PREPARATION AND SOME CHEMISTRY OF
ETHYL 2,3-BIS(ALKYLEDENE)CYCLOBUTANECARBOXYLATES

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We accept this thesis as conforming
to the required standard

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ABSTRACT

This thesis describes the preparation and some chemistry of the cyclobutanecarboxylates 9. Syntheses of larger ring homologs of 9 (compounds 10 and 11) are also presented.

Deconjugation-alkylation of ethyl (Z)- and (E)-3-trimethylstannyl-2-alkenoates 1 and 2 with alkylating agents of general structure 7 affords the ethyl (E)- and (Z)-3-trimethylstannyl-3-alkenoates (see 8), respectively. The diene esters 8a undergo efficient intramolecular palladium(0)-catalyzed cross coupling reactions of the vinyl halide and vinylstannane groups to provide the cyclobutanecarboxylates 9. Similarly, the diene esters 8b and 8c were converted into the coupled products 10 and 11, respectively.

A number of Diels-Alder reactions of the cyclobutanecarboxylates 9 and structurally related substances are described. These studies provided information regarding the relative reactivities of various substrates of general structure 9 and the face-, regio- and stereoselectivities of the Diels-Alder processes. The cycloaddition reactions led to the preparation of the bicyclic cyclobutenes 314 and 315. Diels-Alder reactions were also performed on the diene 318 to provide the bicyclic cyclobutenes 319 and 321. The bicyclic cyclobutenes 322, 324 and 327 were readily prepared from the keto esters 314 and 315.

The stereochemistry of the thermally induced, conrotatory ring opening reaction of each of the bicyclic cyclobutenes 314, 315, 319, 321, 322, 324 and 327 was investigated. Thermolysis of 319, 321 and 322 gave, in each case, the product resulting from exclusive outward rotation of the CH2OR group. In contrast, heating the substituted 3-formylcyclobutenes 324 and 327 resulted in exclusive inward rotation of the formyl group. Thermally induced ring opening of 314
resulted in the predominant outward rotation of the \( \text{CO}_2\text{Et} \) group. On the other hand, the keto ester 315 showed no preference for the direction of rotation of the \( \text{CO}_2\text{Et} \) group during the thermal ring opening process.

\[
\begin{align*}
R &\quad \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} & \quad \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} \\
1 & & 2 \\
R' & \quad \text{SnMe}_3 \quad \text{CO}_2\text{Et} & \quad \text{SnMe}_3 \quad \text{CO}_2\text{Et} \\
8a & n = 1 & 9 & n = 1 \\
8b & n = 2 & 10 & n = 2 \\
8c & n = 3 & 11 & n = 3 \\
X, X' & = \text{Halides} \\
\end{align*}
\]
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ABBREVIATIONS

The following abbreviations have been used throughout this thesis.

- **B-Br-9-BBN** = B-bromo-9-borabicyclo[3.3.1]nonane
- **t-Bu** = tert-butyl
- **d** = doublet
- **DDQ** = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
- **DMAD** = dimethyl acetylenedicarboxylate
- **DME** = 1,2-dimethoxyethane
- **DMF** = \(\text{\textit{N,N}}\)-dimethylformamide
- **DMPU** = \(\text{\textit{N,N}}\),\(\text{\textit{N'}}\)-dimethyl-\(\text{\textit{N,N'}}\)-propylene urea
- **DMSO** = dimethyl sulfoxide
- **equiv** = equivalent (s)
- **Et** = ethyl
- **GLC** = gas-liquid chromatography
- **h** = hour (s)
- **HMPA** = hexamethylphosphoramide
- **\(^1\text{H} \text{NMR}\)** = proton nuclear magnetic resonance
- **IR** = infrared
- **LDA** = lithium diisopropylamide
- **LiIICA** = lithium \(\text{\textit{N}}\)-isopropylicyclohexylamide
- **m** = multiplet
- **Me** = methyl
- **min** = minute (s)
- **MOM** = methoxy methyl
- **MVK** = methyl vinyl ketone
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<tr>
<td>NOE</td>
<td>nuclear Overhauser effect</td>
</tr>
<tr>
<td>Pd(PPh$_3$)$_4$</td>
<td>tetrakis(triphenylphosphine)palladium(0)</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>c-Pr</td>
<td>cyclopropyl</td>
</tr>
<tr>
<td>i-Pr</td>
<td>isopropyl</td>
</tr>
<tr>
<td>q</td>
<td>quartet</td>
</tr>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>TBDMS</td>
<td>tert-butyldimethylsilyl</td>
</tr>
<tr>
<td>TCNE</td>
<td>tetracyanoethylene</td>
</tr>
<tr>
<td>Th</td>
<td>thienyl</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin-layer chromatography</td>
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I. INTRODUCTION

1. The Problem

Previous work in our laboratories had demonstrated that the geometrically isomeric ethyl 3-trimethylstanny1-2-alkenoates 1 and 2 can be synthesized efficiently and stereoselectively.\(^1\) These organostannanes 1 and 2 are found to undergo stereospecific deconjugation\(^2\) (Equations 1 and 2). For example, reaction of ethyl (Z)-3-trimethylstanny1-2-alkenoates (1) with lithium diisopropylamide (LDA) (2.3 equiv) in tetrahydrofuran (THF)-hexamethylphosphoramide (HMPA, 1.5 equiv) (-78°C, 0.5 h; 0°C, 1 h), followed by inverse quenching with a cold (-98°C) solution of acetic acid in diethyl ether, provided the ethyl (E)-3-trimethylstanny1-3-alkenoates (3) exclusively (Equation 1). Similarly, ethyl (E)-3-trimethylstanny1-2-alkenoates (2) were converted into ethyl (Z)-3-trimethylstanny1-3-alkenoates (4) via the same procedure, except that deprotonation was done in the absence of HMPA (Equation 2). These deconjugated organostannanes may be further converted into bifunctional conjunctive reagents* which are useful in organic synthesis.\(^3\)

\[\begin{align*}
\text{R} & - \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} \\
1 & \xrightarrow{(a) \text{LDA, HMPA,} \quad \text{-78°C, THF}} \\
\text{CO}_2\text{Et} & \text{SnMe}_3 \\
\text{R} & - \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} \\
2 & \xrightarrow{(a) \text{LDA, -78°C, THF}} \\
\text{CO}_2\text{Et} & \text{SnMe}_3
\end{align*}\]

\[\begin{align*}
\text{R} & - \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} \\
3 & \xrightarrow{(b) \text{H}^+} \\
\text{CO}_2\text{Et} & \text{SnMe}_3 \\
\text{R} & - \text{Me}_3\text{Sn} \quad \text{CO}_2\text{Et} \\
4 & \xrightarrow{(b) \text{H}^+}
\end{align*}\]

* Bifunctional conjunctive reagents are substances that contain two reactive sites and are incorporated in whole or in part into a substrate molecule.\(^4\)
It seemed obvious that this work could be extended to the deconjugation-alkylation of the organostannanes 1 and 2. Thus, treatment of the substrates 1 and 2 with an appropriate base would result in the formation of the corresponding dienolate anions. These latter species would be expected to react with alkylating agents at the \( \alpha \)-carbon position to give the unsaturated esters 5 and 6, respectively (Equations 3 and 4).5-9 If these reactions were to be done with alkylating agents of general structure 7, the products 8 would contain a vinylstannane and a vinyl halide functionality. It should then be possible to cyclize these products to give compounds 9, 10 and 11, via an intramolecular palladium(0)-catalyzed coupling reaction (Scheme 1). Successful execution of this chemistry would lead to a novel method of synthesizing cyclic molecules with conjugated exocyclic double bonds.

\[
\text{R} - \underset{\text{Me}_3\text{Sn}}{\text{C}} - \underset{\text{CO}_2\text{Et}}{\text{C}} \xrightarrow{\text{Base}} \xrightarrow{\text{R'X}} \text{R} - \underset{\text{CO}_2\text{Et}}{\text{C}} \xrightarrow{\text{SnMe}_3} \]

\[
\text{R} - \underset{\text{Me}_3\text{Sn}}{\text{C}} - \underset{\text{CO}_2\text{Et}}{\text{C}} \xrightarrow{\text{Base}} \xrightarrow{\text{R'X}} \text{R} - \underset{\text{CO}_2\text{Et}}{\text{C}} \xrightarrow{\text{SnMe}_3} \]

In the ground state of isolated conjugated dienes, such as butadiene derivatives, the four carbon atoms constituting the \( \pi \) system must be coplanar for maximum conjugation. According to the proposal in Scheme 1, \textit{cisoid} diene systems would be produced in the highly strained compounds 9 (\( n = 1 \)). Thus, it would be interesting to measure, by the use of X-ray analysis, the extent to which these diene systems are twisted away from planarity. As the cyclobutanecarboxylates 9...
are not expected to be solids, the X-ray analyses would have to be performed on crystalline derivatives, such as 12, 13 and 14.

