transition state geometry for the cyclization of cis-1,3,5-hexatriene (7) has been calculated by three methods\textsuperscript{21, 34, 35} all of which involve potential energy surfaces.

The first method\textsuperscript{21} that of intersecting potential energy surfaces (for product and reactant), which tends to present a transition state that is an average of the products and reactant, offered a non-symmetric transition state with reasonably accurate activation parameters.

The second calculation\textsuperscript{34} from this laboratory, post-dated Herndon's article and presented a simplified approach to empirical reaction surfaces. The reaction geometry was described in terms of two sets of coordinates with three parameters each. The parameters used were $\theta$, a rotation
about the C$_2$-C$_3$ \((C_4-C_5)\) bond; \(\omega\), a rotation about the C$_1$-C$_2$ \((C_5-C_6)\) bond; and \(\eta\), to describe the change in hybridization of C$_1$ \((C_6)\) in going from sp$^2$ to sp$^3$. The rotation angle \(\Theta\) was used as the reaction coordinate. Energies calculated included the pi system, the forming sigma bond, and strain energy which included non-bonded interactions. Initial calculations produced no energy maximum, but judicious adjustment of the Hückel \(\beta\) term (only within the narrow confines of good chemical sense) produced an energy maximum with \(\Theta \approx 135^\circ\) in a symmetrical transition state with considerable C$_1$-C$_6$ bond formation. The disrotatory path was the favored course.

Most recently, the system has been subjected to a rigorous MINDO/2 treatment$^{35}$ which tends to overestimate the stability of cyclic systems$^{33}$. Other than a \(\Delta H^0\) of reaction which was some 17 kcal too large, the calculated parameters agreed with experimental values and predicted a disrotatory pathway via a C$_s$ symmetric transition state (Figure 5) as in the previous work.

Figure 5. An ORTEP II plot of the C$_s$ symmetry transition state.
II. Competitive 1,2 and 1,4 addition to 2-isoproxydromethyl-
enecyclohexanone.

In 1954, Dreiding and Nickel\textsuperscript{36} reported a series of
reactions of 2-hydroxymethylene
enecyclohexanone (9) and its
isopropyl ether (10) with organometallic reagents. Figure
6 summarizes these reactions.

\begin{center}
\includegraphics[width=\textwidth]{figure6.png}
\end{center}

Figure 6. Alkylation of 2-hydroxymethylene
cyclohexanone and its isopropyl ether. – Dreiding and Nickel.\textsuperscript{36}

While these reactions appear to offer access to a number of
substituted cyclohexanes and cyclohexanones, the use of alkyl
ethers of 2-hydroxymethylene
cyclohexanone as synthetic
intermediates is relatively rare. Actually, the enol ether was originally produced to protect one of the carbonyl functions of a \( \beta \)-dione while the other is left in reactive form. The enol ether can then be cleaved with acid (usually in the work-up) to regenerate the original carbonyl. Two of the more recent examples are an alkylation reaction published by Schiess and Chia\(^{37} \)

\[
\begin{align*}
\text{CH} & \equiv \text{CNa} \\
\text{O} & \text{-secBu} \\
\end{align*}
\]

\[
\begin{align*}
\text{OH} & \text{C} \equiv \text{CH} \\
\text{O} & \text{-secBu} \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{O}^+ & \\
\end{align*}
\]

in which dehydration of the alcohol is concurrent with cleavage of the enol ether, and a lithium aluminum hydride reduction by Matoba and Yamazaki\(^{38} \)

\[
\begin{align*}
\text{HO} & \text{CH}_3 \\
\text{HO} & \text{CH}_3 \\
\text{CH}_3 & \text{CH}_3 \\
\text{CH}_3 & \text{CH}_3 \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{O}^+ & \\
\end{align*}
\]

in which again, the dehydrated material is produced.

Actually the latter reaction is just an updated example
Since a large part of this thesis deals with the competitive 1,2 and 1,4 additions to 2-isopropoxymethyl-
enecyclohexanone (10), this portion of the historical section deals with two questions: 1. What factors, in general, promote 1,4 conjugate addition? and 2. What are some of the factors, peculiar to our system, that affect alkylation reactions? The remainder of this section will be concerned with these two topics.

A. Conjugate addition of organometallic reagents to \(\alpha,\beta\)-unsaturated carbonyls.

In general organoalkali metal reagents involving unstable carbanions (e.g. methylolithium, phenylsodium), generally add 1,2 to a carbonyl group whether or not it is \(\alpha,\beta\)-unsaturated. Stabilized anions such as enolates, on the other hand, tend to undergo 1,4 (Michael) addition, alkylating \(\beta\) to the carbonyl. Grignard reagents do not seem to show the same sort of behaviour patterns.
Organomagnesiums corresponding to the more stable carbanions show no tendency toward conjugate addition; in fact, we were unable to document any conjugate additions of either allyl- or ethynylmagnesium bromides. Other organomagnesiums show some sensitivity to the geometry of the carbonyl substrate (\( \alpha,\beta \)-unsaturated aldehydes normally give 1,2 adducts, while sterically inaccessible carbonyl functions may give exclusively 1,4 adducts) but, more usually, \( \alpha,\beta \)-unsaturated carbonyls give mixtures of 1,2 and 1,4 Grignard adducts.\(^4\) Finally, organocopper reagents add exclusively 1,4 to \( \alpha,\beta \)-unsaturated carbonyls.\(^2\)

Unlike the alkali metal salts, Grignard reagents and organocopper reagents both possess an undissociated carbon metal bond. The dissociation of a Grignard reagent involves cleavage of the halo-magnesium bond.\(^3\)

\[
\text{RMgX} \quad \longrightarrow \quad \text{RMg}^+ + X^-
\]

Before delving into the factors controlling 1,4 addition of Grignard reagents, a brief review of the exclusive 1,4 addition reagents (organocopper) will be presented.

The use of organocopper reagents actually grew out of a modified Grignard technique. Until the mid 1960s, 1,4 additions of Grignard reagents were "promoted" by the addition of catalytic amounts of a copper salt. It now appears that these reactions involved the in situ formation of an organocopper reagent which undergoes 1,4
addition and regenerates an active organocopper species.

\[
\text{RMgX + CuY} \rightarrow \text{RCu + MgXY}
\]

\[
X=\text{Cl, Br, I}
\]

\[
Y=\text{Cl, Br, I, CN, (OAc)}_2
\]

\[
\text{R-Cu + Sub} \rightarrow \text{R-SubCu}
\]

\[
\text{R-SubCu + RMgX} \rightarrow \text{R-SubMgX + RCu (etc.)}
\]

The logical way to eliminate the competitive attack of the free organomagnesium would be to change all of the organomagnesium to organocopper prior to the introduction of substrate. Hence, the use of stoichiometric (instead of catalytic) organocopper reagents (circa 1966). Actually the metal originally tied to the "R" group need not be magnesium; any metal above copper in the electromotive series will do (e.g. lead, zinc, magnesium, or lithium). If lithium (most common) is used as a metal, the addition of \(\text{RLi} \) to the cuprous salt gives a lithium dialkylcuprate.

\[
2 \text{RLi + CuX} \rightarrow \text{R}_2\text{CuLi + LiX}
\]

The presence of a non-copper metal is essential for conjugate addition since dialkylcuprates, \(\text{R}_2\text{Cu} \), do not react.

The originally proposed mechanism for the reaction featured a concerted cyclic six-centered transition state consisting of 2 moles of the organocopper reagent and the double bond of the unsaturated carbonyl.
Immediately afterward, the other organometallic species reacts with the C-copper enolate to form an O-metal enolate and expell a mole of organocopper. Hence the process is catalytic in organocopper.

H.O. House (footnote 50 and references cited therein) has shown that, at least in the case of lithium dialkyl cuprates, the first step is the transfer of an electron (formal reduction) from the reactive organocopper species to the $\alpha,\beta$-unsaturated carbonyl. The resultant radical anion and copper species then combine and transfer an R group to give the product enolate.
The rather curious structure for the lithium dialkylcuprate dimer, proposed by House\textsuperscript{50}, represents the four metal atoms in a tetrahedral array with an alkyl group bonded simultaneously to three metal atoms. Though he presents no hard evidence, House contends this structure is compatible with those known structures\textsuperscript{51} of alkyllithium reagents, stable organocopper compounds, and one stable cuprate reagent.

The hypothesis that the rate determining step involves the transfer of an electron (reduction) from the organocopper species to the substrate is supported by the fact that the energetics of the reaction depend upon the reduction potential of the substrate. In fact, House\textsuperscript{50} reports that the presence of an electron-donating $\beta$-alkoxy substituent makes the reduction potential so low that 5,5-dimethyl-3-isobutoxy-2-cyclohexenone (11) does not react with lithium dialkylcuprates. We probably should point out that the corresponding methoxyl compound reacts with lithium dimethylcuprate\textsuperscript{52} as shown:
Also, Coates and Sowerby\textsuperscript{53} have reported the double addition of lithium dimethylcuprate to 2-n-butylthiomethylene-cyclohexanone (12) to give 2-isopropylcyclohexanone (13).

Electron-withdrawing groups at the $\beta$ position, on the other hand, promote reaction with lithium dialkylcuprates to give mono- and di-adducts. Table 4 gives a summary of these reactions\textsuperscript{54}.

It should be noted that the copper binds ethynyl ligands so tightly that these compounds show no tendency to add to $\alpha,\beta$-unsaturated carboxyls\textsuperscript{55}. In fact, mixed lithium dialkylcuprates have been made in which one of the alkyl groups is ethynyl and the other an $sp^2$ or $sp^3$ carbon.
Table 4. Reaction of lithium dimethylcuprate with $\beta$-acetoxy-$\alpha,\beta$-unsaturated carbonyls.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>$(\text{CH}_3)_2\text{CuLi}$ (equiv)</th>
<th>Products</th>
<th>(%) Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{AcO} \backslash \text{OCH}_2\text{CH}_3$</td>
<td>1.1</td>
<td>$\text{AcO} \backslash \text{OCH}_2\text{CH}_3$</td>
<td>91</td>
</tr>
<tr>
<td>$\text{AcO} \backslash \text{cyclopropene}$</td>
<td>1.1</td>
<td>$\text{AcO} \backslash \text{cyclopropene}$</td>
<td>88</td>
</tr>
<tr>
<td>$\text{AcO} \backslash \text{cyclopentene}$</td>
<td>1.0</td>
<td>$\text{AcO} \backslash \text{cyclopentene}$</td>
<td>76, 2</td>
</tr>
<tr>
<td>$\text{AcO} \backslash \text{cyclohexene}$</td>
<td>2.7</td>
<td>$\text{AcO} \backslash \text{cyclohexene}$</td>
<td>2, 81</td>
</tr>
<tr>
<td>$\text{AcO} \backslash \text{cyclohexane}$</td>
<td>1.0</td>
<td>$\text{AcO} \backslash \text{cyclohexane}$</td>
<td>91</td>
</tr>
<tr>
<td>$\text{AcO} \backslash \text{cyclopentene}$</td>
<td>1.0</td>
<td>$\text{AcO} \backslash \text{cyclopentene}$</td>
<td>99</td>
</tr>
</tbody>
</table>
bonded to copper. Such reagents transfer the other R group to the $\beta$-carbon with total specificity. Thus, isophorone (14) reacts in the following manner: 

\[
\begin{align*}
\text{n-C}_3\text{H}_7\text{C}=\text{CCu(Li)}\text{CH}_2\text{Sn(Bu)}_3 & \rightarrow \text{Sn(Bu)}_3 \\
\text{n-C}_3\text{H}_7\text{C}=\text{CCu(Li)}\text{CH}_2\text{Sn(Bu)}_3 & \rightarrow \text{Sn(Bu)}_3 \\
\end{align*}
\]

E.J. Corey has used a modified vinyl reagent to effect what amounts to a formal 1,4 addition of an ethynyl group (Figure 7).

Considerable importance was attached to this scheme since there are no examples involving the direct conjugate addition of an ethynyl group regardless of the metal used.

While 1,2 addition products of Grignard reactions are normally written as proceeding through a polar mechanism,
much evidence has been put forth in support of a single electron transfer process.\textsuperscript{57-64} Grignard reactions present much more of a problem when discussing mechanisms since the nature of the solvent, ketone, R group of the reagent itself, purity of the magnesium, and mode of preparation of the Grignard reagent are all influential in determining the course of the reaction.\textsuperscript{59,62-64} For example,\textsuperscript{63} the reaction of methylmagnesium bromide with benzophenone gives exclusively (> 99.4%) 1,2 addition when "single-crystal magnesium"\textsuperscript{63} is used, but gives 2% benzopinacol (accepted as the coupling product of two ketyl radical anions\textsuperscript{64}) when "Grignard Grade" magnesium is used.

\[
\begin{align*}
\phi_2C &= 0 \quad \xrightarrow{\text{CH}_3\text{MgBr}} \quad \phi_2\text{C}-\text{OH} \quad \xrightarrow{\text{CH}_3} \quad \phi_2\text{C}-\text{C}\phi_2 \quad \text{OH} \quad \text{OH}
\end{align*}
\]

Single Crystal Magnesium \hfill 99.4% \hfill ----
Grignard Grade \hfill 98% \hfill 2%

Among other minor products, a 1,6 adduct is also observed. This example is presented to point out the mechanistic sensitivity that Grignard reagents may display toward seemingly insignificant perturbations.
As mentioned previously, ethynyl and allylic organomagnesiums show no tendency toward conjugate addition to $\alpha,\beta$-unsaturated carboxyls. Vinyl Grignard reagents, as do their alkyl counterparts, seem to "pick and choose" between 1,2 and 1,4 addition modes. Boccarra and Maitte, in a series of three articles, have presented dozens of reactions of various vinyl Grignard reagents with both saturated and unsaturated esters, ketones, and aldehydes in an attempt to correlate electronic and steric effects with the mode(s) of addition. While they did produce some axioms (e.g. $\alpha,\beta$-unsaturated aldehydes bearing an $\alpha$-hydrogen always add 1,2 with vinyl Grignard reagents), it appears that product compositions can be "predicted" only on an empirical basis and can be rationalized after the observation. The chief observation that can be extracted from their work is that 1,4 additions of vinyl Grignard reagents is never exclusive (>95%) and does not occur in high overall yield. The most exclusive 1,4 addition occurred with 1-propenylmagnesium bromide and methyl styryl ketone to give 92:8 ketone to alcohol in 40% overall yield.

\[
\begin{align*}
\text{CH}_3\text{CH=CH}-\text{C}=\text{CH}_3 + \text{CH}_2\text{CH}=\text{CHMgBr} & \rightarrow \text{CH}_3\text{CH}=\text{CH}-\text{C}=\text{CH}_3 + \text{CH}=\text{CH}-\text{CH}_3 \\
\text{92:8} & (40\% \text{ overall})
\end{align*}
\]
The best yield of a 1,4 addition occurs with only a 2:1 preference of the conjugate addition.

\[
\begin{align*}
&\text{O-C-CH}_3 & \xrightarrow{\text{CH}_3\text{CH}_2\text{OMgBr}} & \text{O-C-CH}_3 \\
&\text{C=CH}_2 & & \text{C-CH}_3 \\
&\text{CH}_3 & & \text{CH}_3
\end{align*}
\]

(78% overall)

B. Nature of the \(\alpha,\beta\)-unsaturated substrate.

We have already mentioned that steric hindrance, while having no effect on the mode of addition of organo-copper reagents, may in the case of Grignard additions promote either 1,2 or 1,4 additions, depending upon the particular substrate. Thus for our system (\(\beta\)-isopropoxy group) we have a fairly bulky \(\beta\)-substituent, which might tend to discourage 1,4 attack on steric grounds. Alkylations with organometallics can be run directly on the precursor of the enol ether as demonstrated by Conia.68
This reaction requires two moles of Grignard, one of which is destroyed by the acidic hydrogen of the substrate. It is unclear exactly which species is being attacked in this case.

Without a knowledge of which structure represents the substrate, it is impossible to assess the mode of addition. If, instead of the free hydroxyl compound, the alkyl enolate is examined, these assessments become clear. This enol ether is formed by treating the hydroxyl compound with the appropriate halide in the presence of base.

Here, we run into the problem of specifically alkylating the aldehyde oxygen. Writing the three tautomers
for the 2-formylcyclonones,

\[
\begin{align*}
\text{(CH}_2\text{)}_n\text{H} &\rightleftharpoons \text{(CH}_2\text{)}_n\text{OH} \\
\text{(CH}_2\text{)}_n\text{H} &\rightleftharpoons \text{(CH}_2\text{)}_n\text{OH}
\end{align*}
\]

one can see that base catalyzed (usually K\textsubscript{2}CO\textsubscript{3}) alkylation can lead to C-alkylation or two different O-alkylated products. The relative abundance of the three tautomers has been studied\textsuperscript{69} for rings \(n=3\) to 7 and there seems to be little relation between the abundance of the tautomers and the formation of the corresponding alkylated products. Branched alkylation groups (i-Pr-Br or sec-Bu-Br) tend to alkylate on the sterically less hindered aldehydic oxygen rather than at the tertiary carbon or the cyclic carbonyl oxygen. The reaction should probably be envisioned as attack by the substrate anion on the alkylating agent:

\[
\begin{align*}
\text{C} &\text{C} \\
\text{C} &\text{C} \\
\text{C} &\text{C} \\
\text{C} &\text{C}
\end{align*}
\]
Alkylating agents, which are derivatives of the more stable anions or are themselves readily alkylated, lead to C-alkylated products.

\[
\begin{align*}
R_1OH & + CH_2=CH-COCH_3 & \xrightarrow{\text{or } R_1=iPr, R_2=CH_3} & \xrightarrow{\text{70}} \text{C-alkylated product} \\
R_2 & & & \\
\end{align*}
\]

More extensive comparisons have been run on 2-carb-ethoxycyclopentanone.

\[
\begin{align*}
\text{Cyclopentenone} & + CH_3I & \xrightarrow{72} & \text{Product} \\
\end{align*}
\]

\[
\begin{align*}
\text{Cyclopentenone} & \xrightarrow{k_2CO_3} & \text{Product} \\
\end{align*}
\]

with CH\textsubscript{3}I, CH\textsubscript{3}SO\textsubscript{4}, CH\textsubscript{2}=CH-CH\textsubscript{2}Br, n-pentyl-Br, BrCH\textsubscript{2}CO\textsubscript{2}Et

with iPrI, OCH\textsubscript{2}OCH\textsubscript{2}Cl, ClCO\textsubscript{2}Et
Here, without the sterically more accessible aldehyde oxygen available, some reagents (most notably isopropyl) still show a preference for O-alkylation.

One might then expect that the production of 2-isopropoxymethylenecyclohexanone (10) from 2-hydroxymethylene-cyclohexanone (9) would be competitive with alkylation of the other oxygen on the ring to form 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15). Previous workers\textsuperscript{36,72} have not observed this product.
RESULTS AND DISCUSSION

INTRODUCTION

During the course of our investigations into syntheses of cis-1,3,5-hexatriene analogs, 2-isopropoxymethylene cyclohexanone (10) was used as an intermediate. While eventually a successful synthesis was developed, a major portion of this thesis resulted from the unexpected reactions of this intermediate, which we had occasion to investigate in some detail. Indeed, these studies strayed so far from our original goal (triene synthesis) that they will be discussed under a separate heading.

Another approach to the triene series involved the use of a modified Wittig reaction to form the central cis double bond. While this did not lead to the desired triene, a known but unanticipated reaction of this Wittig reagent occurred. As a result of these events the investigation took on a rather diverse character. Consequently it has, for organizational reasons, been necessary to divide this discussion into four separate sections.

I. Synthesis and thermolysis of ethyl 3-(2-vinyl-1-cyclohexenyl)propenoate.

II. The Schlosser-Wittig reaction of (2-phenyl-2-propenyl)triphenylphosphonium bromide with acrolein.

III. The alkylation of 2-isopropoxymethylene cyclohexanone with organometallic reagents.
IV. Further reactions of the derivatives of 2-isopropoxymethylenecyclohexanone.

I. The synthesis and thermolysis of ethyl 3-(2-vinyl-1-cyclohexenyl)propenoate.

In order to complete our studies of the influence of substituents at the terminal carbon of a cis-1,3,5-hexatriene system, it was necessary to investigate the effects of an electron-withdrawing group at the terminal position. The carbethoxyl group was chosen, for not only is it a good electron-withdrawing group, but it is known to enhance greatly the rate of cyclization when it is placed in the 2-position. Also, for synthetic convenience, the 1,2-divinylcyclohexene series was chosen. Thus, ethyl 3-(2-vinyl-1-cyclohexenyl)propenoate (16) was the reactant selected.
A. Synthesis.

While the use of P$_2$I$_4$ to convert 1,2-dihydroxy-1,2-dialkenylcyclohexanes to dialkenylcyclohexenes has proved of some synthetic utility in this laboratory, it suffers from poor to moderate yields. Also, the incorporation of the desired carbethoxyl group would necessitate severe reorganization of the synthetic scheme. Since 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (17) had been synthesized by a convenient procedure,$^3$ it could be converted readily via a Wadsworth-Emmons Wittig reaction into the desired substrate.

This modified Wittig reaction gives isomerically pure trans alkenes.$^7$ In addition, the phosphorus-containing by-product of the reaction, NaOP(OEt)$_2$, is easily removed from the product mixture. The overall scheme, somewhat modified from that of Schiess, is presented in Figure 8.

The formylation of cyclohexanone is a well-known and often repeated process.$^7$ However, it was improved slightly by the use of sodium shot which reduces the reaction time from 16 hours to about 20 minutes. Use of methyl formate instead of ethyl formate seems to make stirring easier and reduces the solvent required by about one half. The crude 2-hydroxymethylenecyclohexanone (9) is essentially pure and distillation offers no apparent further purification while decreasing the yield about 20%. The product does
not store well and should be used as soon as possible after preparation.

Figure 8. Synthesis of ethyl 3-(2-vinylcyclohexen-1-yl)-propenoate.

Three methods of alkylating 9 were studied. The first, originally employed by Claisen and van Auwers, 76 involved refluxing the reactants in acetone over potassium carbonate for three days. It seemed likely that the use of dimethyl sulfoxide as solvent would shorten the reaction time - this
was found to be quite true. We also examined direct isolation of the sodium salt of 2-hydroxymethylenecyclohexanone (18) from

\[
\text{\begin{center}
\includegraphics{structure.png}
\end{center}}
\]

the formylation reaction followed by alkylation in dimethyl sulfoxide. While the yield for this one step process approached the overall yield for the two step procedure using DMSO, the latter was the method of choice because it gave a purer product and was experimentally easier to run.

In any case, 2-bromopropane was used to reduce C-alkylation, and no C-alkylation product was observed, but 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15), a second O-alkylated product, was obtained in 15-20% yield. This structure was assigned on the basis of infrared, ultraviolet, and proton magnetic resonance spectra. The infrared showed a strong doublet at 1615 and 1665 cm\(^{-1}\), typical of a conjugated carbonyl with an alkoxy group in
the $\beta$-position (the $\beta$-alkoxy group is responsible for the peak at 1615 cm$^{-1}$ while the conjugated carbonyl vibrates at 1665 cm$^{-1}$ as does 2-cyclohexenone$^{78}$). Both calculated$^{79}$ and experimental ultra-violet absorptions are tabulated below:

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>Observed (EtOH)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Structure 10" /></td>
<td>260 nm</td>
<td>277 nm ($\varepsilon=16,900$)</td>
</tr>
<tr>
<td><img src="image2.png" alt="Structure 15" /></td>
<td>259 nm</td>
<td>276 nm ($\varepsilon=15,500$)</td>
</tr>
</tbody>
</table>

This method of calculation does not correct for the fact that 10 is forced into an s-cis conformation which can be relieved somewhat by twisting the six membered ring. The s-cis conformation might be expected to raise the maximum absorbance value as in the case of carbon-carbon double bonds in 5-, 6- and 7-membered rings, but apparently the effect is not observed when both double bonds are exocyclic as with 2-ethylidenecyclohexanone whose calculated (242 nm) and observed (230 nm)$^{80}$ values agree without considering the s-cis configuration. The differences in observed and
calculated values are the same for both compounds. The proton magnetic resonance spectrum indicates O-alkylation - the methine proton of the isopropyl group resonated at δ 4.46 (carbon attached to an oxygen) and the aldehyde proton appeared at δ 10.06. It might be well to mention at this point that the "trans" structure was assigned to 10 from the observation of allylic splitting (J=2.5 cps) on the olefinic proton. The aldo ether (15) seemed to be less stable than the keto ether (10) and may be lost if the work-up is delayed or during distillation.

The conversion of 2-isopropoxymethylenecyclohexanone (10) to 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (17) via 2-ethynyl-3,4,5,6-tetrahydrobenzaldehyde (19) was carried out with results similar to those described by Schiess and Chia.37
Though vinyl metal reagents show a greater tendency to add 1,4 than do ethynyl, we felt that 10 could be converted directly to 17 by use of an appropriate vinylic alkylating agent. Vinylmagnesium bromide, the first candidate, produced some interesting chemistry which will be discussed later, but did not give the desired aldehyde (17). Vinyllithium, on the other hand, gave a smooth conversion to 17.

An infrared spectrum of the initial product shows a moderate intensity broad hydroxyl peak. The compound responsible was not isolated but was converted directly to the aldehyde. While the yields were slightly higher using vinyllithium, product separation proved more difficult.

The Wadsworth-Emmons Wittig reaction of triethyl phosphonoacetate (20) with 17 proceeded smoothly to give
exclusively ethyl trans-3-(2-vinylcyclohexen-1-yl)propenoate (16).

\[
\begin{array}{c}
\text{17} + (\text{EtO})_2\text{PCH}_2\text{CO}_2\text{Et} \\
\overset{0}{\underset{20}{\text{NaH}}} \\
\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3 \\
\rightarrow \\
\text{CO}_2\text{Et}
\end{array}
\]

The following spectral evidence was used for structural identification. In the ultra-violet region, a maximum at 299 nm (\(\varepsilon = 22,700\)) appears with shoulders at 291 nm and 305 nm. Trienes typically show this sort of triplet absorption with high extinction coefficients. The infrared spectrum shows a conjugated ester carbonyl absorption at 1720 cm\(^{-1}\) and the proton magnetic resonance spectrum is reproduced in Figure 9. The trans geometry was assigned on the basis of the \(H_g - H_1\) coupling constant of 16 Hz.
B. Thermolysis.

On thermolysis in cyclohexane, 16 would be expected to give 2-carbethoxy-2,3,5,6,7,8-hexahydronaphthalene (21). While 21 may indeed be formed initially (see below), it was not isolated from the reaction. Instead what appears to be
2-carbethoxy-2,3,4,6,7,8-hexahydronaphthalene (22) was the observed product. Assignment was based on spectral evidence: the ultra-violet spectrum has a maximum at 241 nm, which rules out a homoannular diene. The double exocyclic hexahydronaphthalene absorbs at 242 nm. Interestingly, that was the thermolysis product isolated from 1,2-divinylcyclohexene. The infrared spectrum of the product reveals a non-conjugated ester carbonyl at 1731 cm\(^{-1}\). The proton magnetic resonance displays, aside from the carbethoxy protons, two olefinic protons, and seven allylic protons. The isomer of 22 with the carbethoxy group at the 3-position has nine allylic protons (the proton α- to the carbethoxy group should resonate in the allylic region) but certainly fits the rest of the data and could possibly occur as a mixture with 22. Unfortunately the allylic proton α- to the carbethoxy group in 22 was not clearly separated from the rest of the allylic region by proton magnetic resonance. The appearance of a 287 nm peak in the ultraviolet spectra of some of the kinetic samples has been attributed to the
expected thermal product, but the compound responsible for this peak was never isolated.