Scheme 1

The compounds 15 with a cisoid exocyclic diene system should undergo Diels-Alder reactions readily (Scheme 2). It would be logical to investigate the regio- and/or stereoselectivity of these reactions with various dienophiles, such as dimethyl acetylenedicarboxylate (DMAD), tetracyanoethylene (TCNE), methyl vinyl ketone (MVK), nitroethylene and methyl propynoate.

It is well known that simple cyclobutenes can be converted into 1,3-dienes via a thermally allowed conrotatory ring opening process. Therefore, the bicyclic
cyclobutenes 16 obtained via Diels-Alder reactions would be expected to undergo the thermolytic ring opening (Scheme 2). An interesting aspect of the thermolyses of 16 is that, in each case, the conrotatory ring-opening process allows the substituent on the cyclobutene ring to rotate inwardly or outwardly (Equation 5). Houk has postulated a theory suggesting that the direction of rotation of a substituent on the cyclobutene ring is dependent on the electronic nature of the substituent.\textsuperscript{10} Although simple cyclobutenes with substituents at the C-3 and C-4 positions have been extensively investigated,\textsuperscript{10-13} there is very little information regarding this opening process in complex cyclobutenes such as 16. As different substituents on the cyclobutene ring of 16 can be easily obtained, the cyclobutenes 16 can be used to further correlate Houk's theory with experimental results. Finally, the thermolysis products 17 can undergo Diels-Alder reactions to provide highly substituted octalin systems 18 (Scheme 2).
In summary, the primary objectives of the projected work are the following:

a) to investigate deconjugation-alkylation of ethyl 3-trimethylstanny1-2-alkenoates 1 and 2;

b) to synthesize the cyclobutane compounds 9 and larger ring homologs via palladium(0)-catalyzed coupling reactions;

c) to investigate the structures and Diels-Alder reactions of the cyclobutane compounds 15;

d) to investigate the thermolysis of the bicyclic cyclobutenes 16 and the Diels-Alder reactivity of the resultant thermolysis products 17.

The following chapters discuss the progress made in these areas of research. However, a brief summary of some background information is first presented.
2. Background Information

2.1. Synthesis of Alkyl 3-Trimethylstannyl-2-alkenoates

Morton and Chong, in our laboratories, have extensively studied the synthesis of alkyl 3-trimethylstannyl-2-alkenoates 21 and 22, via stannylcuprate reactions on $\alpha,\beta$-acetylenic esters. It has been observed that the various stannylcuprate reagents (e.g. 26-30) undergo conjugate addition of the trimethylstannyl group to $\alpha,\beta$-acetylenic esters. Table 1 shows examples of these reactions with ethyl 2-butynoate (23).

The conjugate addition of lithium (phenylthio)(trimethylstannyl)cuprate (26) to ethyl 2-butynoate (23) can be controlled experimentally to produce either of the geometrically isomeric products 24 and 25 (Table 1). For example, reaction of 23 with 26 (THF, -48°C, 4 h), followed by protonation, provided the $Z$-isomer 24 (98% isomerically pure). In contrast, reaction of 23 with 26 (THF, -78°C, 4 h) in the presence of a small amount of methanol produced the $E$-isomer 25 (>99% isomerically pure).

Applying the nature of the stannylcuprate reagent also affects the stereochemical outcome of these reactions. For example, the reagents, 28-30, reacted with ethyl 2-butynoate (23) under various conditions to provide predominantly the $E$-isomer 25 (Table 1).

Thus, various geometrically isomeric alkyl 3-trimethylstannyl-2-alkenoates 21 and 22 were prepared efficiently and stereoselectively via these stannylcuprate reactions from the corresponding $\alpha,\beta$-acetylenic esters (Table 2).
Table 1

Reaction of Various Stannylcuprate Reagents with Ethyl 2-Butynoate

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \rightarrow \quad (A) \\
23 & \quad \rightarrow \quad \text{Me}_3\text{Sn} \quad \text{H} \quad \text{CO}_2\text{Et} \\
24 & \quad \quad \quad \text{Me}_3\text{Sn} \\
25 & \quad \quad \quad \text{Me}_3\text{Sn}
\end{align*}
\]

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<th>Entry</th>
<th>Reagent, Conditions (A)</th>
<th>Ratio of 24 : 25</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Me₃SnCuSC₆H₅]Li (26), THF, -48°C, 4 h</td>
<td>98 : 2</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>[Me₃SnCuSC₆H₅]Li (26), THF, -78°C, 4 h, MeOH</td>
<td>&lt;1 : &gt;99</td>
<td>79</td>
</tr>
<tr>
<td>3</td>
<td>[Me₃SnCuSnMe₃]Li (27), THF, -48°C, 4 h</td>
<td>68 : 32</td>
<td>74</td>
</tr>
<tr>
<td>4</td>
<td>[Me₃SnCuC≡CC(Me₂)OMe]Li (28), THF, -48°C, 4 h</td>
<td>&lt;1 : &gt;99</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>Me₃SnCu·SMe₂ (29), THF, -48°C, 3 h</td>
<td>&lt;1 : &gt;99</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td>Me₃SnCu·SMe₂ (29), THF, -78°C, 3 h</td>
<td>&lt;1 : &gt;99</td>
<td>76</td>
</tr>
<tr>
<td>7</td>
<td>[Me₃SnCuCN]Li (30), THF, -48°C, 3 h</td>
<td>4 : 96</td>
<td>86</td>
</tr>
</tbody>
</table>
Table 2

Conversion of $\alpha,\beta$-Acetylenic Esters to (Z)- and (E)-3-Trimethylstannyl-2-alkenoates

R$\equiv$CO$_2$R' $\rightarrow$ R$\equiv$H $\rightarrow$ R$\equiv$CO$_2$R'  

Me$_3$Sn

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>R</th>
<th>R'</th>
<th>Me$_3$Sn</th>
<th>Ratio of 21:22</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>Et</td>
<td>Et</td>
<td>26, -48°C, 4h &gt;99:&lt;1 (35:36)</td>
<td>76</td>
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<tr>
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<td>32</td>
<td>Et</td>
<td>Et</td>
<td>26, -78°C, 3h, &lt;1:&gt;99 (35:36)</td>
<td>80</td>
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<td></td>
<td></td>
<td>MeOH</td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>Et</td>
<td>Et</td>
<td>29, -48°C, 4h 98:2 (35:36)</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>i-Pr</td>
<td>Me</td>
<td>26, -78°C, 3h, &lt;1:&gt;99 (37:38)</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MeOH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
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<td>i-Pr</td>
<td>Me</td>
<td>29, -48°C, 4h 94:6 (37:38)</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>TBDMSO(CH$_2$)$_2$, Et</td>
<td>26, -48°C, 4h &gt;99:&lt;1 (39:40)</td>
<td>79</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>34</td>
<td>TBDMSO(CH$_2$)$_2$, Et</td>
<td>26, -78°C, 6h, &lt;1:&gt;99 (39:40)</td>
<td>71</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>MeOH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>TBDMSO(CH$_2$)$_2$, Et</td>
<td>29, -48°C, 4h 96:4 (39:40)</td>
<td>81</td>
<td></td>
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</tr>
</tbody>
</table>
2.2. Stereospecific Deconjugation of Alkyl 3-Trimethylstannyl-2-alkenoates

Our initial interest in the area of protonation-deconjugation of alkyl 3-trimethylstannyl-2-alkenoates 41 was to develop new methods for the preparation of the bifunctional conjunctive reagents 44, which are useful in natural product syntheses. The readily available geometrically pure alkyl 3-trimethylstannyl-2-alkenoates 41 could be subjected to protonation-deconjugation to furnish the required esters 42 with isomerization of the double bond. Then, the chlorides 44 could be easily obtained from the esters 42 via standard reduction and chlorination reactions (Scheme 3).