We felt that if \( \text{22} \) were the result of a base catalyzed rearrangement, the most acidic proton of \( \text{21} \) (\( \alpha \) to the carbethoxyl group) would be involved, leading to a diene conjugated with the ester function. It is, however, uncertain whether or not this is an acid catalyzed process since base (ammonia) washed glassware still gave the same result. In any event, the direct conversion of \( \text{21} \) to \( \text{22} \) via a 1,3 hydrogen shift seems unlikely.

**Kinetics.**

Since the triene \( \text{16} \) and the cyclized product have ultraviolet maxima separated by 60 nm and the extinction coefficient of the triene was much larger than that of the product, the disappearance of \( \text{16} \) was monitored using the ultraviolet absorbance at 299 nm. Since the absorbance is proportional to the concentration (checked over the absorbance range of the investigation), the initial absorbance, \( A_0 \), and absorbance at time \( t \), \( A_t \), may be used directly in the rate equation.

As expected, a plot of \( \ln (A_0/A_t) \) versus time gave a straight line indicating first-order kinetics. For each temperature, the experimental data were fitted to a straight line using a least-squares program on a Hewlett-Packard 9100A calculator. The results, along with the corresponding
correlation coefficients, are summarized in Table 5.

Table 5. Kinetic results for the cyclization of ethyl trans-3-(2-vinyl-1-cyclohexenyl)propenoate.

<table>
<thead>
<tr>
<th>Temp.(°K)</th>
<th>k(sec⁻¹)</th>
<th>Correlation Coef.</th>
</tr>
</thead>
<tbody>
<tr>
<td>400.2</td>
<td>3.91 x 10⁻⁵</td>
<td>0.999</td>
</tr>
<tr>
<td>403.8</td>
<td>5.77 x 10⁻⁵</td>
<td>0.999</td>
</tr>
<tr>
<td>409.8</td>
<td>1.03 x 10⁻⁴</td>
<td>0.999</td>
</tr>
<tr>
<td>413.7</td>
<td>1.53 x 10⁻⁴</td>
<td>0.992</td>
</tr>
<tr>
<td>423.0</td>
<td>2.36 x 10⁻⁴</td>
<td>0.999</td>
</tr>
</tbody>
</table>

A plot of ln k versus 1/T gave a straight line from which an activation energy, Ea = 27.0 kcal-mole⁻¹ (correlation coefficient of 0.986 by least-squares) was derived. The following formulae\(^81\) then can be used to provide the activation parameters \(\Delta H^\ddagger\) and \(\Delta S^\ddagger\).

\[
\Delta H^\ddagger = \frac{\text{Ea}}{T}
\]

and

\[
\Delta S^\ddagger = 4.576(\log k - \log T - 10.75) + \frac{\text{Ea}}{T}
\]

\[
\Delta H^\ddagger_{400.2^\circ K} = 26.2 \text{ kcal-mole}^{-1}
\]

\[
\Delta S^\ddagger_{400.2^\circ K} = -14 \text{ cal-mole}^{-1} \text{K}^{-1}
\]

Previous work in this laboratory\(^2\) gave the following results for the thermolysis of 1,2-divinylcyclohexene.
Figure 10. Thermolysis of ethyl trans-3-(2-vinyl-1-cyclohex-
Thus, the presence of the carbethoxy group in the terminal position has virtually no effect on the rate of ring closure in this 1,3,5-hexatriene ring system.

**Mechanistic Implications.**

We now have a wide range of effects (or lack of them) from which to draw conclusions about the transition state. Neither electron-donating nor electron-withdrawing groups attached to the terminal carbons show any large effect on reaction rate as long as they are in the **trans** position. Such **trans** substituents are not only electronically uninvolved in the transition state, but they also exhibit no steric effect on the reaction.

Many of the same substituents offer considerable rate
retardation when in the cis position. Since their inductive effect is not expected to change, this retardation is attributed solely to steric effects. Terminal substituents in the cis geometry have considerable non-bonded interaction in the transition state while those in the trans geometry do not.

The fact that the 2 (and 5) position behaves as if, in transition state, it possesses a partially isolated p-orbital while the 1 (and 6) position does not, indicates that not only are these positions no longer involved with each other, but that the terminal atom no longer bears a p-orbital at all. The logical inference is that the terminal carbons have undergone extensive rehybridization (from sp$^2$ to sp$^3$) and bond formation (with each other) by the time the transition state is attained.

Substituent effects at the 3 (and 4) position are somewhat harder to assess. In terms of the transition state (see Figure 11), substituents which stabilize an isolated double bond should help stabilize the transition state to about the same extent which they stabilize the ground state. While it appears unlikely that such substituents would be sterically involved in the transition state [1-(x-styrl)-2-vinylcyclohexene (8) is an exception], they may raise the ground state energy enough to effect the rate of the reaction.

It is of course gratifying to note that predictions based on the calculated transition-state geometry (either
Ours or McIver's) agree very well with the experimental results. (Both calculations predict a C(1) to C(6) bond distance of about 2 Å which corresponds to about two-thirds of the energy of the forming bond. Experimentally, bond formation in the transition state could be even further advanced.)

Thus, starting from the triene in an s-trans, s-trans conformation and maintaining C₅ symmetry, the reaction proceeds as shown in Figure 11. Note that orbital symmetry is conserved via the disrotation and that groups which were cis on the terminal carbons show considerable interaction in the transition state.

![Diagram of cyclization process](image)

**Figure 11.** Cyclization of cis-1,3,5-hexatrienes showing transition-state geometry and p-orbital utilization.
II. Synthetic approach directed toward cis-2-phenyl-1,3,5-hexatriene.

Failure to observe a large rate enhancement in the thermolysis of 1-(α-styryl)-2-vinyl-cyclohexene (8), which was attributed to non-bonded interaction between hydrogens on the cyclohexene ring and the phenyl group indicated the need for a kinetic study of the analog without additional substituents – cis-2-phenyl-1,3,5-hexatriene (23).

Since Padwa\textsuperscript{11} had already described the formation of the central double of a triene with three phenyl substituents, his route seemed the synthetic method of choice.
To enhance the amount of the cis isomer formed, a salt-free system and a non-polar solvent was used; this is the Schlosser modification\textsuperscript{13} of the Wittig reaction. Since the phenyl substituent was expected to increase reactivity in the electrocyclic reaction dramatically, the reaction was run at 0° to retard cyclization.

\(\alpha\)-Bromomethylstyrene (24) was synthesized according to the method of Reed\textsuperscript{82} in comparable yields. This method also gives some \(\beta\)-bromo-\(\alpha\)-methylstyrene, but since the vinylic bromide is not expected to form an adduct with triphenylphosphorous, we did not separate it (\(\sim\)5\%) from the desired product. The \(\alpha\)-bromomethylstyrene was mixed with triphenylphosphine and the product was recrystallized from chloroform-pentane to give (2-phenyl-2-propenyl)triphenylphosphonium bromide (25), which was identified by melting point and proton magnetic resonance spectrum.

One equivalent of a benzene solution of the ylide was added to acrolein at 0° and the entire work-up was done at 0°. Two products were obtained from the reaction by glc separation. The major product had a maximum in the ultraviolet at 272 nm and its proton magnetic resonance showed a ratio of olefinic to aliphatic protons of 3:4. Hydrogenation gave a mixture of 1-phenylcyclohexene (26) and phenylcyclohexane (27). Though 1-phenyl-1,3-cyclohexadiene (28) would be expected to be the product from cyclization of 23, the ultraviolet spectrum indicates
that this was not the product obtained experimentally. Both the ultraviolet and proton magnetic resonance spectral data are in complete agreement with the published data for 2-phenyl-1,3-cyclohexadiene (29).\(^3\)

\[
\begin{align*}
\text{28} & \\
\text{29}
\end{align*}
\]

The minor product has three maxima in the ultraviolet region at 251, 262, and 270 nm. Since hydrogenation of the crude reaction product from the Wittig reaction gives 2-phenylhexane as well as phenylcyclohexane,\(^5\) this minor product was assumed to be trans-2-phenyl-1,3,5-hexatriene.

Although it seems unlikely that all 28 could be converted to the 29 by basic catalysis (ylide), this possibility was eliminated experimentally. A sample of 28 was prepared by a modification of Grisdale's synthesis.\(^3\) The overall procedure is illustrated in Figure 12. Dehydration of the Grignard adduct gave better yields with phosphorus oxychloride/pyridine instead of aqueous oxalic acid (indeed, we could not repeat Grisdale's method of dehydration), and cleavage of the benzylxy group by lithium aluminum hydride vastly improved this step.
Figure 12. Synthesis of 1-phenyl-1,3-cyclohexadiene and 1-phenyl-1,4-cyclohexadiene.
The 3-methyl xanthate ester (35) was not purified and the crude mixture was pyrolyzed directly on the glc to give the two isomeric phenylcyclohexadienes, (28) and (36). The first, 28, gave a uv max at 302 nm, while the 1,4-cyclohexadiene gave a uv max at 249 nm. These values agree well with those of Grisdale83 (303 nm and 249 nm). The 1-phenyl-1,3-cyclohexadiene (28) did not rearrange when treated with a solution of α-styryl-triphenylphosphonium methyldie.

There remains the problem of explaining the appearance of the unexpected product 29. A search of the literature revealed similar reactions with some ketones and esters. In fact, Padwa, using his own previously described Wittig procedure, has described a "synthesis of substituted 1,3-cyclohexadienes" in which the product does not correspond to the thermal product of the expected triene.

The reaction was first reported by Büchi85 in 1971 and he stated that the appearance of the rearranged product (the
"expected" product was not observed) was enhanced by salt-free conditions. W.G. Dauben has since carried out many such reactions and he points out that only one example of a "normal" allylidene triphenylphosphorane-ketone adduct has been reported.

\[
\text{RCH} = \text{CHCH}_2 - \text{R} \quad \text{RCH} = \text{CHCH}_2 - \text{R}
\]

Dauben used this procedure in the preparation of some rather strained cyclohexadienes and has shown that they were not the result of triene cyclization. His mechanistic pathway is presented in Figure 13.

**Figure 13.** Mechanistic proposal for the formation of the abnormal Wittig adduct, - W.G. Dauben
Büchi, Dauben and Padwa all suggested the same mechanism for the reaction which is shown in Figure 13. This mechanism involves reaction of the 4-carbon of the allylidene-phosphorane with the β-carbon of the unsaturated carbonyl, followed by proton rearrangement and a "normal" intramolecular Wittig reaction.

As far as we have been able to determine, ours is the first example of a 1,4 Wittig addition to an unsaturated saturated aldehyde. Since we apparently observed some trans-2-phenyl-1,3,5-hexatriene formation, normal Wittig addition is competitive with the preponderant Michael addition.

There is, however, another mechanistic pathway which may have some merit. This pathway (Figure 14) involves normal Wittig attack to give two diastereomeric betaines. The betaine rotates until the phosphorus and oxygen atoms are eclipsed. Triphenylphosphine oxide is then eliminated to give the appropriate triene. In the case of the cis-triene precursor rotation is hindered by the large groups and is supplanted by a Cope rearrangement, after which the reaction proceeds in the same manner as the previously proposed mechanism. In the presence of a carbonium ion, the Cope rearrangement is known to proceed readily even at -15°C.90
Figure 14. Production of abnormal Wittig product via a Cope rearrangement.
III. Reactions of isopropoxymethylene cyclohexanone with organometallic reagents.

During the triene synthesis described earlier, it was observed that 2-isopropoxymethylene cyclohexanone (10) exhibits some unusual behavior in its reactions with organometallic reagents. Specifically, two reactions were found in which nucleophilic attack at the carbonyl carbon gave the corresponding alcohol. However, a third reaction which would have been expected to lead to some of the same product presented an altogether different mode of addition.
Compound 10 adds two moles of vinyl Grignard to give 2-propenylidene-1-vinylcyclohexanol (37).

This is a most unusual result since the first mole of vinyl Grignard adds 1,4 and, presumably after loss of alkoxide, the second mole adds 1,2 to an unsaturated carbonyl.

Thus given this reaction, one is led to take a second look at 2-isopropoxymethylenecyclohexanone (10) as a substrate in organometallic reactions.

An organometallic reagent, symbolized as $R^-M^+$, can add to the $\alpha, \beta$-unsaturated carbonyl in either a 1,2 or a 1,4 manner.
The 1,4 adduct can react further in a manner vinylogous to a normal ester to eliminate a mole of alkoxide.

This regenerates another $\alpha,\beta$-unsaturated carbonyl, which is subject to either 1,2 or 1,4 addition by an additional $R^-M^+$. With the vinyl Grignard the second addition could occur in a 1,6 manner, though this was not observed.
Thus, addition may occur in the following modes:

1.) Normal 1,2 addition to the carbonyl, 2.) 1,4 addition which is followed by 1,2 addition, or 3.) 1,4 addition followed by a second 1,4 addition.

Before one begins to investigate the reactions of this compound, one must be sure that the 2-isopropoxymethylene-cyclohexanone (10) is free of 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15). This compound is also subject to all of the modes of addition described above, but with a very different set of products. Indeed, the 1,4 adduct of 15, after alkoxide elimination, is identical to the 1,2 adduct of 10 after acid hydrolysis.
Since previous workers were apparently unaware of the presence of the aldo-ether (15), consideration must be given to its reactions when analyzing their results.

Reactions of 10 with two organometallic reagents have already been described in detail. Both sodium acetylide and vinyllithium proceed via 1,2 addition to the carbonyl.

Vinylmagnesium bromide, as noted above, adds in a very different manner leading to a double adduct. The product of the reaction absorbed three moles of hydrogen over platinum oxide (Adam's catalyst) to give 1-ethyl-2-propylcyclohexanol (38), which was identified by comparison with an authentic sample prepared from cyclohexanone via 2-allylcyclohexanone (39) and 2-propylcyclohexanone (40).
Actually, the hydrogenation of the trienol (37) gave two alcohols, each giving a molecular ion at 170 amu and a most abundant ion at 141 amu. These are presumed to be the two isomers of 1-ethyl-2-propylcyclohexanol (38). The fact that the reaction of 40 with ethylmagnesium bromide gives only one isomer is not surprising.

Additional support for the assigned structure comes from the spectroscopic data. The infrared spectrum in carbon tetrachloride shows two very sharp peaks at 3590 cm\(^{-1}\) and 3320 cm\(^{-1}\), typical of a tertiary alcohol. The ultraviolet spectrum has a maximum at 237 nm – identical with that of propenylidenecyclohexane. The proton magnetic resonance spectra, besides showing 6 aliphatic protons, 2 allylic protons and the hydroxyl proton displays seven olefinic protons, which can be further analyzed: the furthest down field (\(\delta 6.53\)) is a doublet of doublets of doublets with coupling constants of 10, 11 and 17 Hz; followed by a doublet (\(J=11\) Hz) at \(\delta 6.01\) which overlaps a doublet of doublets (\(J=11,18\) Hz) at \(\delta 5.99\). The remaining four olefinic protons appear at 4.9 to 5.4 as a complex multiplet. In terms of the proposed structure, the assignments are as follows:
It is most interesting that the first addition goes 1,4 despite the obvious steric hindrance, while the second addition goes exclusively 1,2 even though 1,6 addition is completely free from steric hindrance.

Next on the list of organometallic reagents is a normal aliphatic Grignard reagent, ethylmagnesium bromide. When the reaction is run in ether at room temperature with a two to one - Grignard to substrate ratio - 2-(3-pentyl)cyclohexanone (41) is produced in good yield.
The product was identified by boiling point, refractive index, and an infrared spectrum which shows a carbonyl stretch at 1710 cm$^{-1}$. This reaction obviously proceeds by a 1,4 addition, loss of alkoxide, and another 1,4 addition. No product resulting from 1,2-addition was observed.

In an attempt to isolate the intermediate $\alpha,\beta$-unsaturated ketone, 2-propylidene cyclohexanone (42), a solution of ethyl Grignard was added to the substrate at 0° C.
While the monoaddition product was observed, an approximately equal amount of the double addition product also was obtained. The new product was identified by comparison with an authentic sample. Apparently, the loss of alkoxide (magnesium isopropoxide) is facile even at 0°C, and the resulting 2-propylidencyclohexanone (42) competes effectively with the keto ether (10) for ethylmagnesium bromide.

Thus, the vinyl and ethyl Grignard reagents follow two different modes of addition. To complete the sequence, an acetylenic Grignard reagent should be studied. Since, unlike sodium acetylide, acetylenemagnesium bromide is unstable due to disproportionation, propynyl Grignard was used.

Propynylmagnesium bromide was prepared by bubbling propyne through a solution of ethylmagnesium bromide. When 2-isopropoxymethylenecyclohexanone (10) was added to an excess of this Grignard reagent, a double addition, similar to that observed with vinylmagnesium bromide, occurred to give 2-(2-butynylidene)-1-(1-propynyl)cyclohexanol (43).

\[
10 \quad \text{excess} \quad \text{CH}_3\text{C}=\text{CMgBr} \quad \xrightarrow{\text{excess} \quad \text{CH}_3\text{C}=\text{CMgBr}} \quad 43
\]
The infrared spectrum reveals an O-H stretch at 3570 cm\(^{-1}\) and the triple bond stretch at 2225 cm\(^{-1}\). The ultraviolet spectrum has a maximum at 234 nm, very close to the peak for the vinylic compound. The mass spectrum shows a small molecular ion at 188 amu with a strong peak at 170 amu corresponding to the expected loss of water. Indeed, dehydration occurs so readily that a satisfactory analysis of 43 was unattainable. Instead, the compound was allowed to dehydrate on a glc column and the product collected.

The product, 3-(2-butynylidene)-2-(1-propynyl)cyclohexene (44), produces an ultraviolet maximum at 272 nm, no hydroxyl stretch in the infrared, and the proton magnetic spectrum is shown in Figure 15. Assignments were made on the basis of decoupling experiments. When the multiplet at \(\delta\) 5.80 was irradiated, the three proton doublet at \(\delta\) 2.03 collapsed to a singlet and the triplet of doublets at \(\delta\) 2.56 went to a triplet. Irradiation of the other olefinic proton, a
triplet at \( \delta 6.11 \), transformed the two proton allylic quartet at \( \delta 2.26 \) to a triplet.

Figure 15. Pmr spectrum of 3-(2-butynylidene)-2-(1-propynyl)-cyclohexene.

Thus, 1-propynylmagnesium bromide does indeed behave as does vinylmagnesium bromide in its reaction with compound 10: 1,4-addition, loss of alkoxide, and a subsequent 1,2-addition.

Since the compound shows a marked tendency to initial 1,4 addition and at least a potential for subsequent 1,4
addition, reaction might be directed by using a reagent which tends to add 1,4, such as lithium dialkylcuprate. However the prognosis for the reaction is not entirely clear. Two problems might alter the situation. First, some question has been raised about the ability of lithium dialkylcuprate to add to \( \alpha,\beta \)-unsaturated carbonyl systems with an electron-donating alkoxy group on the \( \beta \)-carbon since such groups lower the reduction potential of the unsaturated carbonyl. It is also possible that if initial 1,4 addition does not occur alkoxide elimination may not, thus preventing the second addition.

No products resulted from our initial attempts to add lithium divinylcuprate, using the procedure described by E.J. Corey and R.L. Carney. When lithium dimethylcuprate is used instead, double 1,4 addition does occur to give 2-isopropylcyclohexanone (13).

No attempt was made to isolate a mono addition product.
Summary

The reactions of 2-isopropoxymethyleneecyclohexanone (10) are compiled in Figure 16. Reaction occurs in three stages: 1.) initial addition, 2.) formation of a new \( \alpha,\beta \)-unsaturated carbonyl, 3.) a second addition. These topics will be dealt with in order.

1.) Initial addition. Both of the alkali metal salts add in a normal 1,2 fashion to the carbonyl. It is interesting to note that Dreiding and Nickel\textsuperscript{36} found that phenyllithium and methyllithium both gave 1,4 addition products with 10. While the 1,4 adduct with methyllithium is a minor product and might be explained as the 1,2 adduct of 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (15) occurring as an undetected impurity in 10, the phenyllithium adduct can only be explained by 1,4 addition since the product retains the isopropoxy group. This is also the only 1,4 adduct of 10 which does not eliminate alkoxide under the reaction conditions.

Grignard reagents give exclusively conjugate addition products with 10. While we promised not to draw any mechanistic conclusions from this work, the tendency toward conjugate addition - even to the point of including acetylenic Grignard reagents (which 'never' add 1,4) - is so strong that it must be attributed to the presence
Figure 16. Reactions of 2-isopropoxymethylenecyclohexanone described in this work.
of the isopropoxyl group in the β-position either due to its electron-donating nature or its ability to coordinate to magnesium thus directing addition to the 4-position.

![Chemical structures](image)

The 1,4 addition of lithium dialkylcuprate has already been discussed in detail, and does not involve initial coordination to oxygen.

2.) Formation of a new α,β-unsaturated carbonyl. After 1,2 addition, the enol ether must be hydrolyzed with aqueous acid to produce the carbonyl. Presumably concurrent elimination of water affords the α,β-unsaturated system, though we have no evidence to determine whether water is eliminated before or after ether hydrolysis.

![Additional chemical structures](image)
This procedure destroys any organometallic reagent in the mixture precluding addition of a second mole of organometallic reagent to the product.

Grignard adducts, on the other hand, permit elimination in a non-aqueous, basic medium. A uni-molecular mechanism can be written:

\[
\begin{align*}
&\text{OMgBr} \\
&\text{OiPr} \\
&\text{R} \\
&\rightarrow \\
&\text{OMgBr} \\
&\text{OiPr} \\
&\text{R} \\
&\rightarrow \\
&\text{R} \\
&\rightarrow \\
&\text{R} \\
&\rightarrow \\
\end{align*}
\]

The reaction need not be concerted, but this scheme does offer a six-membered ring transition state and isopropoxide is not a particularly good leaving group. Regardless, the elimination is quite facile, even at 0°C (R = ethyl).

The elimination of acetate from the lithium dialkylcuprate – \( \beta \)-acetoxy- \( \alpha,\beta \)-unsaturated carbonyl adduct has already been described and occurs rapidly enough to compete with rotation about the "3"-"4" bond. It seems probable that loss of alkoxide would occur at a slower rate and might even need some help from a metal ion acting as a Lewis acid.

3.) Addition of a second mole of organometallic reagent. The Grignard reactions and lithium dimethylcuprate reaction are the only ones which need be considered
under this heading, and of these, the lithium dimethyl-cuprate is a well-documented reaction

\[
\text{CH}_2=\text{CHLi} \rightarrow \text{CH}_2=\text{CCH}_3
\]

which has already been discussed.

The Grignard reactions, however, present a more complex situation:

\[
\begin{align*}
\text{CH}_2=\text{CHLi} + \text{EtMgBr} & \rightarrow \text{CH}_2=\text{CCH}_3 + \text{EtLi} \\
\text{CH}_2=\text{CHLi} + \text{CH}_2=\text{CHMgBr} & \rightarrow \text{CH}_2=\text{CCH}_3 + \text{CH}_2=\text{CHMgBr} \\
\text{CH}_2=\text{CHLi} + \text{CH}_3=\text{C}≡\text{CHMgBr} & \rightarrow \text{CH}_2=\text{CCH}_3 + \text{CH}_3=\text{C}≡\text{CHMgBr}
\end{align*}
\]
Ethylmagnesium bromide adds in a 1,4 fashion presumably for steric reasons since nucleophilic attack at the $\beta$-carbon does not seem to be electronically favored. On the same grounds vinylmagnesium bromide would be expected to show conjugate addition since 1,6 addition is entirely free from steric hindrance – it adds in a 1,2 manner. Finally the ethynylmagnesium bromide reverts to form and adds in a 1,2 fashion to give the alcohol. Without the presence of the $\beta$-alkoxyl group it becomes once again difficult to predict the mode of addition except in the case of ethynyl Grignard reagents.

IV. Further reactions of the derivatives of 2-isopropoxy-methylene cyclohexanone.

Given the pi system of 2-propenylidene-1-vinylcyclohexanol (37) one is intrigued by its possibilities for acid-catalyzed, thermal, or photochemical reactions.
The first of these three conditions, acid catalysis, presumably will produce the heptatrienylium ion (45).

\[
\text{\includegraphics[width=0.2\textwidth]{45.png}}
\]

To this end, p-toluenesulfonic and sulfuric acids were employed but gave no isolable products. Finally, reaction with acetic acid gave 1-(3-acetoxy-1-propenyl)-2-vinylcyclohexene (46) in good yield.

\[
\begin{align*}
37 & \xrightarrow{\text{HOAc}} 46 \\
\text{\includegraphics[width=0.2\textwidth]{46.png}}
\end{align*}
\]

The proton magnetic resonance spectrum of 46 is shown in Figure 17 and should be compared with that of ethyl 3-(2-vinyl-1-cyclohexenyl)propenoate (16) (see Figure 9) since the structural assignment was based largely on this
comparison. Without the carbethoxyl group conjugated with the triene, the olefinic protons are shifted upfield as can be seen in Table 6.

Figure 17. Proton magnetic resonance spectrum of 1-(3-acetoxy-1-propenyl)-2-vinylcyclohexene.
Table 6. Proton magnetic resonance spectral comparison of 16 and 46.

<table>
<thead>
<tr>
<th></th>
<th>R=CO₂Et(16)</th>
<th>CH₂OAc(46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₁</td>
<td>5.735</td>
<td>5.68</td>
</tr>
<tr>
<td>H₂</td>
<td>7.93</td>
<td>6.89</td>
</tr>
<tr>
<td>H₃</td>
<td>7.12</td>
<td>6.95</td>
</tr>
<tr>
<td>H₄</td>
<td>5.19</td>
<td>5.04</td>
</tr>
<tr>
<td>H₅</td>
<td>5.31</td>
<td>5.16</td>
</tr>
<tr>
<td>J₁₂</td>
<td>16Hz</td>
<td>16.5</td>
</tr>
<tr>
<td>J₃₄</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>J₃₅</td>
<td>17</td>
<td>17</td>
</tr>
</tbody>
</table>

The effect of the carbethoxyl group is most noticeable on the proton (H₂) to the substituent since this proton is sterically most accessible to the shielding effects of the carbethoxyl group. The proton magnetic resonance spectrum of the acetoxy compound has some additional features: H₁ is a doublet of triplets, being split (J=7Hz) by two protons on the allylic carbon attached to oxygen (doublet at δ 4.56); and the acetyl methyl displays a sharp singlet at δ 1.93. The ultraviolet spectrum of 46 has a maximum at 274 nm with the three fingered fine structure and high extinction coefficient (33000) typical of conjugated trienes.

While no direct cyclization was realized in the
acetolysis reaction, the fortuitous production of a linearly conjugated triene gives not only a route to cyclization, but also a possible synthetic pathway to longer polyene systems or a variety of terminal substitution patterns on the divinylcyclohexene system. Pyrolysis of methyl allyl ethers is known to lead to reductive elimination of formaldehyde with rearrangement of the allylic system.

\[
\begin{align*}
\text{CH}_2\text{CH}_2\text{H} & \xrightarrow{300-400^\circ} \text{C} = \text{C} + \text{CH}_2 \\
\text{C} = \text{C} & \text{C} \text{C} \text{H}_2
\end{align*}
\]

This reaction has received considerable attention and, although a somewhat doubtful looking transition state has been proposed,\textsuperscript{95-98} the conclusion that the reaction is a clean unimolecular process appears sound. This is important because a free-radical chain process, as occurs in the case of the thermolytic cleavage of non-allylic ethers,\textsuperscript{98} might lead to very different products considering the butadiene system of the substrate.