Previous studies on the protonation-deconjugation of alkyl 3-trimethylstannyl-2-alkenoates 41, carried out by Gavai in our laboratory, showed that this process is highly stereospecific. Thus, when ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) was allowed to react with lithium diisopropylamide (2.3 equiv) in THF-HMPA (1.5 equiv) (-78°C, 0.5 h; 0°C, 1 h) and the resulting solution (recooled to -78°C) was transferred (cannula) to a cold (-98°C) solution of acetic acid in diethyl ether, ethyl (E)-3-trimethylstannyl-3-pentenoate (46) was produced exclusively in 87% yield.
(Equation 6). In a similar manner, the (Z)-trimethylstannyl esters 39 and 45 were converted cleanly and efficiently into the (E)-β,γ-unsaturated esters 47 and 48 in yields of 81% and 77%, respectively (Equation 6).

\[
\begin{align*}
\text{(a) } & \text{LDA, HMPA,} \\
\text{Me}_3\text{Sn} & \text{CO}_2\text{R'} \\
\text{R} & \text{(b) } \text{H}^+ \\
\text{Me}_3\text{Sn} & \text{CO}_2\text{R'} \\
\end{align*}
\]

\[
\begin{align*}
35, \text{ R} = \text{Me, } R' = \text{Et} & \quad 46, \text{ R} = \text{Me, } R' = \text{Et, } 87\% \\
39, \text{ R} = \text{TBDMSO(CH}_2)_2, \text{ R'} = \text{Et} & \quad 47, \text{ R} = \text{TBDMSO(CH}_2)_2, \text{ R'} = \text{Et, } 81\% \\
45, \text{ R} = \text{c-Pr, } R' = \text{Me} & \quad 48, \text{ R} = \text{c-Pr, } R' = \text{Me, } 77\% \\
\end{align*}
\]

Protonation-deconjugation of the (E)-trimethylstannyl esters 36, 40 and 49 also occurred with complete stereoselectivity, producing exclusively the alkyl (Z)-3-trimethylstannyl-3-alkenoates 50, 51 and 52, respectively (Equation 7). The procedure employed for these reactions was very similar to that used for the (Z)-trimethylstannyl esters except that deprotonation was done in the absence of HMPA.

\[
\begin{align*}
\text{(a) } & \text{LDA, } -78^\circ\text{C, THF} \\
\text{Me}_3\text{Sn} & \text{CO}_2\text{R'} \\
\text{R} & \text{(b) } \text{H}^+ \\
\text{Me}_3\text{Sn} & \text{CO}_2\text{R'} \\
\end{align*}
\]

\[
\begin{align*}
36, \text{ R} = \text{Me, } R' = \text{Et} & \quad 50, \text{ R} = \text{Me, } R' = \text{Et, } 82\% \\
40, \text{ R} = \text{TBDMSO(CH}_2)_2, \text{ R'} = \text{Et} & \quad 51, \text{ R} = \text{TBDMSO(CH}_2)_2, \text{ R'} = \text{Et, } 83\% \\
49, \text{ R} = \text{c-Pr, } R' = \text{Me} & \quad 52, \text{ R} = \text{c-Pr, } R' = \text{Me, } 79\% \\
\end{align*}
\]

2.3. Palladium(0)-Catalyzed Coupling Reactions

There has been great interest in recent years in the use of organometallic reagents to form carbon-carbon bonds efficiently and stereoselectively. One common method employed is the cross coupling of an organometallic reagent (RM) with an
organic electrophile \((R'X)\), normally in the presence of a group VIII transition metal catalyst such as palladium (Equation 8). An important outcome of this method is a route to synthesize selectively and stereospecifically conjugated dienes by cross coupling of two alkenyl partners (i.e. both \(R\) and \(R'\) are alkenyl groups in Equation 8). This route is desirable since 1,3-dienes are required as substrates for Diels-Alder reactions and many natural products contain 1,3-diene systems (e.g. carotenoids, insect pheromones).

\[
RM + R'X \xrightarrow{\text{Pd (0) catalyst}} RR' + MX
\]  

The generality and degree of success for the cross coupling of two alkenyl groups greatly depends on the nature of the organometallic partner. Therefore, some of the desirable characteristics of the organometallic reagent are listed below:

- a) it should be readily available;
- b) it should be fairly stable and easy to handle;
- c) it should tolerate a wide variety of functional groups.

Organostannanes have emerged as one of the more popular organometallic reagents for this palladium(0)-catalyzed cross coupling reaction as they fit all of these characteristics.\(^{14,15}\) Furthermore, the coupling reaction of organostannanes with vinylic electrophiles generally takes place in high yields under mild conditions.

Stille and co-workers have extensively studied the intermolecular cross coupling of vinylstannanes with acyl halides,\(^{16}\) allyl halides,\(^{17}\) aryl halides\(^{18}\) and benzyl halides.\(^{18b}\) In addition to these works, they also have reported intermolecular cross coupling of vinylstannanes with vinyl triflates\(^{19}\) and vinyl halides\(^{20}\) to provide conjugated dienes. These coupling reactions are found to be highly stereospecific.

The cross coupling reactions of vinylstannanes with vinyl triflates are generally done in the presence of lithium chloride and the catalyst normally used is tetrakis(triphenylphosphine)palladium(0) (\(\text{Pd(PPh}_{3}\text{)}_{4}\)). For example, 4-\textit{ tert}-butyl-
cyclohex-1-enyl triflate (53) coupled in high yield with tri-\textit{n}-butylstannylethylene (54) in the presence of 2 mol\% of Pd(PPh₃)₄ and 3 equivalents of lithium chloride in refluxing THF to give 1-vinyl-4-\textit{tert}-butylcyclohexene (55) (Equation 9). In the absence of lithium chloride, no coupling was observed.

\[
\begin{align*}
\text{Cyclohex-1-enyl triflate (53)} & \quad + \quad \text{tri-n-butylstannylethylene (54)} \\
& \quad \xrightarrow{\text{Pd(PPh₃)₄ (2 mol\%), THF (reflux), LiCl, 91\%}} \text{1-vinyl-4-\textit{tert}-butylcyclohexene (55)}
\end{align*}
\]

In contrast, the coupling reactions of vinylstannanes with vinyl halides were done without lithium chloride. Thus, the coupling of 1-iodocyclohexene (56) with (Z)-3-tri-\textit{n}-butylstannylpropen-1-ol (57) in the presence of 2 mole \% of Pd(PPh₃)₄ (DMF, room temperature, 23 h) afforded a 90\% yield of the conjugated diene (58) (Equation 10).

\[
\begin{align*}
\text{1-iodocyclohexene (56)} & \quad + \quad \text{(Z)-3-tri-\textit{n}-butylstannylpropen-1-ol (57)} \\
& \quad \xrightarrow{\text{Pd(PPh₃)₄ (DMF), 90\%}} \text{conjugated diene (58)}
\end{align*}
\]

Other catalysts (e.g. (MeCN)₂PdCl₂, PhCH₂Pd(Cl)(PPh₃)₂, (Ph₃P)₂PdCl₂) are also used in these coupling reactions. For example, (\textit{E})-\textit{\beta}-iodostyrene (59) underwent a coupling reaction with tri-\textit{n}-butylstannylethylene (54) in the presence of a catalytic amount of bis(acetonitrile)dichloropalladium(II) at room temperature to provide the diene 60 in 85\% yield (Equation 11).