The procedure of Diner and co-workers\textsuperscript{99} for the methylation of 2-hydroxymethyl-3,4-dihydro-2H-pyran, also an acid-sensitive compound, was employed for the methylation of 37 with good success.
The spectral data (uv, pmr, ir) of ether (47) are virtually the same as those of the parent alcohol with the exception of an O-methyl group in the proton magnetic resonance spectrum at δ 3.02 and the lack of an O-H in the infrared spectrum.

When the ether was subjected to pyrolysis in the gas phase at 350° for two minutes expulsion of formaldehyde (trapped as the 2,4-DNPH adduct) was observed and a yellow oil was recovered in about 80% yield. This yellow oil appeared to contain one main component judged from its behaviour on a number of glc columns. A sample was obtained from preparative glc and spectral data refer to that sample.
The mass spectrum indicates a molecular weight of 148 amu \( (C_{11}H_{16}) \) confirming the loss of formaldehyde. Exhaustive hydrogenation over platinum oxide gave two products in a ratio of about three to one. The major product had a molecular weight of 154 and contained no double bonds as determined by ultraviolet end absorption and the allylic region of the proton magnetic resonance spectrum. Thus, the pyrolysis product contains three double bonds and one ring. Additionally, the two of the double bonds are conjugated since the ultraviolet spectrum shows a maximum absorption at 242 nm with an extinction coefficient of about 12,000. The proton magnetic resonance structure of the pyrolysis product is shown in Figure 18.

This spectrum was repeated several times on different samples. From slight differences in integration, an impurity was detected which manifests itself at \( \delta 0.9 \) as a doublet and in the large olefinic multiplet at \( \delta 5.3 \) to \( \delta 5.7 \). If the doublet is assigned as a methyl group and
the molecular formula of the impurity is also C_{11}H_{16}, integrations indicate that it constitutes from 25 to 35% of the pyrolysis product and contains 2 or 3 olefinic protons. Since we were unable to eliminate this impurity, it became evident that structural assignments of the major product would be speculative. The 242 nm chromophore and proposal of one ring and three double bonds appears viable and our integration arithmetic suggests three or four olefinic protons in the main product.

Figure 18: Proton magnetic resonance spectrum of the pyrolysis product of methyl 2-propenylidene-1-vinyl-cyclohexyl ether.
Extensive decoupling experiments were run on the above spectrum and when the olefinic multiplet is irradiated the large doublet at 6 1.7 (which integrates to about six protons) collapses. This suggests two allylic methyl groups, each attached to a carbon bearing a hydrogen. The initial loss of formaldehyde could account for one of these methyl groups and a 1,5 hydrogen shift.

\[ \text{CH}_3 \quad \Delta \quad -\text{CH}_2\text{O} \]

would give a second such group.

\[ \text{CH}_3 \quad \Delta \quad \text{CH}_3 \]

\[ \text{H}_a \quad \text{H}_b \quad \text{H}_c \quad \text{H}_d \]
Hence 3-ethylidene-2-(1-propenyl)cyclohexene (48) was tentatively proposed as the product. Due to the steric nature of the formaldehyde elimination and the 1,5 hydrogen shift both double bonds would be in a cis configuration. The doublet of multiplets at δ 5.89 corresponds to H_d and the splitting constant of 11Hz is in agreement with the cis assignment. H_a, H_b, and H_c should appear as a doublet of doublets, a finely split quartet, and a doublet of quartets, respectively, all with about the same chemical shifts. Although the close proximity of their shifts and those of the impurity prevent a clean assignment, the decoupling experiments suggest that this is correct.

The longest chromophore of 48 with a calculated value of 244 nm, agrees with the ultraviolet maximum of 242 nm.

The major hydrogenation product 1-ethyl-2-propyl-cyclohexane (49) was identified by comparison with an authentic sample prepared from 1-ethyl-2-propylcyclohexanol (38) via 1-ethyl-2-propylcyclohexene (50).
The dehydration of 38 with p-toluenesulfonic acid gave a mixture of isomers as evidenced by a multiplet at 5.32 and a quartet (J = 6Hz) at 5.12 in the proton magnetic spectrum. This mixture was not separated but was hydrogenated with difficulty to give 49 whose proton magnetic resonance spectrum is virtually identical with that of the hydrogenated pyrolysis product.

The mass spectrum of the hydrogenated pyrolysis product revealed that it is actually a mixture of 50 and 49. The saturated hydrocarbon (49) is responsible for the small molecular ion at m/e= 154 while every major peak in the mass spectrum of 50 (above-mentioned mixture of isomers) is represented in the spectrum of the hydrogenated pyrolysis product (i.e. m/e= 152, 123, 110, 109, 79 and 58, none of which is prominent in the spectrum of 49). The major peaks of 49 (especially m/e= 125, 111, 83 and 69 which do not appear in the spectrum of 50) also appear in the spectrum.

Since 50 was reduced to 49 only with difficulty, the hydrogenation of the triene (48) might be expected to produce some 50 as a semi-hydrogenated product.
The minor hydrogenation product appears to be 2-methyl-1,2,3,4,5,6,7,8-octahydronaphthalene (51) from its ultraviolet, proton magnetic resonance and mass spectra.

This would correspond to a minor pyrolysis product of a 2-methyl-hexahydronaphthalene which could arise from the cyclization of an initially produced triene.
Finally 47 was photolyzed in ether at 251 nm (unsensitized) to show smooth disappearance of the starting material over a four-hour period. However, we were unable to isolate any major products. We had expected that 47 might undergo a di-$\pi$-methane rearrangement [as does artemisia triene (52)98] to form a divinyl cyclopropane.

No such product was observed.
EXPERIMENTAL

Introduction

All pmr spectra were run on either Varian HA-100 or a Varian EM360 (noted), uv spectra on a Cary model 15, ir spectra on either a Beckman IR8 or a Perkin-Elmer 137, and mass spectra on a Varian CH7-MAT. All boiling points given are uncorrected while melting points (taken on a Büchi "schmeltzpunktbestimmungsapparat") were corrected.

2-Hydroxymethylenecyclohexanone (2). The preparation was run under nitrogen according to the method of C. Ainsworth as described in "Organic Synthesis". To a mixture of 300 ml dry ether, 29.4 g (0.30 mole) redistilled cyclohexanone, and 27.0 g (0.45 mole) methyl formate in a 1000 ml three-necked flask equipped with a mechanical stirrer, stopper, and a mercury bubbler, was added 6.90 g (0.30 g-atom) sodium shot. The reaction was initiated by the addition of 3 ml of methanol to the stirred mixture, which was then placed in a cold water bath. The mixture became quite thick after ten minutes and stirring was difficult. The mixture was stirred for an additional two hours, and then was poured onto 100 g of ice. The ether layer was separated and washed with 50 ml of water. The combined aqueous extracts were washed with two 40 ml portions of ether, and the aqueous layer was acidified with
50 ml of 6 N hydrochloric acid. The mixture was extracted with two 100 ml portions of ether, and the ether extracts were washed with 25 ml of saturated ammonium chloride solution, dried (sodium sulfate), and concentrated, giving 35.3 g (92%) of 2-hydroxymethylenecyclohexanone (9). This material need not be further purified before use, but may be distilled under vacuum: bp 57-59° (2.3 mm); [lit75 bp 39-40° (0.10 mm)]; pmr (CCl4) δ 1.2-1.5 (m, 4H) 1.6-1.9 (m, 4H) 8.61 (s, 1H) 13.5 (dependent upon concentration) (s, 1H).

2-Isopropoxymethylenecyclohexanone (10) & 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15).

METHOD A (W. S. Johnson and H. Posvic)72: The crude product of the previous reaction, 63.0 g (0.500 mole) of 2, 40.0 g (0.579 equivalent) of ignited potassium carbonate, and 73.8 g (0.600 mole) of 2-bromopropane were placed in 200 ml of redistilled acetone and the mixture was refluxed for 72 hrs. The mixture was filtered, the solution concentrated, and the residue distilled, giving 52.1 g (62%) of a mixture of 0-alkylated products.

METHOD B: The sodium salt of 2-hydroxymethylenecyclohexanone was taken from the preparation of 2-hydroxymethylenecyclohexanone (9) without work-up. i.e. after "...The mixture was stirred for an additional two hours...". The ether was removed with an aspirator, and the residue placed under reduced pressure (1 mm). The nitrogen atmosphere was
reintroduced and dry dimethylsulfoxide (DMSO), 200 ml, was added, followed by 49.2 g (0.400 mole) of 2-bromopropane and the mixture was stirred overnight. After 200 ml of ether had been added, the DMSO was removed by repeated washing with water, followed by a final washing with a saturated solution of ammonium chloride. The ether solution was dried (sodium sulfate), concentrated, and distilled under vacuum, giving 27.8 g (55%) of a mixture of O-alkylated products.

METHOD C: Again, the crude material, 63.0 g (0.500 mole) of 2-hydroxymethylenecyclohexanone (9), 40.0 g (0.579 equivalent) of ignited potassium carbonate, and 73.8 g (0.600 mole) of 2-bromopropane were placed in 200 ml of DMSO, heated to 50° and stirred overnight. The supernatent solution was decanted and the residue washed with two 100 ml portions of ether. The DMSO was removed by repeated washings with water, followed by a final washing with a saturated solution of ammonium chloride. The solution was dried (sodium sulfate), concentrated, and the residue distilled under vacuum, giving 69.2 g (83%) of a mixture of O-alkylated products.

The mixtures of O-alkylated products consisted of 15-20% 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15) and 85-80% 2-isopropoxymethylenecyclohexanone (10) as determined by pmr regardless of the method of preparation. Separation was effected by fractionation on a spinning band column,
giving 2-isopropoxymethylene cyclohexanone (10): \( \text{bp } 72-74^\circ (0.10 \text{ mm}) \); \( \text{lit.}^{36} \text{ bp } 72-73^\circ (0.1 \text{ mm}) \); pmr (CCl\(_4\)) \( \delta 1.29 \) (d,\( 6H, J=6 \)) 1.5-1.9 (m,\( 4H \)) 2.1-2.5 (m,\( 4H \)) 4.20 (septet,\( 1H, J=6 \)) 7.24 (t,\( 1H, J=2.5 \)); uv max (95% EtOH) 277 nm (\( \epsilon 16,900 \)).

Also obtained was an enriched fraction of 2-isopropoxy-3,4,5,6-tetrahydrobenzaldehyde (15) (90% by pmr): \( \text{bp } 76-78^\circ (0.10 \text{ mm}) \). An analytical sample was obtained on a 6 ft by \( \frac{3}{4} \) inch 5% FFAP on Chromosorb G column at 100\(^\circ\); pmr (CCl\(_4\)) \( \delta 1.25 \) (d,\( 6H, J=6 \)) 1.5-1.9 (m,\( 4H \)) 2.1-2.4 (m,\( 4H \)) 4.46 (septet,\( 1H, J=6 \)) 10.06 (s,\( 1H \)); ir (neat) 3060-2920 (s), 2890 (m), 1665 (s), 1615 (s), 1380 (m), 1190 (s) and 1160 cm\(^{-1} \) (s); uv max (95% EtOH) 276 nm (\( \epsilon 15,500 \)).


2-Ethynyl-3,4,5,6-tetrahydrobenzaldehyde (10). Schiess and Chia had prepared this compound using sec-butyloxymethylene cyclohexanone as a starting material.\(^37\) To a stirred mixture of sodium acetylide in liquid ammonia [prepared from 20.7 g (0.900 g-atom) of sodium and purified (two sulfuric acid traps followed by a calcium chloride drying tube) acetylene] was added 15.1 g (90.0 mmoles) of 10 in 50 ml dry tetrahydrofuran (THF). After the mixture was stirred for 2 hrs, 57 g of ammonium chloride and 350 ml of ether were added and the ammonia was allowed to evaporate. Cold water was added and the organic layer was separated and washed with water, saturated sodium chloride solution, and dried (sodium sulfate).
The solvent was removed and the residue was dissolved in 125 ml of 100% ethanol. The alcohol solution was mixed with 65 ml of 2N sulfuric acid and the solution was stirred for 3 hrs at room temperature. About 500 ml of water was added and the mixture was extracted with three 125 ml portions of ether. The combined ether extracts were washed with three portions of 2N sodium hydroxide, water, saturated sodium chloride solution, and then dried over sodium sulfate. The solution was concentrated and the residue distilled to give 6.34 g (51%) of 2-ethynyl-3,4,5,6-tetrahydrobenzaldehyde (19): bp 45-80° (0.2 mm). The material was recrystallized from ether-petroleum ether to give pale yellow plates: mp 49-51.5° (lit.37 50-52°); pmr (CDCl₃, EM360) δ 1.5-2.0 (m, 4H) 2.0-2.6 (m, 4H) 3.45 (s, 1H) 10.12 (s, 1H).

2-Vinyl-3,4,5,6-tetrahydrobenzaldehyde (17).

METHOD A (Schiess and Chia)37: A solution of 2.894 g (21.6 mmole) of 19 in 60 ml of a 30:70 ethyl acetate : hexane mixture, was added to 1.02 g of activated Lindlar catalyst in 100 ml of the same solvent mixture. Hydrogen uptake was monitored and stopped after the addition of one mole (520 ml at 20° and 756 mm). The mixture was filtered, the solution concentrated, and the residue distilled to give 2.48 g (84%) of 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (17): bp 48-50° (0.10 mm).

METHOD B: To a stirred solution of 20.5 g (0.122 mole) of 10 in 500 ml of dry THF at 0°, was added 155 ml (0.122
mole) of 0.79M vinyl lithium in THF over a 30 min period. The solution was stirred for 1 hr at 0° and carefully hydrolyzed with 125 ml of saturated ammonium chloride solution. One liter of ether was added and the THF removed with repeated washing with water, followed by saturated sodium chloride solution. The ethereal solution was dried (calcium chloride), the solvent was removed on the rotary evaporator, and the residue was treated with a mixture of 100 ml ethanol and 100 ml 2N sulfuric acid for 3 hrs at room temperature. The mixture was shaken with ether and the organic layer was separated, dried over calcium chloride and the solvent removed. The residue was distilled, giving 8.46 g (51%) of 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (17): bp 46-48° (0.10 mm) [lit.37 bp 45° (0.02 mm)(sic)]; pmr (CCl₄) δ 1.5-1.9 (m, 4H) 2.2-2.6 (m, 4H) 5.39 (d, 1H, J = 11) 5.48 (d, 1H, J = 17) 7.34 (dd, 1H, J = 11, 17) 10.26 (s, 1H).

Triethyl phosphonoacetate. The method described by G.M.Kosolapoff was used without modification.98 Ethyl bromoacetate (9.23 g, 55.1 mmoles) and 9.83 g triethyl phosphite were heated over a 45 min period until the temperature had reached 150°. The product was isolated by vacuum distillation; 10.87 g (78%) bp 93-95° (0.60 mm) [lit.98 bp 140° (10 mm)]; glc analysis (4 ft by 1/8 inch 2% SE-30 on Chromosorb G, 140°) showed the material to be greater than 95% pure, with a trace of triethyl phosphite present.
**Ethyl 3-(2-vinyl-1-cyclohexenyl)propenoate (16).** The reaction was run under a nitrogen atmosphere. A suspension of 0.425 g (10.5 mmols) of sodium hydride (57% in a mineral oil suspension which was not pre-washed) in 4 ml of dry benzene was treated with 2.552 g (11.3 mmols) of triethyl phosphonoacetate (a water bath was used to cool the solution), followed by 0.727 g (5.35 mmols) of 2-vinyl-3,4,5,6-tetrahydrobenzaldehyde (17) in 1 ml of dry benzene. The mixture was warmed gently to about 70°, then cooled to 0° and the phosphorous compounds allowed to precipitate (~1 hr). The benzene solution was poured from the precipitate, the solvent removed on the rotary evaporator, and the residue distilled to give 0.661 g (60%) of ethyl-3-(2-vinyl-1-cyclohexenyl)propenoate (16): bp 87-88° (0.025 mm); pmr (CCl₄) δ 1.27 (t, 3H, J=7) 1.68 (m, 4H) 2.31 (m, 4H) 4.16 (quartet, 2H, J=7) 5.19 (d, 1H, J=11) 5.31 (d, 1H, J=11) 5.73 (d, 1H, J=11) 7.12 (dd, 1H, J=11, 17) 7.93 (d, 1H, J=16); ir (CCl₄) 1720, 1625, 1300, 1178, 1161 cm⁻¹; uv max (EtOH) 291 nm (ε 16,400), 299 nm (ε 22,700), 305 nm (ε 16,800).

**Anal.** Calc'd for C₁₃H₁₈O₂: C 75.69, H 8.80.

**Found:** C 75.45, H 8.99.

**Thermolysis of ethyl 3-(2-vinylcyclohexen-1-yl)propenoate (16).**

**Product.** A solution of 100 mg of ethyl 3-(2-vinylcyclohexen-1-yl)propenoate (16) in 6 ml of spectral grade cyclohexane was heated to 140° for 12 hrs in a sealed bomb. (see "Kinetic
Data" for details) The solvent was removed to give 100 mg of yellow oil, which was purified by column chromatography on alumina, Activity Grade III, eluting with cyclohexane. The product was distilled giving 30 mg of a pale yellow oil: bp 75° (0.025 mm); pmr (CCl₄) δ 1.10 (t, 3H, J=7) 1.4-2.0 (m, 4H) 2.0-2.6 (m, 7H) 4.08 (quartet, 2H, J=7) 5.3-5.6 (m, 2H); irr (CCl₄) 2950, 1731, 1440, 1365 cm⁻¹; uv max (95% EtOH) 241 nm (ε 14,000).

Kinetic Data. All kinetic data were taken from samples which consisted of approximately 1.5 mg of compound 16 in 100 ml of spectral grade cyclohexane. Prior to each run, 150 μl of a 500 mg/100 ml solution was diluted to 50 ml in spectral grade cyclohexane under nitrogen. Four to 6 ml of solution was then syringed into each of the previously prepared bombs. Bombs were washed with sulfuric acid-potassium dichromate solution, distilled water, 28% ammonia solution, and CO₂-free distilled water, and left in the annealing oven overnight. The samples were degassed at 0.05 mm and sealed at -78° at 0.05 mm. Each kinetic run used six bombs placed simultaneously into a preheated oil bath, set at the desired temperature. Temperatures were regulated using an American Instrument Co. "Quickset" type regulator. A 0°-360° Hg thermometer, calibrated against a Pt-resistance thermometer, was used (all temperatures given are corrected). At appropriate time intervals, a bomb was taken out and immediately cooled (10 sec) to -79°. The bomb was then opened and the
TABLE 7: KINETIC DATA

<table>
<thead>
<tr>
<th>T=400.2°K, A₀=1.90</th>
<th>t(min)</th>
<th>60.0</th>
<th>120</th>
<th>210</th>
<th>300</th>
<th>390</th>
<th>480</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.63</td>
<td>1.37</td>
<td>1.13</td>
<td>0.914</td>
<td>0.730</td>
<td>0.605</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T=403.8°K, A₀=1.750</th>
<th>t(min)</th>
<th>60.0</th>
<th>120</th>
<th>182</th>
<th>241</th>
<th>300</th>
<th>362</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.586</td>
<td>1.256</td>
<td>1.038</td>
<td>0.842</td>
<td>0.663</td>
<td>0.563</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T=409.8°K, A₀=1.750</th>
<th>t(min)</th>
<th>60.0</th>
<th>90.0</th>
<th>160</th>
<th>190</th>
<th>260</th>
<th>290</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.217</td>
<td>1.001</td>
<td>0.799</td>
<td>0.686</td>
<td>0.571</td>
<td>0.482</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T=413.7°K, A₀=2.18</th>
<th>t(min)</th>
<th>30.0</th>
<th>50.0</th>
<th>75.0</th>
<th>105</th>
<th>135</th>
<th>165</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.61</td>
<td>1.59</td>
<td>1.22</td>
<td>0.892</td>
<td>0.661</td>
<td>0.504</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T=423.0°K, A₀=1.05</th>
<th>t(min)</th>
<th>15.9</th>
<th>34.0</th>
<th>40.8</th>
<th>47.8</th>
<th>56.8</th>
<th>68.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.740</td>
<td>0.581</td>
<td>0.530</td>
<td>0.529</td>
<td>0.415</td>
<td>0.356</td>
<td></td>
</tr>
</tbody>
</table>
the solution was allowed to thaw. After the solution had been thoroughly mixed, a uv cell was rinsed with the solution and the uv spectrum was run from 340 nm to 220 nm. The absorbance at 299 nm was recorded and the appearance of the 242 nm peak noted. A spurious peak at 287 nm appeared in some samples and some of these were checked on the glc to confirm that this peak did not affect the absorbance value at 299 nm. Six samples were taken on each run, over a time span of about two half-lives. Due to the heat capacity of the large bombs, accurate zero-point times were unattainable, but the absorbance of the starting solution was used as the initial absorbance value.

\( \alpha-(\text{Bromomethyl})\text{styrene (24)} \): The method of S. F. Reed was used. A mixture of 122.7 g (1.04 moles) of freshly distilled \( \alpha \)-methylstyrene, 112.1 g (0.992 mole) of N-bromo-succinimide, and 65 ml of carbon tetrachloridewere placed in a 1 l round-bottomed flask equipped with a magnetic stirrer and an efficient condenser. The mixture was heated to \( \approx 170^\circ \), and the violently exothermic reaction was controlled with an ice-water bath. After the reaction had been brought under control (about 5 min), the ice-water bath was removed and the mixture was allowed to cool over a 3 hr period. The mixture was filtered; the solvent was removed from the filtrate, and the resultant yellow oil was distilled, giving 90.4 g (46%) of \( \alpha-(\text{bromomethyl})\text{styrene (24): bp 70-80^\circ (1 mm) [lit}^79 \text{ bp 66-67^\circ (0.9 mm)].} \)
2-Phenyl-2-propenyl triphenylphosphonium bromide (25).

The procedure described by Schlosser and Christmann was employed.13 A mixture of 90.4 g (0.458 mole) of α-(bromo-methyl)styrene (24), 141 g (0.538 mole) of triphenylphosphine and 700 ml of benzene was stirred overnight. The product was isolated by filtration and recrystallized from chloroform-pentane to give 128 g of 2-phenyl-2-propenyl triphenylphosphonium bromide (25). Another 27.4 g (74% total yield) of product was recovered by stirring the filtrate (above) for an additional 48 hrs: mp 216-18° (lit.13 mp 224-25°); pmr (CDCl₃, EM360) δ 5.26 (d, 2H, J=14) 5.57 (s, 1H) 5.62 (s, 1H) 7.3 (s, 5H) 7.7-8.1 (m, 15H).

Reaction of acrolein with α-styryl triphenylphosphonium methide. To a mixture of 20.5 mmoles of freshly prepared sodamide [from 0.472 g (20.5 mg-atom) sodium] in 50 ml of benzene in an inert (N₂) atmosphere was added 9.17 g (20.0 mmoles) of 25. The mixture was refluxed for 4 hrs and allowed to stand overnight. The mixture was filtered under nitrogen to give a wine-red solution of the salt-free ylide: 67% yield as determined by neutralization with ethereal hydrochloric acid and back titration with aqueous sodium hydroxide (phenolphthalein end-point). This solution was stored (frozen) without apparent deterioration for limited periods (up to one week). To 10 mmoles of a vigorously stirred solution of the salt-free ylide at 0° was added 0.62 g (11 mmoles) of freshly distilled acrolein
in 2 ml dry benzene. After 3 hrs, the benzene was lyophilized under high vacuum (∼1 mm, 0°) and replaced with 45 ml of dry ether. Still at 0°, the mixture was stirred vigorously and filtered under nitrogen: glc analysis (4 ft by 1/8 inch 4% SE-30 on Chromosorb W at 105°) shows acrolein (15%), a partially resolved doublet (∼15%), and a main peak (∼60%). The main peak was collected by glc (12 ft by 1/4 inch 2% SE-30 on Chromosorb G at 140°) and identified as 2-phenyl-1,3-cyclohexadiene (36): pmr (CCl₄) δ 1.8-2.4 (m,4H) 5.8-6.4 (m,3H) 7.0-7.2 (m,5H) [the pmr spectrum matches that of 2-2-phenyl-1,3-cyclohexadiene (24) rather than that of 1-phenyl-1,3-cyclohexadiene (28) as reported]; uv max (95% EtOH) 272nm (ε 6200) [lit. uv max (cyclohexane) 276 nm (ε 8140)]. The minor product (doublet) gave a uv triplet at 251, 262, and 271 nm (ε ~20,000).

Hydrogenation of 2-phenyl-1,3-cyclohexadiene (26). Twenty mg (0.13 mmole) of the main product (above) were collected on the glc, dissolved in 3 ml of spectral grade cyclohexane, and hydrogenated over 6 mg of platinum oxide to give a 50:50 mixture of phenylcyclohexane (27) and 1-phenylcyclohexene (26) as determined by comparison with authentic samples.

1-Phenylcyclohexene (26). A solution of 5.80 g (59.3 mmoles) of cyclohexanone in 100 ml of dry ether under nitrogen was cooled to 0° and treated with 19 ml (57 mmoles) of 3M phenyllithium in ether. The reaction mixture was stirred
for one hour. After work-up, the solution was dried over calcium chloride, and the solvent was removed to give 8.32 g (83%) of crude 1-phenylcyclohexanol: glc (4 ft by 1/8 inch 4% SE-30 on Chromosorb W at 105°) showed the material to be 85% pure. This material was dissolved in 80 ml of benzene containing 1.0 g of p-toluenesulfonic acid. The solution was refluxed for two hours while the water (∼ 0.7 ml) was collected in a Dean-Starck trap. The solvent was distilled and the residue was dissolved in ether. p-Toluenesulfonic acid was washed out with aqueous sodium bicarbonate. After the ether solution had been dried (calcium chloride), the solvent was removed and the product was distilled to give 6.39 g of 1-phenylcyclohexene (26): bp 65-67° (0.025 mm) [lit.29 bp 126-128° (16 mm)]; pmr (CCL₄, EM360) δ 1.5-2.5 (m,8H) 5.9-6.1 (m,1H) 7.0-7.4 (m,5H); 95% pure by glc analysis (4 ft by 1/8 inch 4% SE-30 on Chromosorb W at 105°).

Phenylcyclohexene (27). Aluminum chloride, 6.9 g (0.52 mole), was added in small portions to a stirred solution containing 14.5 g (0.177 mole) of cyclohexene and 13.8 g (0.177 mole) of benzene at 0°. The mixture was refluxed for 4 hrs and allowed to cool to room temperature. One hundred mililiters of ether and 30 ml of water were added. The ether layer was washed with water and dried over calcium chloride. The ether was removed on the rotary evaporator and the residue distilled to give 10.5 g (42%, based on aluminum chloride) of phenylcyclohexene (27): bp 58-60°
108

(0.05 mm) [lit.\textsuperscript{100} bp 230-245\degree (760 mm)], which is better than 95\% pure by analysis on a 4 ft by 1/8 inch 4\% SE-30 on Chromosorb G column at 105\degree; pmr (CCl\textsubscript{4}, EM360) \delta 0.9-2.0 (m,1H) 2.1-2.6 (m,1H) 7.1 (s,5H); uv max (95\% EtOH) 211 nm.