The solvents favored by Stille and co-workers for the coupling reactions are tetrahydrofuran (THF) and \textit{N},\textit{N}-dimethylformamide (DMF). However, other
solvents such as DME, dioxane, HMPA, DMPU and DMSO, which can act as catalyst ligands or have the ability to solubilize lithium chloride, are also employed.\textsuperscript{19a}

\begin{equation}
\begin{array}{c}
\text{Ph} \quad \text{I} \\
\text{59}
\end{array}
\quad + \quad
\begin{array}{c}
\text{n-Bu}_3\text{Sn} \\
\text{54}
\end{array}
\quad \xrightarrow{(\text{MeCN})_2\text{PdCl}_2 (2 \text{ mol}%),} 
\quad \text{DMF, 25°C, 85%} 
\quad \begin{array}{c}
\text{Ph} \\
\text{60}
\end{array}
\end{equation}

The coupling reaction is relatively insensitive to steric hindrance. For example, coupling of 2,5,5-trimethylcyclopent-1-enyl triflate (61) with the vinylstannane 62 under the standard reaction conditions afforded cleanly, in 80% yield, the diene 63 (Equation 12).\textsuperscript{19b}

\begin{equation}
\begin{array}{c}
\text{OTf} \\
\text{61}
\end{array}
\quad + \quad
\begin{array}{c}
\text{n-Bu}_3\text{Sn} \\
\text{62}
\end{array}
\quad \xrightarrow{\text{Pd(PPh}_3)_4 (2 \text{ mol}%),} 
\quad \text{THF (reflux), LiCl, 80%} 
\quad \begin{array}{c}
\text{63}
\end{array}
\end{equation}

Stille and co-workers have performed some mechanistic studies on the palladium(0)-catalyzed cross coupling of vinylstannanes with vinyl triflates.\textsuperscript{19b} Thus, for the cross coupling reaction of tri-n-butylstannylethylene (54) with 4-\textit{tert}-butylcyclohex-1-enyl triflate (53) in Equation 9, they propose the catalytic cycle shown in Scheme 4. Initially, oxidative addition of the vinyl triflate 53 to the \text{PdL}_4 in the presence of lithium chloride gives the intermediate 66 and lithium triflate. The formation of the intermediate 66 is proposed to take place via one of two different pathways (Equations 13 and 14).
Oxidative addition of the vinyl triflate 53 to PdL₄ to give the corresponding organopalladium(II) triflate complex 64, followed by reaction with lithium chloride, would yield 66 (Equation 13). Alternatively, a reversible reaction of lithium chloride with PdL₄ could form a salt such as 65. Then, oxidative addition of vinyl triflate 53 would generate 66 (Equation 14). Stille and co-workers suggested that the reaction most likely proceeds via the latter pathway from the observation of the
$^{31}$P NMR spectral data for 65 and 66. The organostannane 54 undergoes transmetalation with 66 to yield the trans-bis(organo)palladium(II) complex 67. The complex 67 undergoes trans/cis isomerization to provide 68, which, upon reductive elimination, affords the coupled product 55 and regenerates the palladium(0) catalyst.

The nature of the organic group on tin determines the group to be transferred in the transmetalation step. For example, the rate of transfer of groups follows the order of the sequence, PhRC=CR'-CH$_2$=CR-Ph > Me. Therefore, when an organostannane contains three alkyl groups and one alkenyl group, the latter group will transfer exclusively.

Friesen and Keay, in our laboratory, have utilized the intramolecular palladium(0)-catalyzed coupling reaction of vinyl triflates and vinylstannanes to
synthesize conjugated dienes. Examples involving new synthetically useful annulation sequences, are shown in Scheme 5. Transformation of the ketones 69 into the corresponding enol triflates 70 was accomplished via a procedure very similar to that reported by McMurry and Scott.\textsuperscript{21} Treatment of the triflates 70 with a catalytic amount of Pd(PPh\textsubscript{3})\textsubscript{4} in refluxing THF effected efficient ring closure, producing the bicyclic dienes 71 in good yields (83-86%).\textsuperscript{22} It must be noted that these reactions were done in the absence of lithium chloride. Qualitative experiments on the coupling reaction showed that the rate of the process and isolated yield of the reaction product decreased in the presence of lithium chloride.

![Scheme 5](image)

The intramolecular coupling reaction of vinylstannanes and vinyl triflates has proved to be useful in natural product syntheses. An example is illustrated by the synthesis of (±)-(14S)-dolasta-1(15),7,9-trien-14-ol (75) (Scheme 6).\textsuperscript{23} Treatment of the ketone 72 with lithium diisopropylamide (THF-HMPA, -78°C to 0°C), followed by trapping the enolate with N-phenyltrifluoromethanesulfonimide, afforded the enol
triflate 73. The enol triflate 73 underwent the intramolecular coupling reaction in the presence of a catalytic amount of Pd(PPh₃)₄ to provide the bicyclic compound 74 with conjugated endocyclic double bonds. This material was subsequently converted into the natural product 75.

\[
\begin{align*}
\text{K} & \quad \text{SnMe}_3 \\
\text{72} & \quad \text{(a) LDA} \\
\text{73} & \quad \text{(b) Tf}_2\text{NPh} \\
\text{74} & \quad \text{Pd(PPh}_3\text{)}_4 \\
\text{75} & \quad \text{78\% from 72}
\end{align*}
\]

Recently, Stille and co-workers also performed this coupling reaction intramolecularly to synthesize large-ring lactones.²⁴ For example, cyclization of the substrate 76 containing a vinylstannane and a vinyl triflate group at the termini of the ester-containing chain was accomplished with a catalytic amount of Pd(PPh₃)₄ and lithium chloride in refluxing THF (Equation 15). Under these reaction conditions, no \(E\) to \(Z\) isomerization of the internal double bond and no rearrangement of the exocyclic double bond were observed.
2.4. Previous Synthetic Work on 1,2-Dimethylenecyclobutane and Related Substances

There are a number of methods reported in the literature for the synthesis of 1,2-dimethylenecyclobutane (79) and related substances. However, most of these methods are cumbersome, inefficient and stereochemically ambiguous.

One of the most obvious methods for the synthesis of these compounds is the thermal dimerization of allene or its derivatives. This dimerization process is presumed to proceed via a thermal $[\pi^2_a + \pi^2_s]$ cycloaddition.\textsuperscript{25} For example, allene gas (78) was passed through a tube packed with glass balls at 500°C. The pyrolysate, which contained a mixture of unreacted allene, allene dimers and higher oligomers, was collected in a flask cooled in dry ice. Fractional distillation, with recycling of the pyrolysate, afforded 1,2-dimethylenecyclobutane (79) in 25% yield (Equation 16).\textsuperscript{26}

\[
\begin{array}{c}
\text{78} \\
\text{500°C, 25%} \\
\text{79}
\end{array}
\]
Another example is the dimerization of methylallene (80) reported by Gajewski and Shih.\textsuperscript{27} Methylallene (80) was heated in a static system at 170°C for 13 h to produce a mixture of the dimers, 81-87 (29%) and unreacted methylallene (80) (32%) (Equation 17). Clearly, this method is very inefficient as there is no control of the stereochemical outcome of the reaction.

\[
\text{H}_2\text{C} = \text{C}(\text{CH}_3) + \Delta (170^\circ\text{C}) \rightarrow \begin{array}{c}
\text{C}_6\text{H}_{12} \\
80 \rightarrow 29\% \\
\text{C}_6\text{H}_{12} \\
81 \\
82 \\
83 \\
84 \\
85 \\
86 \\
87
\end{array}
\]

Other methods for the synthesis of 1,2-dimethylenecyclobutane (79) and related compounds involve chemical manipulation of substrates containing the four-membered ring system. For example, the synthesis of 1,2-bis(dideuteriomethylene)cyclobutane (91) was reported by Gajewski and Shih (Scheme 7).\textsuperscript{28} The predominantly \textit{trans}-1,2-cyclobutanedicarboxylic acid (88) was first esterified in acidic ethanol to produce diethyl 1,2-cyclobutanedicarboxylate (89). The diester 89 was reduced with lithium aluminum deuteride and the resultant diol was treated with excess \textit{p}-toluenesulphonyl chloride in pyridine to produce 90. Displacement of the tosylate groups in compound 90 with sodium iodide in acetone and, finally, double dehydroiodination with molten potassium hydroxide afforded the diene 91 in a 22% overall yield.
Bickelhaupt and co-workers also employed chemical manipulation of a substrate containing a four-membered ring to synthesize 1,2-dimethylene cyclobutane (79). In their procedure, the cyclobutanone 92 was subjected to a Wittig reaction followed by a Hofmann degradation to yield 79 in an overall yield of less than 10% (Equation 18). However, their method was more successful in synthesizing the larger ring homologs of 79.