\textbf{4-Benzoyloxy cyclohexanol (30).} According to the method described by R.S. Monson\textsuperscript{101}, a solution containing 46.9 g (0.418 mole) of 1,4-cyclohexanediol and 108 ml of dry pyridine in 140 ml of dry chloroform was cooled to 3\degree (ice bath), 46.5 ml (0.400 mole) of benzoyl chloride in 120 ml of dry chloroform was added with stirring. The rate of addition was regulated so that the temperature did not rise above 5\degree. After standing overnight at room temperature, the chloroform solution was washed four times with water, followed with 5\% sulfuric acid, and finally with saturated sodium chloride solution. The solution was dried (sodium sulfate), concentrated, the solvent was removed with the rotary evaporator, and the residue was distilled, giving 44.3 g (50.3\%, based on benzoyl chloride) of 4-benzoyloxy cyclohexanol (30): bp 148-153\degree (0.1 mm) [lit.\textsuperscript{101} 175-8\degree (2.0 mm)]; ir (neat) 3500, 2990, 1710, 1270 cm\textsuperscript{-1} (broad).

\textbf{4-Benzoyloxy cyclohexanone (31).} Using the method of R.S. Monson\textsuperscript{102} a stirred solution of 44.3 g (0.202 mole) of 4-benzoyloxy cyclohexanol (30) in 80 ml of acetic acid was treated, dropwise, with a solution of 19.4 g (0.194 mole, 0.291 equivalent) of chromium trioxide in 12 ml of water
and 46 ml of acetic acid. The temperature was maintained below 35° throughout the addition by means of a water bath. After 12 hrs, 300 ml of ether was added, and the resulting solution was washed with two 200 ml portions of water, followed with two 200 ml portions of saturated sodium bicarbonate solution, and finally with 200 ml of water. After being dried over sodium sulfate, the solution was placed in a crystalizing dish and the solvent evaporated. The solid residue was pumped on (ca 0.1 mm) for one hour to give 35.2 g (80.2%) of 4-benzoyloxy-4-cyclohexanone (31): mp 60-63° (lit. mp 62-63°); pmr (CCl₄, EM360) δ 1.8-2.7 (m, 8H) 5.1-5.4 (t, 1H, J=4) 7.2-7.5 (m, 3H) 8.01 (dd, 2H, J=2, 7).

4-Benzoyloxy-1-phenylcyclohexene (32). A mixture of 21.8 g (0.100 mole) 31 and 30 ml dry ether was treated with a solution of 0.0983 mole of phenylmagnesium bromide [prepared from 15.4 g (0.0983 mole) of phenyl bromide and 2.44 g (0.101 g-atom) of magnesium] in 75 ml of dry ether. When an oily precipitate formed, 30 ml of dry benzene was added to the mixture and the addition was resumed. The usual work-up gave 30 g (~100%) crude 4-benzoyloxy-1-phenylcyclohexanol. A pmr spectrum (CDCl₄, EM360) showed that the ratio of aromatic protons to the proton on the carbon bearing benzoyloxy group (δ 5.3) was 9.5 to 1 (theoretical 10 to 1 with two phenyl groups). This material was dissolved in 150 ml of pyridine and the solution was cooled to 0° under nitrogen. Then 33.4 g (0.220 mole) of phosphorous oxychlor-
ide was added, dropwise, to the stirred solution. The temperature was maintained below 5° throughout the addition and for 2 hrs afterward. After standing overnight at room temperature, the solution was poured over 250 g of ice. The usual work-up gave 11.3 g (43%, based on phenylmagnesium bromide) of 4-benzoyloxy-1-phenylcyclohexene (32) as a white solid, which was recrystallized from ethanol-water to give white needles: mp 108-110° (lit. mp 114-116°); pmr (CDCl₃, EM360) δ 1.8-2.3 (m, 2H) 2.3-2.7 (m, 4H) 5.2-5.5 (t, 1H, J=6) 5.9-6.1 (m, 1H) 7.2-7.6 (m, 8H) 7.9-8.2 (m, 2H).

4-Phenyl-3-cyclohexenol (33). To a stirred mixture of 1.00 g (26.4 mmoles) of lithium aluminum hydride in 25 ml of dry ether under nitrogen, was added 4.38 g (15.2 mmoles) of 32 dissolved in 75 ml of dry ether. Stirring was continued for 15 min and the mixture was then treated with a saturated solution of ammonium chloride until the inorganic salts congealed as a tacky precipitate. The supernatant solution was decanted, concentrated with the rotary evaporator, and the residue was held in vacuo (0.05 mm) for 2 hrs, giving 2.35 g (89%) of 4-phenyl-3-cyclohexanol (33) as a white solid: mp 77-80° (lit. 80-82°).

S-Methyl xanthate ester of 4-phenyl-3-cyclohexenol (34). A solution containing 1.16 g (7.5 mmoles) of 33 in 20 ml of dry ether (under nitrogen) was treated with 4.0 ml (8.0 mmoles) of 2M n-butyllithium in hexane. This addition was
followed by 1.4 g (18 mmoles) dry carbon disulfide. The mixture was stirred for 1.5 hrs. Then 2.43 g (17.1 mmoles) of methyl iodide was added and the mixture was stirred overnight. The mixture was filtered and the residue was washed with ether. The combined filtrates were washed with saturated ammonium chloride solution, dried (sodium sulfate), and the solvent removed to give 1.9 g (~100%) of crude S-methyl xanthate ester of 4-phenyl-3-cyclohexenol (34) as an orange oil.

1-Phenyl-1,3-cyclohexadiene (28) and 1-phenyl-1,4-cyclohexadiene (35). The crude S-methyl xanthate ester of 4-phenyl-3-cyclohexenol (34) was run through a glc column (6 ft by \( \frac{1}{4} \) inch 5% FFAP on Chromosorb G at 150° with injector and detector temperatures of 250° and 230°, respectively) and the products were collected: 1-phenyl-1,3-cyclohexadiene (28) \{uv max (EtOH) 302 nm (ε 12,000) \[lit.80\] uv max (cyclohexane) 303 nm (ε 13,800)\} appeared at nine minutes and 1-phenyl-1,4-cyclohexadiene (35) \{uv max (EtOH) 249 nm (ε 8000) \[lit.80\] uv max (cyclohexane) 249 nm (ε 9300)\} followed immediately afterward at 10.5 minutes.

About 30 mg (0.13 mmole) of 28 in 3 ml of benzene was treated with 2 mmoles of salt-free α-styryl triphenylphosphonium methyldi in 5 ml of benzene. The solvent was removed under vacuum (1 mm) and the residue was washed with 5 ml of ether. This solution showed a strong (10,000) uv absorption at 302 nm when 10 l of the supernatent liquid was diluted to 3 ml in 95% ethanol.
Vinyl bromide. This method of preparation was first described by P.N. Kogerman in 1930. To 90.0 g (1.61 equivalents) of potassium hydroxide in 500 ml of 95% ethanol at room temperature was added 300 g (1.65 moles) of 1,2-dibromoethane. The mixture was heated to 80° and the product, a colorless liquid, collected using a dry ice-acetone trap. This material was dried over sodium sulfate, and redistilled to give 142 g (84%) of vinyl bromide: bp < 20°; (lit. bp 16°).

2-(2-Propanalidene)-1-vinylcyclohexanol (37). A solution of vinyl bromide (53.5 g, 0.500 mole) in 150 ml of dry THF was added to a stirred mixture of 11.25 g (0.460 g-atom) of magnesium in 500 ml dry THF under nitrogen. The vinyl bromide was retained by means of a dry ice condenser. After all of the magnesium had been consumed (about four to six hours), the red-brown solution was cooled to 0°, and 33.6 g (0.200 mole) of 10 in 50 ml of dry THF was added. The mixture was allowed to warm to room temperature and was stirred overnight. The reaction was quenched with 500 ml of cold 3N ammonia saturated with ammonium chloride. One liter of ether was added and the THF was washed out with water, followed by a final washing of 3N ammonia saturated with ammonium chloride. The solution was dried (sodium sulfate), the solvent removed, and the residue was fractionated under vacuum with a six inch glass
bead column to give 17.1 g (52%) of 2-(2-propenylidene)-1-vinylcyclohexanol (37): bp 74-6° (0.25 mm). An analytical sample was obtained using a 6 ft by ½ inch 5% DEGS on Chromosorb G column at 140°. Pmr (CCl₄) δ 1.3-1.8 (m, 6H) 1.98 (concentration dependent) (s, 1H) 2.0-2.6 (m, 2H) 4.9-5.4 (m, 4H) 5.99 (dd, 1H, J=11, 18) 6.01 (d, 1H, J=11) 6.53 (ddd, 1H, J=10, 11, 17; ir (CCl₄) 3590 (sharp), 3320 (sharp), 3100, 2990, 1640, 1460, 925 cm⁻¹; uv max (cyclohexane) 237 nm (ε 22,000).


2- Allyl cyclohexanone (39). This procedure is described by C.A. Vanderwerrf and L.V. Lemmerman in "Organic Synthesis." A suspension of 0.25 mole of freshly prepared sodamide in 200 ml of dry ether, under nitrogen, was treated with 27.4 g (0.28 mole) of cyclohexanone, and the mixture was refluxed for 3 hrs. The mixture was cooled to 0° and 30.3 g (0.25 mole) of allyl bromide in 100 ml dry ether was rapidly added. After the initial exothermic reaction had subsided, the mixture was refluxed overnight. The usual work-up gave an ethereal solution which was dried (sodium sulfate), concentrated, and the residue distilled to give 11.18 g (27%) of 2-allyl cyclohexanone (39): bp 101-104° (30 mm) [lit. bp 90-2° (17 mm)]; single peak on glc analysis (6 ft by ½ inch 5% DEGS on Chromosorb G, 125°); pmr (CCl₄) δ 1.2-2.6 (m, 10H) 4.92 (d, 1H, J=12) 4.98 (d, 1H, J=17) 5.5-
2-Propylcyclohexanone (40). A solution of 1.227 g (8.90 mmoles) of 2-allylcyclohexanone (39) in 25 ml of cyclohexane was hydrogenated over PtO$_2$ (61 mg) at ambient temperature and pressure. The mixture was filtered, the solvent removed, and the residue was distilled to give 1.153 g (90%) of 2-propylcyclohexanone (40): bp 63$^\circ$ (0.1 mm) [lit.105 bp 80-81$^\circ$ (1.2 mm)]; the compound showed one peak on glc analysis (6 ft by 1/8 inch 5% DEGS on Chromosorb G, 120$^\circ$).

1-Ethyl-2-propylcyclohexanol (38). A solution containing 10 mmoles of ethylmagnesium bromide in 20 ml of ether, under nitrogen, was prepared from 0.234 g (10.0 mg-atom) of magnesium. After the reaction had subsided, this was cooled to 0$^\circ$ and 0.794 g (5.57 mmoles) of 40 in 5 ml dry ether was added dropwise and the mixture was refluxed for 30 min. After the usual work-up, the solvent was removed with the rotary evaporator and the residue was distilled, giving 0.773 g (82%) of 1-ethyl-2-propylcyclohexanol (38): bp 43-5$^\circ$ (0.1 mm) [lit.105 bp 60-68$^\circ$ (2 mm)].

Hydrogenation of 2-(2-propenylidene)-1-vinylcyclohexanol (37). A cyclohexane solution (0.6 ml) of 55 mg of 37 was hydrogenated over platinum oxide (16.7 mg) in the presence of sodium bicarbonate (22 mg) at ambient temperature
and pressure. The hydrogen uptake was 21 ml (2.9 equivalents) over 90 min. Glc analysis (6 ft by 1/8 inch 10% FFAP on Chromosorb W, 130°, 100 ml/min) showed no starting material and two peaks of approximately equal area. Both hydrogenation products were collected from a 6 ft by 1/8 inch 5% FFAP on Chromosorb G column at 120°, and their mass spectra were taken. Both spectra are essentially the same with a very small molecular ion at 170 m/e, and moderate 141 peak, and a most abundant ion at 85. One of these products was identified as 38 when compared with an authentic sample on: 1. 6 ft by 1/8 inch DEGS on Firebrick + 6 ft by 1/8 inch FFAP on Chromosorb W at 130°; and 2. 6 ft by 1/8 inch 20% Apiezon M on Chromosorb W at 180°.

Reactions of 2-isopropoxymethylenecyclohexanone with ethylmagnesium bromide.

A. EXCESS GRIGNARD REAGENT. A solution of 3.68 g (21.9 mmoles) of 10 in 75 ml of dry ether was added to a stirred solution of 40.3 mmoles ethylmagnesium bromide [prepared from 0.9801 g (40.3 mg-atom) magnesium and 4.8250 g (40.5 mmoles) bromoethane] in 200 ml of ether. The solution was stirred for an additional hour and then was treated with 100 ml of cold saturated ammonium chloride solution. After the usual work-up, the ethereal solution was dried, the solvent removed, and the residue distilled to give 3.39 g (71%, based on magnesium) of 2-(3-pentyl)cyclohexanone (41).
bp 46-48° (0.06 mm), \( n_{D}^{22^\circ} = 1.4620 \text{ [lit.] bp 108° (15 mm)}, n_{D}^{25^\circ} = 1.4597 \); ir (neat) 2930 (s), 2900 (m), 1710 (s), 1460 (m), 1125 (m) cm\(^{-1}\).

B. INVERSE ADDITION OF GRIGNARD REAGENT. A solution of 19.6 mmol of ethylmagnesium bromide [made from 0.475 g (19.6 mg-atom) magnesium and 2.21 g (20.2 mmol) bromo-ethane] in 100 ml of ether was added, dropwise, to a stirred solution of 3.72 g (22.1 mmol) of 10 in 200 ml of dry ether at 0°. After having been stirred 1 hr, the solution was allowed to warm to room temperature. The Grignard adduct was hydrolyzed with 60 ml of 3N ammonia saturated with ammonium chloride. After the usual work-up, the product was isolated by solvent removal leaving 3.21 g (\( \sim 90\% \)) of light yellow oil. Glc analysis (1/8 inch by 4 ft 4% SE-30 on Chromosorb G at 105°) showed this material to contain 51% starting material, 18% 2-(3-pentyl)cyclohexanone (41), and 20% 2-propenyldiene-cyclohexanone (42). The 2-propenyldiene-cyclohexanone (42) was identified by comparison (above-mentioned glc column) with an authentic sample.

3-(2-Butenyldiene)-2-(1-propynyl)cyclohexene (14).

To a stirred solution containing 0.119 mole of ethyl magnesium bromide [made from 2.91 g (0.119 g-atom) of magnesium and 13.2 g (0.120 mole) of ethyl bromide] in 625 ml of dry ether was added 20 ml (\( \sim 0.4 \) mole) propyne (kept in solution by means of a dry-ice condenser). The
solution was stirred for 4 hrs and the excess propyne allowed to evaporate. The solution was cooled to 0° and 6.66 g (0.0396 mole) of 2-isopropoxymethylene cyclohexanone (10) in 30 ml of dry ether was added over a 30 min period. The mixture was refluxed for 30 min and then was treated with 3N aqueous ammonia saturated with ammonium chloride. After the usual work-up and drying, the solvent was removed and the residue was distilled to give 4.73 g (64%) 2-(2-butynylidene)-1-(1-propynyl)cyclohexanol (43) as a yellow oil: bp 80-85° (0.005 mm); mass spectrum m/e (rel intensity) 188 (2), 170 (35), 155 (30); ir (neat) 3570 (m,broad), 3350 (w), 3060 (w), 2990 (s), 2225 (w), 1430 (m), 1070 (m), 980 (m) cm⁻¹; uv max (95% EtOH) 234 nm (ε 8000). This material dehydrated on the glc (either 5% FFAP on Chromosorb G at 190° or 5% Carbowax on Chromosorb W at 170°) to give 3-(2-butynylidene)-2-(1-propynyl)cyclohexene (44): bp 80° (0.005 mm); pmr (CCl₄) δ 1.72 (~quintet, 2H, J=6) 1.89 (s, 3H) 2.03 (d, 3H, J=3) 2.26 (~quartet, 2H, J=5-6) 2.56 (dt, 2H, J=2, 6) 5.80 (m, 1H) 6.11 (t, 1H, J=5); ir (neat) 3080 (w), 3000 (s), 2225 (w), 1430 (m), 980 (m), 850 (m) cm⁻¹; uv max (95% EtOH) 272 nm (ε 8600) and a shoulder at 227 nm.

Anal. Calc'd for C₁₃H₁₄: C 91.71, H 8.29; Found: C 90.26, H 8.23.

Reaction of 2-isopropoxymethylene cyclohexanone with lithium dimethylcuprate. A mixture of 3.60 g (18.9 mmoles) of copper(I) iodide and 70 ml of dry ether at 0° was treated
with 25.0 ml (34.5 mmoles) of 1.38M methyl lithium in ether. The color of the mixture changed successively from pale yellow to tan, and, finally, gray, during the course of the addition. This mixture was stirred for 10 min, and then 1.11 g (6.69 mmoles) of 10 in 50 ml of dry ether was added during 15 min. The mixture (now yellow) was stirred for 1 hr at 0° and then was poured into 200 ml of ice cold 3N ammonia saturated with ammonium chloride. The aqueous layer was extracted twice with ether, and the combined ethereal layers were washed with water, and with 3N ammonia saturated with ammonium chloride. This solution was dried, concentrated, and the residue distilled to give 0.767 g (82%) of 2-isopropylcyclohexanone (13): bp 96-97° (28 mm) [lit. 97° (14 mm)]; ir (neat) 2980 (s) and 1710 (s) cm⁻¹; semicarbazone, recrystallized from EtOH: mp 183.5-185° (lit. 180° and 17°).

1-(3-Acetoxy-1-propenyl)-2-vinylcyclohexene (46). A solution containing 3.28 g (20.0 mmoles) 2-propenylidene-1-vinylcyclohexanol (37) in 10 ml of glacial acetic acid was stirred for 24 hrs. Twenty-five milliliters of ether was added to the distinctly yellow solution. This ethereal solution was washed with three portions of water, followed by two portions of saturated sodium bicarbonate solution. The organic layer was dried (sodium sulfate), the solvent removed on the rotary evaporator, and the residue distilled
under vacuum to give 2.76 g (67%) of 1-(3-acetoxy-1-propenyl)-2-vinylcyclohexene (46): bp 58-64° (0.025 mm). This material was about 85% pure by glc analysis (6 ft by 1/8 inch 2% SE-30 on Chromosorb G, 140°). An analytical sample was collected from the glc (1/4 inch by 6 ft 1% SE-30 on Chromosorb G column at 100°): pmr (CCl₄) δ 1.6-1.8 (m,4H) 1.93 (s,3H) 2.1-2.4 (m,4H) 4.56 (d,2H, J=7) 5.04 (d,1H, J=11) 5.16 (d,1H, J=17) 5.68 (d,t,1H, J=16½,7) 6.89 (d,1H, J=16½) 6.95 (d,d,1H, J=11,17); ir (neat) 3100 (w), 2940, 1738, 1215 (broad), 950, and 900 cm⁻¹; uv max (95% EtOH) 274 nm (ε 33,000).

Anal. Calc'd for C₁₃H₁₈O₂: C 75.69, H 8.80.
Found: C 75.50, H 8.88.

**Methyl 2-propenylidene-1-vinyl-1-cyclohexyl ether (47).**

To a cooled and stirred solution of 3.28 g (20.0 mmoles) of 2-propenylidene-1-vinylcyclohexanol (37) and 3.53 g (25.0 mmoles) of methyl iodide in 15 ml of dry 1,2-dimethoxyethane, was added 0.927 g (22.0 equivalents) of a 57% sodium hydride-mineral oil dispersion. After the mixture had been stirred for 1 hr, the solvent was removed, and 25 ml of ether was added to the residue. This ethereal solution was decanted and the residue washed with an additional 10 ml of ether. The combined ether solutions were concentrated and distilled to give 3.07 g (85%) of methyl 2-propenylidene-1-vinyl-1-cyclohexyl ether (47): bp 45-48° (0.05 mm); pmr (CCl₄) δ 1.2-1.9 (m,6H) 2.17 (dd, 1H, J=14,11) 2.54 (dt,1H, J=14,4) 3.02 (s,3H) 5.0-5.3
\( (m,4H) 5.88 \ (dd,1H, J=8,17) \ 5.97 \ (d,1H, J=10) \ 6.59 \ (ddd,1H, J=10,11,17); \ ir \ (neat) \ 3120 \ (w), \ 3120 \ (w), \ 3000 \ (s, \ broad), \ 1645 \ (m), \ 1445 \ (m), \ 1070 \ (s), \ 990 \ (s), \text{and} \ 905 \ (s) \ \text{cm}^{-1}; \ uv \ max \ (95\% \ EtOH) \ 234 \ nm \ (e 16,000). \)

**Anal.** Calc'd for \( \text{C}_{12}\text{H}_{18}O: \ C \ 80.85, \ H \ 10.18. \) Found: \( C \ 80.79, \ H \ 10.11. \)

**Pyrolysis of 2-propenylidene-1-vinyl-1-cyclohexyl methyl ether \((47)\).** The apparatus (described in the thesis of Michael P. Fleming,109 this department) consisted of a quartz tube filled with pieces of broken quartz (free volume of 98 ml). A Pyrex inlet tube (filled with broken pieces of Pyrex) was fitted with a septum and a nitrogen inlet. The inlet was heated to 250\(^\circ\) C with heating tape and the column set at 350\(^\circ\). Effluents were collected in an ice cold trap, followed by a dry ice-acetone trap, and finally by a solution of 2,4-dinitrophenylhydrazine in ethanol. With the nitrogen flow rate set at 50 ml per minute (two minutes contact time), 921 mg (5.17 mmoles) of substrate \(47\) was added using a micrometer syringe. Addition took place over a 5 min period. At the end of the reaction, 754 mg (99\%, based on a molecular weight of 148 corresponding to a loss of \(\text{CH}_2\text{O}\)) of yellow oil was recovered from the 0\(^\circ\) trap, nothing from the -79\(^\circ\) trap, and a heavy yellow precipitate, identified as the 2,4-dinitrophenylhydrazone of formaldehyde [after recrystallization from ethanol, mp 158-160\(^\circ\) (lit.\(^{110}\) mp 166\(^\circ\))], was
recovered from the DNPH solution. Analysis of the yellow oil on glc (6 ft by 1/4 inch 5% FFAP on Chromosorb G at 145°; 4 ft by 1/8 inch 4% SE-30 on Chromosorb W at 105°; 12 ft by 1\ inch in 5% OV-17 on Chromosorb W at 140°; 12 ft by 1/2 inch 5% TCEP on Chromosorb P at 135°; and 6 ft by 1/2 inch 5% DEGS on Firebrick at 145°) showed one major peak (~ 80% of the product mixture), a few nondescript low-intensity peaks, and no starting material (with one minute contact time about 20% of the starting material remained). The main peak was collected by glc (either 5% OV-17 or 5% DEGS described above); the pmr (CCl₄) of this material is shown below.
Extensive decoupling experiments showed the following results.

1. When the allylic region was irradiated (δ -noted), the following changes occurred in the vinyllic region.

2. When the vinyllic region was irradiated, the allylic region appeared as follows.
3. Irradiation of the doublet at $\delta$ 0.98 gave no change in the vinyllic region.

Mass spectroscopy gave a molecular ion of 148 m/e$^-$ and a uv spectrum (95% EtOH) had a maximum at 342nm ($E$ 11,800, based on a molecular weight of 148). This material (50mg) was hydrogenated over platinum oxide (5mg) in 5 ml of cyclohexane. After removal of the catalyst and the solvent, two products were collected by glc (5% DEGS above); major product: pmr ($CCL_4$) $\delta$ 0.8-1.0 (m, 6H) 1.0-1.5 (m, 16H); uv (95% EtOH) end absorption at 200 nm ($E$ 1200); mass spectrum m/e (rel intensity) 154(2), 152(12), 125(5), 123(26), 111(8), 110(23), 109(33), 81(85), 69(30), 67(85), 58(47), 43(320), 41(120); and the minor product: pmr ($CCL_4$) $\delta$ 0.95 (d, 3H, $J=6$Hz) 1.4-2.1 [two groups of multiplets with the more downfield group (1.7-2.1) being larger, 8H]; uv (95% EtOH) end absorption at 200 nm ($E$ 7200); mass spectrum molecular ion 150 m/e$. The major product was identified as 1-ethyl-2-propylcyclohexane (49) with some 1-ethyl-2-propylcyclohexene (50) as an impurity by comparison with authentic samples.

1-Ethyl-2-propylcyclohexene (50). 1-Ethyl-2-propyl-
cyclohexanol (38) (610 mg, 3.59 mmole) was treated with a solution of 85.5 mg of p-toluenesulfonic acid in 5 ml of benzene at 60$^0$ for 1 hr to give 550 mg (~100%) of dehydrated products: pmr ($CCL_4$, rel integration) $\delta$ 0.8-
1.1 (m, 49) 1.1-1.8 (m, 83) 1.8-2.2 (m, 52) 5.12 (quartet, 3, \( J = 6 \text{Hz} \)) 5.32 (m, 3); mass spectrum m/e (rel intensity) 152(30), 123(42), 110(42), 109(100), 81(87), 79(23), 67(90), 58(22), 55(31), 43(66), 41(41). The mixture contains about 40% of 50.

1-Ethyl-2-propylcyclohexane (49). Hydrogenation of 103 mg of the above mixture of olefins containing 50 over 23 mg of PtO\(_2\) in 5 ml of cyclohexane containing 50 \( \mu l \) of 12 N aqueous HCl (the hydrogenation did not proceed without this acid) gave 100 mg (98%) of 49; pmr (CDCl\(_3\), EM360) \( \delta \) 0.7-1.0(m, 6H) 1.0-1.6(m, 16H) (virtually identical with that of the major hydrogenation product above); mass spectrum m/e (rel intensity) 154(17), 125(52), 111(74), 83(39), 81(29), 69(100), 67(34), 55(74), 43(32), 41(63).

Photolysis of 47. A solution containing 196.5 mg (1.10 mmoles) of 47 in 650 ml of dry ether was irradiated for 4.5 hrs using a 450 watt mercury lamp in a Hanovia quartz internal immersion cell with a Vycor (251 nm) filter. Mixing was effected by means of a nitrogen bubbler. The disappearance of starting material was monitored spectroscopically using 150 l aliquots. Smooth disappearance \( (t_{1/2} = 90 \text{min}) \) of the starting material (234 nm) was observed with no appearance of another chromophore (210-320 nm). The solvent was removed to give 183.2 mg (93%) of light
yellow oil. The sample gave many peaks on glc analysis (6 ft by $\frac{1}{4}$ inch 5% DEGS on Firebrick, 120° or 4 ft by 1/8 inch 4% SE-30 on Chromosorb W, 105°) only one of which could be collected (5% DEGS above) in reasonably pure (by re-injection) form. Only 7 mg was obtained from the glc collection; pmr (CCl₄) δ 0.8-1.0 [m, 53 (integration)] 1.2-1.5 (s,81) 2.35 (s,8) (shift appears to be concentration dependent) 3.50 (d,16,$J=2.5$Hz).


5. C.E. Delphey, unpublished results, Oregon State University, Corvallis, Oregon.


26. See Ref. 2, Footnote 15.


51. See Ref. 77, Footnotes 7, 8 and 9.


64. E.C.Ashby and T.L.Wiesemann, ibid, 96, 7117 (1971).


79. Cf. Ref. 78, p.76.


93. Courtesy of Suae-Chen Cheng, Oregon State University, Corvallis, Oregon.


96. See Ref. 98, Footnote 47.


103. T.M. Berry and E.E. Reed, ibid., 49, 3142 (1927).