A further example of chemical manipulation of a substrate containing a four-membered ring to synthesize 1,2-dimethylene cyclobutane derivatives was reported by Schimpf and Heimbach. The readily accessible cis-1,2-divinylcyclobutane (95), which was formed catalytically in 40% yield from butadiene, underwent isomerization on treatment with potassium tert-butoxide in dimethylsulfoxide at 40-
60°C to give a mixture of the conjugated dienes 85, 86 and 96, in 87% yield (Equation 19).

\[
\text{r-BuOK, DMSO, 40-60°C} \quad \begin{array}{c}
\text{95} \quad \xrightarrow{\Delta} \quad \text{85} \quad + \quad \text{86} \quad + \quad \text{96}
\end{array}
\]

Ratio 3 : 3 : 2

Although the examples discussed here are not exhaustive, they indicate some of the difficulties encountered in synthesizing 1,2-dimethylene cyclobutane (79) and related compounds efficiently and stereoselectively.

2.5. Thermolysis of Cyclobutenes

\[
\text{97} \quad \xrightarrow{\Delta} \quad \text{98} \quad + \quad \text{99}
\]

Cyclobutene can be converted into butadiene via a thermally allowed conrotatory ring opening process. The allowed conrotatory process is estimated to be 15.0 kcal/mol more favorable than the disrotatory process.\textsuperscript{31} However, in a substituted cyclobutene, this conrotatory process can occur in two directions (Equation 20). Early studies by Criege, Winter, Trey and their co-workers on the thermolysis of simple cyclobutenes showed that alkyl substituents preferentially opened outward.\textsuperscript{11} For example, 3-methylcyclobutene (100) opened exclusively with the methyl group rotating outward to give \textit{trans}-piperylene (101) (Equation 21), and \textit{trans}-1,2,3,4-tetramethylcyclobutene (102) gave only \((E,E)-3,4\)-dimethyl-
2,4-hexadiene (103) (Equation 22). These results were rationalized on the basis of steric arguments. Thus, it was proposed that the steric repulsion destabilizes the corresponding transition states for inward rotation even though the inward opening of the substituents is allowed by orbital symmetry.

\[ \begin{align*}
\text{100} & \xrightarrow{\Delta} \text{101} \\
\text{102} & \xrightarrow{\Delta} \text{103}
\end{align*} \quad (21)
\]

However, Curry and Steven reported that steric effects do not have a significant influence on the outcome of the conrotatory opening of cyclobutenes.\(^{12}\) Thus, 3-methyl-3-isopropylcyclobutene (104) opened at 180°C to provide a mixture of two isomers 105 and 106 in the ratio of 1:1.9, respectively (Equation 23). The major isomer 106 resulted from inward rotation of the isopropyl group. At the same time, 3-methyl-3-\textit{tert}-butylcyclobutene (107) did not show a preference in the direction of opening, since, in this case, the ratio of the isomers 108 and 109 was 1:1 (Equation 24). A more dramatic case was reported by Dolbier \textit{et al.}\(^{13}\) They observed that the \textit{trans}-perfluoro-3,4-dimethylcyclobutene 110 exclusively opened to give the (Z),(Z)-isomer 111, in which both trifluoromethyl groups had preferentially rotated inward (Equation 25). These data contradict the simple idea that the thermal ring opening of cyclobutenes is governed by steric factors.
Table 3

Calculated Activation Energies (kcal/mol) for Electrocyclic Reactions of 3-Substituted-cyclobutenes Relative to the Calculated Activation Energy for Cyclobutene Opening

<table>
<thead>
<tr>
<th>Substituent</th>
<th>Direction of Rotation</th>
<th>inward</th>
<th>outward</th>
<th>inward-outward</th>
</tr>
</thead>
<tbody>
<tr>
<td>-OH/-OR</td>
<td>7.1</td>
<td>-9.3</td>
<td></td>
<td>16.4</td>
</tr>
<tr>
<td>-CO₂⁻</td>
<td>0.9</td>
<td>-6.4</td>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>-CH₃</td>
<td>5.7</td>
<td>-0.7</td>
<td></td>
<td>6.4</td>
</tr>
<tr>
<td>-CN</td>
<td>2.3</td>
<td>-2.3</td>
<td></td>
<td>4.6</td>
</tr>
<tr>
<td>-CO₂H</td>
<td>-2.0</td>
<td>-4.3</td>
<td></td>
<td>2.3</td>
</tr>
<tr>
<td>-CO₂Me</td>
<td>-1.3</td>
<td>-3.0</td>
<td></td>
<td>1.7</td>
</tr>
<tr>
<td>-CHO</td>
<td>-6.9</td>
<td>-2.3</td>
<td></td>
<td>-4.6</td>
</tr>
<tr>
<td>-C(OH)₂⁺</td>
<td>-15.8</td>
<td>-11.0</td>
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<td>-4.8</td>
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</tbody>
</table>
Recently, Houk and co-workers have performed extensive theoretical calculations on the effect of substituents on the cyclobutene ring opening reaction. Their theoretical studies suggest that this type of reaction is influenced mainly by the electronic nature of the substituents. Table 3 summarizes their results derived from calculations of the activation energies for outward or inward rotation of various substituents. An alkoxy or a hydroxy substituent is predicted to favor outward rotation by 16.4 kcal/mol. The methyl and the methyl ester groups are calculated to favor outward rotation by 6.4 and 1.7 kcal/mol, respectively. It is apparent that the preference for the direction of rotation is not based on steric control alone as the preference for outward rotation decreases along the series OR > CH₃ > CO₂Me; whereas, the sizes, as measured by the A values* of substituents, decrease in the order CH₃ > CO₂Me > OR.

Houk and co-workers also reported some experimental results to verify their theory. For example, they predicted that 3-formylcyclobutene (112) would rotate the formyl group inward during the ring opening process. The calculated activation energy preference for inward rotation of the formyl group is 4.6 kcal/mol (Table 3). The experimental test for this prediction showed that 3-formylcyclobutene (112) underwent ring opening at 50-70°C to produce exclusively (Z)-2,4-pentadienal (113) (Equation 26). This preference for the inward rotation is not likely to arise from product stabilities as (Z)-2,4-pentadienal (113) is suggested to be 3.1 kcal/mol less stable than the (E)-isomer.

\[ \text{112} \xrightarrow{\Delta} \text{113} \]

* A simple measure of steric effects by the conformational free-energy difference between equatorial and axial substituents on a cyclohexane ring.
Houk and co-workers suggested that a hydroxy or alkoxy group on the cyclobutene ring strongly favors rotating outward in the electrocyclic reaction. Their experimental results also supported this prediction. For example, when 2-tert-butyl-3-(trimethylsilyloxy)cyclobutene (114) was heated in deuteriochloroform at 95-100°C for 1.5 h, (E)-2-tert-butyl-1-trimethylsilyloxy-1,3-butadiene (115) was obtained exclusively (Equation 27). In addition, 3-tert-butyl-3-(trimethylsilyloxy)cyclobutene (116) was heated (CDCl₃, 90-100°C, 4 h) to yield exclusively (E)-1-tert-butyl-1-trimethylsilyloxy-1,3-butadiene (117) (Equation 28). The reaction was not controlled by a steric effect because a smaller alkoxy group, such as a methoxy group, was used and a similar result was obtained. Thus, 3-tert-butyl-3-methoxycyclobutene (118) was heated (C₆D₆, 90-95°C, 6 h) to produce exclusively (E)-1-tert-butyl-1-methoxy-1,3-butadiene (119) (Equation 29). Therefore, from all these experimental and theoretical data, Houk and co-workers suggested that the electronic effect of the substituent played an important role in the cyclobutene ring opening reaction.
II. DISCUSSION

1. Synthesis of Ethyl 3-Trimethylstannyl-2-alkenoates

1.1. Preparation of the $\alpha,\beta$-Acetylenic Esters 121

The 1-alkynes (120) required as starting materials for the preparation of the $\alpha,\beta$-acetylenic esters (121) were either commercially available or were prepared by protection of the appropriate alkyn-1-ol with methoxymethoxy or tert-butyl-dimethylsilyloxy groups. Reaction of 4-pentyn-1-ol (123) with chloromethyl methyl ether (1.5 equiv) in the presence of diisopropylethylamine (1.5 equiv) in dichloromethane (0°C, 1.5 h) provided, after distillation of the crude reaction product, 5-methoxymethoxy-1-pentyne (125) in 95% yield (Equation 30). The $^1$H NMR spectrum of 125 exhibited the expected signals for the methoxymethoxy group at $\delta$ 3.39 (a 3-proton singlet) and $\delta$ 4.63 (a 2-proton singlet). In a similar fashion, 2-propyn-1-ol (122) was converted into 3-methoxymethoxy-1-propyne (124) in 88% yield (Equation 30).$^{33}$ 6-tert-Butyldimethylsilyloxy-1-hexyne (127) was prepared by reaction of 5-hexyn-1-ol (126) with tert-butyldimethylsilyl chloride and imidazole in $N,N$-dimethylformamide (room temperature, 12 h) (Equation 31).$^{34}$

\[
\text{(30)} \quad \begin{array}{c}
\text{122} \quad n = 1 \\
\text{123} \quad n = 3 \\
\end{array}
\]

\[
\begin{array}{cccc}
\text{124} & n = 1, & 88\% \\
\text{125} & n = 3, & 95\% \\
\end{array}
\]
The 1-alkynes (120) were converted into the corresponding \( \alpha,\beta \)-acetylenic esters (121) via the procedure outlined in Table 4. Addition of methyllithium (1 equiv) to a THF solution of 1-butyne (130) (-78°C, 15 min; -20°C, 1 h) afforded the corresponding alkynyllithium species, which, upon reaction with ethyl chloroformate (-20°C, 1 h; room temperature, 1 h) yielded ethyl 2-pentynoate (131) (93%, work-up and distillation). In a similar manner, the other \( \alpha,\beta \)-acetylenic esters, 132-134, were prepared from the corresponding 1-alkynes 124, 125, and 127, respectively (Table 4).

The spectral data for these \( \alpha,\beta \)-acetylenic esters (131-134) were in agreement with the assigned structures. For example, the \(^1\text{H} \) NMR spectrum of 131 displayed the expected signals for an ethyl ester moiety (a 3-proton triplet at \( \delta 1.32, J = 7 \text{ Hz} \), and a 2-proton quartet at \( \delta 4.22, J = 7 \text{ Hz} \)) and an ethyl moiety (a 3-proton triplet at \( \delta 1.21, J = 7 \text{ Hz} \), and a 2-proton quartet at \( \delta 2.35, J = 7 \text{ Hz} \)). In addition, the IR spectrum of 131 exhibited a weak C=C stretching frequency at 2239 cm\(^{-1} \) and a C=O stretching frequency at 1713 cm\(^{-1} \).

Ethyl 2-butynoate (23) is commercially available.
Table 4

Preparation of $\alpha, \beta$-Acetylenic Esters

\[ \begin{array}{c}
\text{Entry} \\
1 & 2 & 3 & 4 \\
\text{Substrate} & 130 & 124 & 125 & 127 \\
\text{R} & \text{CH}_3 & \text{CH}_3\text{OCH}_2\text{O} & \text{CH}_3\text{OCH}_2\text{O}(\text{CH}_2)_2 & r-\text{BuMe}_2\text{SiO}(\text{CH}_2)_3 \\
\text{Product} & 131 & 132 & 133 & 134 \\
\text{Yield} & 93 & 84 & 83 & 76 \\
\end{array} \]

(a) MeLi (1 equiv), THF, -78°C, 15 min; -20°C, 1 h,

(b) Ethyl chloroformate (1 equiv), -20°C, 1 h; room temperature, 1 h.

II Yield of purified, distilled product.
1.2. Preparation of Ethyl (Z)- and (E)-3-Trimethylstannyl-2-alkenoates (1 and 2)

\[
\begin{align*}
&[\text{Me}_3\text{SnCuSPh}]\text{Li} & [\text{Me}_3\text{SnCuCN}]\text{Li} & [\text{Me}_3\text{SnCu(2-Th)CN}]\text{Li}_2 \\
&26 & 30 & 141
\end{align*}
\]

Previous work in our laboratories demonstrated that various trimethyl-stannylcopper reagents,* such as 26 and 30, smoothly transfer one trimethyl-stannyl group to the β-position of α,β-acetylenic esters (121). Generally, these cuprate reagents are thermally unstable, and sensitive to both oxygen and traces of inorganic salts. Thus, it must be noted that maintaining an appropriate temperature with stringently clean glassware in an oxygen-free atmosphere is vital to the success of the reaction.

For the preparation of most of the (Z)-trimethylstannyl esters 1, the reported procedure that utilized lithium trimethylstannyl(phenylthio)cuprate (26) was employed. In accordance with the procedure, addition of a THF solution of ethyl 6-methoxymethoxy-2-hexynoate (133) to a solution of the cuprate reagent 26 (1.3 equiv in THF (-78°C, 15 min; -48°C, 4 h), followed by quenching with a proton source, work-up, and chromatography of the crude product, afforded ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (136) in 74% yield (Entry 3, Table 5). The results for the other α,β-acetylenic esters are summarized in Table 5. All of the required (Z)-trimethylstannyl esters 1, except 135, were obtained cleanly and efficiently via this procedure. Reaction of the α,β-acetylenic ester 132 with the cuprate reagent 26 under the standard reaction conditions (THF; -78°C, 15 min; -48°C, 4 h) did not provide the expected (Z)-trimethylstannyl ester 135. Instead, transfer of the phenylthio group occurred and the major products, therefore,

* The formulations of these cuprate reagents are not meant to represent actual structures, but are used for convenience and to show stoichiometry.
Table 5
Preparation of Ethyl (Z)-3-Trimethylstanny1-2-alkenoates

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>R</th>
<th>Procedure</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>131</td>
<td>CH₃</td>
<td>A</td>
<td>35</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>132</td>
<td>CH₃OCH₂O</td>
<td>B</td>
<td>135</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>133</td>
<td>CH₃OCH₂O(CH₂)₂</td>
<td>A</td>
<td>136</td>
<td>74</td>
</tr>
<tr>
<td>4</td>
<td>134</td>
<td>t-BuMe₂SiO(CH₂)₃</td>
<td>A</td>
<td>137</td>
<td>71</td>
</tr>
</tbody>
</table>

I Procedure A: [Me₃SnCuSPh]Li (26) (1.3 equiv), THF, -78°C, 15 min; -48°C, 4 h.

I Procedure B: [Me₃SnCu(2-Th)CN]Li₂ (141) (1.3 equiv), THF, -78°C, 15 min; -48°C, 4 h.

II Yield of purified, distilled product.
were compounds 138 (Equation 32). Earlier reports noted that reaction of the cuprate reagent 26 with the \( \alpha,\beta \)-acetylenic ester 139 under similar conditions gave the phenylthio transfer product 140 (35%) (Equation 33).\(^1\) It is not clear why the \( \alpha,\beta \)-acetylenic esters, 132 and 139, containing an ether function on the \( \gamma \)-position, behave in this anomalous manner. However, one can speculate that this abnormal behavior might be due to the electron-withdrawing effect of the oxygen functionality which is situated near to the \( \alpha,\beta \)-acetylenic ester moiety of these substrates. Recently, Tillyer, in our laboratory, prepared a new, higher order cuprate reagent 141 and showed that this species adds to the \( \alpha,\beta \)-acetylenic esters 121 to give the (Z)-trimethylstannyl esters 1 under specified conditions.\(^{36}\) Thus, addition of a THF solution of the \( \alpha,\beta \)-acetylenic ester 132 to a solution of dilithium trimethylstannyl(2-thienyl)(cyano)cuprate (141) in THF (-78°C, 4 h) afforded, after chromatography and distillation of the crude reaction product, the (Z)-trimethylstannyl ester 135 in 51% yield (Entry 2, Table 5).

The (E)-trimethylstannyl esters 2, on the other hand, were obtained by reaction of the \( \alpha,\beta \)-acetylenic esters 121 with lithium trimethylstannyl(cyano)cuprate (30).\(^1\) The choice of the cuprate reagent 30 was mainly due to the easy workup procedure. Thus, in accordance with the reported procedure, addition of ethyl
Table 6

Preparation of Ethyl (E)-3-Trimethylstannyl-2-alkenoates

\[
\begin{align*}
\text{R} & \quad \equiv & \quad \text{CO}_2\text{Et} & \quad \rightarrow & \quad \text{R} & \quad \equiv & \quad \text{CO}_2\text{Et} \\
121 & & & & & \text{Me}_3\text{Sn} & \quad \text{H}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>( R )</th>
<th>Product</th>
<th>Yield ((%)^{\text{II}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>H</td>
<td>25</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>131</td>
<td>\text{CH}_3</td>
<td>36</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>132</td>
<td>\text{CH}_3\text{OCH}_2\text{O}</td>
<td>142</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>133</td>
<td>\text{CH}_3\text{OCH}_2\text{O(\text{CH}_2)_2}</td>
<td>143</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>134</td>
<td>\text{t-BuMe}_2\text{SiO(\text{CH}_2)_3}</td>
<td>144</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^{\text{I}}\) [\text{Me}_3\text{SnCuCN}]\text{Li} (30) (1.3 equiv); THF; \(-78^\circ\text{C}, 4\) h.

\(^{\text{II}}\) Yield of purified, distilled product.
6-methoxymethoxy-2-hexynoate (133) in THF to a solution of the cuprate reagent 30 in THF (-78°C, 4 h) afforded, after chromatography and distillation of the crude product, the (E)-trimethylstannyl ester 143 in 76% yield (entry 4, Table 6). The results for the various (E)-trimethylstannyl esters obtained via this procedure are summarized in Table 6. A small amount of the (Z)-trimethylstannyl ester 1 (<10%) was also produced in each case, but was easily removed by chromatography.

The structural assignments for the (Z)- and (E)-trimethylstannyl esters 1 and 2 were supported by the 1H NMR spectral data obtained from these compounds. Three notable differences in the 1H NMR spectra of the (Z)- and (E)-trimethylstannyl esters 1 and 2 are the chemical shifts of the allylic protons, the chemical shifts of the vinyl proton, and the tin-proton coupling values (3J_{Sn-H}) associated with coupling between the olefinic proton and the 117Sn and 119Sn isotopes (Table 7). For example, the 1H NMR spectrum of the (Z)-trimethylstannyl ester 136 exhibited the signals expected for a trimethylstannyl group (a 9-proton singlet at δ 0.19 with satellite peaks due to Sn-H coupling, 2J_{Sn-H} = 56 Hz), a methoxymethoxy group (a 3-proton singlet at δ 3.37 and a 2-proton singlet at δ 4.63) and an ethyl ester moiety (a 3-proton triplet at δ 1.29, J = 1 Hz, and a 2-proton quartet at δ 4.20, J = 7 Hz). In addition, the presence of a 2-proton quintet (J = 7 Hz) due to the homoallylic methylene protons at δ 1.71, a 2-proton triplet of doublets (J = 7, 1 Hz) due to the allylic methylene protons at δ 2.52, a 2-proton triplet (J = 7 Hz) due to the methylene group next to the methoxymethoxy moiety at δ 3.52 and a 1-proton broad triplet (J = 1 Hz) due to the vinyl proton at δ 6.38 (with satellite peaks due to Sn-H coupling, 3J_{Sn-H} = 120 Hz) were observed.

On the other hand, the 1H NMR spectrum of the geometrically isomeric (E)-trimethylstannyl ester 143 with the three expected exceptions is very similar to that of the (Z)-trimethylstannyl ester 136. Firstly, the position of the allylic methylene protons of the (E)-trimethylstannyl ester 143 (δ 2.96) is considerably
Table 7: The Partial $^1$H NMR and IR Spectral Data for (Z)- and (E)-3-Trimethylstanny1-2-alkenoates

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compounds 1 and 2</th>
<th>$\delta$ of allylic methylene protons</th>
<th>$\delta$ of olefinic proton</th>
<th>$^3J_{\text{Sn-H}}$ of the olefinic proton (Hz)</th>
<th>C=O stretching (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me$_3$Sn-CO$_2$Et</td>
<td>2.42</td>
<td>6.34</td>
<td>120</td>
<td>1703</td>
</tr>
<tr>
<td>2</td>
<td>Me$_3$Sn-CO$_2$Et</td>
<td>2.88</td>
<td>5.91</td>
<td>73</td>
<td>1718</td>
</tr>
<tr>
<td>3</td>
<td>MOMOMe$_3$Sn-CO$_2$Et</td>
<td>4.37</td>
<td>6.68</td>
<td>110</td>
<td>1702</td>
</tr>
<tr>
<td>4</td>
<td>MOMOMe$_3$Sn-CO$_2$Et</td>
<td>4.80</td>
<td>5.95</td>
<td>71</td>
<td>1712</td>
</tr>
<tr>
<td>5</td>
<td>MOMO(CH$_2$)$_3$Me$_3$Sn-CO$_2$Et</td>
<td>2.52</td>
<td>6.38</td>
<td>120</td>
<td>1703</td>
</tr>
<tr>
<td>6</td>
<td>MOMO(CH$_2$)$_3$Me$_3$Sn-CO$_2$Et</td>
<td>2.96</td>
<td>5.99</td>
<td>72</td>
<td>1714</td>
</tr>
<tr>
<td>7</td>
<td>TBDMSO(CH$_2$)$_4$Me$_3$Sn-CO$_2$Et</td>
<td>2.41</td>
<td>6.33</td>
<td>120</td>
<td>1704</td>
</tr>
<tr>
<td>8</td>
<td>TBDMSO(CH$_2$)$_4$Me$_3$Sn-CO$_2$Et</td>
<td>2.89</td>
<td>5.95</td>
<td>75</td>
<td>1718</td>
</tr>
</tbody>
</table>
downfield from that of the (Z)-trimethylstannyl ester 136 (δ 2.52). This difference is in accord with the fact that the γ-protons are cis to the ester group in the (E)-trimethylstannyl ester 143 but trans to the ester group in the (Z)-trimethylstannyl ester 136. Secondly, the chemical shift of the vinyl proton in the (E)-trimethylstannyl ester 143 is at δ 5.99 which is at slightly higher field than that of the corresponding vinyl proton in the (Z)-trimethylstannyl ester 136. Again, this difference is reasonable, since in general, vinyl protons in unsaturated organotin compounds are shielded by a cis vicinal trialkylstannyl substituent. Thirdly, the tin-proton coupling constant of the vinyl proton in the (E)-trimethylstannyl ester 143 is approximately 50 Hz smaller (3J_Sn-H = 72 Hz for 143, whereas 3J_Sn-H = 120 Hz for 136) than that of the (Z)-trimethylstannyl ester 136. Since it is well established that the couplings between the ¹¹⁷Sn and ¹¹⁹Sn isotopes and a vicinal olefinic proton are much stronger (larger 3J_Sn-H value) when the R₃Sn group and the proton are trans than when they are cis, this further indicates that the assignment of the stereochemistry of the (Z)- and (E)-trimethylstannyl esters 136 and 143 is correct.

The IR spectra of the (Z)- and (E)-trimethylstannyl esters 1 and 2 are very similar to each other except for their carbonyl stretching frequencies. For example, this absorption band in the (E)-trimethylstannyl ester 143 was observed to be at 1714 cm⁻¹, whereas, the corresponding value for the (Z)-trimethylstannyl ester 136 was at 1703 cm⁻¹.

As in previous cases, the molecular ions for these trimethylstannyl compounds were not observed in their mass spectra. The high resolution mass spectrometric measurements were performed on the z/e M⁺-15 peaks.

The reaction of the cuprate reagent 26 with the α,β-acetylenic esters 121 can be rationalized as shown in Scheme 8. The cuprate reagent 26 initially adds in
a cis manner to the α,β-acetylenic ester 121 to provide the vinyl cuprate species 145a (the "kinetic intermediate"). Under low temperature conditions and in the presence of a proton source, the species 145a is converted into the "kinetic" product 2. However, at higher temperatures (e.g. -48°C) the species 145a can rearrange to the allenoate 146a which, upon protonation, provides stereoselectively the (Z)-trimethylstannyl ester 1.

The stereoselectivity observed in the kinetic protonation of the allenoate 146a can be rationalized in the following manner. The trimethylstannyl group on the allenoate 146a is bulkier than the RCH2 group and it would be expected to hinder the approach of an external protonating reagent. Thus, protonation of the allenoate
146a would take place on the side opposite to the trimethylstannyl group and the (Z)-trimethylstannyl ester 1 would be the observed product.

The fact that different stereochemical results are observed with the other cuprate reagents 30 and 141 may be related to the ease of rearrangement of the initially formed intermediate 145 to the allenoate 146 (Scheme 8). For example, in the reaction of 121 with the cuprate reagent 30, it appears that the intermediate 145b is fairly stable and does not rearrange readily to the allenoate 146b. Thus, upon protonation, the reaction yields stereoselectively the (E)-trimethylstannyl ester 2.

On the other hand, the initial intermediate 145c, which is obtained from cis-addition of the cuprate reagent 141 to the \( \alpha,\beta \)-acytylenic ester 121, is, apparently, very unstable and rearranges to the allenoate 146c even at a low temperatures (-78\(^\circ\)C). Subsequent protonation provides the (Z)-trimethylstannyl ester 1.

In summary, the (Z)- and (E)-trimethylstannyl esters 1 and 2 were readily prepared by the use of the appropriate procedures described above.
2. Deconjugation-Alkylation of Ethyl (Z)- and (E)-3-Trimethylstannyl-2-alkenoates

2.1 The Alkylating Agents

The next stage of the proposed research program involved deconjugation-alkylation of the (Z)- and (E)-trimethylstannyl esters 1 and 2 with alkylating agents incorporating a vinyl halide functionality. Although 2,3-dibromopropene (147) is commercially available, the other required alkylating agents had to be prepared. The preparation of the alkylating agents will be discussed in this section of the thesis.

2.1.1. Preparation of the ω-Halo-2-bromo-1-alkenes 154

Suzuki and co-workers reported that \( B \)-bromo-9-borabicyclo[3.3.1]nonane (\( B \)-Br-9-BBN) reacts readily with 1-alkynes. The bromoboration reaction proceeds through a Markovnikov addition of the Br-B moiety to the C=C bond in a \textit{cis} manner. Protonolysis of the bromoboration intermediates with acetic acid gives the corresponding 2-bromo-1-alkenes in excellent yields.\(^4\) For example, 1-decyne (148) and cyclohexylethyne (149) were converted into 2-bromo-1-decene (150) (88\% yield) and 2-bromo-2-cyclohexylethylene (151) (80\% yield), respectively, via this method (Equation 34).

\[
\begin{align*}
\text{R} & \equiv \text{H} & \text{a)} & \text{B-Br-9-BBN} & \Rightarrow & \text{R} & \equiv \text{Br} \\
\text{b) AcOH} & & & \text{CH}_2\text{Cl}_2 & & & \\
148 \text{ R} = \text{CH}_3(\text{CH}_2)_9 & & & 150 \text{ R} = \text{CH}_3(\text{CH}_2)_9 & & & 88\% \\
149 \text{ R} = & & & 151 \text{ R} = & & & 80\% 
\end{align*}
\]
Therefore, it appeared that the $\omega$-halo-2-bromo-1-alkenes 154 could be synthesized via this methodology (Scheme 9). The $\omega$-halo-1-alkynes 153 were obtained from the corresponding alkyne alcohols 152 (commercially available) via standard procedures as typified by the preparation of 4-iodo-1-butyne (156).\textsuperscript{41} A solution of 3-butyn-1-ol (155) in dichloromethane was added slowly to a solution of triphenylphosphine diiodide (prepared \textit{in situ}) in dichloromethane (room temperature, 3 h) to afford, after chromatography and distillation of the crude reaction product, 4-iodo-1-butyne (156) in 83% yield (Equation 35). The $^1$H NMR spectrum of 156 displayed the expected signals for a terminal alkyne proton (a 1-proton triplet at $\delta$ 2.16, $J = 2$ Hz), and two different methylene groups (a 2-proton triplet of doublets at $\delta$ 2.78, $J = 7$, 2 Hz, and a 2-proton triplet at $\delta$ 3.24, $J = 7$ Hz). The IR spectrum of 156 showed a strong $\equiv$C-H stretching band at 3295 cm$^{-1}$ and a weak C$\equiv$C stretching band at 2121 cm$^{-1}$. Furthermore, high resolution mass spectrometry showed that 156 had a molecular formula of C$_4$H$_5$I.

\begin{equation}
\text{\begin{align*}
\text{155} & \xrightarrow{\text{Ph}_3\text{PI}, \text{CH}_2\text{Cl}_2} & \text{156} \\
\text{83%} & & \\
\end{align*}}
\end{equation}
6-Bromo-1-hexyne (159) was prepared via a procedure similar to that described above, except that triphenylphosphine dibromide was used (Equation 36). The $^1$H NMR and IR spectral data of 159 were consistent with the assigned structure. However, the low and high resolution mass spectra did not exhibit the molecular ion ($M^+$) peak. The two peaks with largest mass corresponded to formulae of $C_4H_7Br$ and $C_4H_5Br$, which result from the loss of a $C_2H_4$ fragment from the molecular ion. Possible pathways for the loss of this fragment involve McLafferty type rearrangements (Scheme 10). The bromine atom migrates to the unsaturated portion of the molecule and the $C_2H_4$ fragment is then lost. Similar observations with 6-chloro-1-hexyne (158) and 5-hexyn-1-ol (126) were reported by Arseniyadis and co-workers.\textsuperscript{42}

\[ \text{Scheme 10} \]

5-Chloro-1-pentyne (157) is commercially available.
The readily available \( \omega \)-halo-1-alkynes 153 were subjected to the bromoboration reaction to provide the corresponding 2-bromo-1-alkenes 154. In accordance with the reported procedure, addition of a dichloromethane solution of 4-iodo-1-butyne (156) to a solution of \( B \)-Br-9-BBN in dichloromethane (0°C, 3 h), followed by protonolysis with glacial acetic acid, afforded, after chromatography and distillation of the crude reaction product, 2-bromo-4-iodo-1-butene (160) in 95% yield (Equation 37). The \( ^1 \)H NMR spectrum of 160 exhibited the expected signals for the different methylene groups (two 2-proton triplets at \( \delta \) 2.95 and \( \delta \) 3.34, \( J = 7 \) Hz in each case) and two geminal olefinic protons (two 1-proton doublets at \( \delta \) 5.56 and \( \delta \) 5.68, \( J = 1 \) Hz in each case). The IR spectrum of 160 displayed a moderate C=C stretching band at 1631 cm\(^{-1}\). The high resolution mass spectrum showed that 160 had a molecular formula of \( \text{C}_4\text{H}_6\text{BrI} \).

\[
\begin{array}{c}
\text{equiv} \\
\begin{array}{c}
\equiv \left( \right)_n \\
153
\end{array}
\text{a) } B\text{-Br-9-BBN,} \\
\begin{array}{c}
\text{CH}_2\text{Cl}_2, \\
b) \text{AcOH}
\end{array}
\rightarrow \\
\begin{array}{c}
\equiv \left( \right)_n \\
154
\end{array}
\end{array}
\]

(37)

156 \( n = 2, X = \text{I} \) 
157 \( n = 3, X = \text{Cl} \) 
159 \( n = 4, X = \text{Br} \)

160 \( n = 2, X = \text{I}, 95\% \)
161 \( n = 3, X = \text{Cl}, 92\% \)
162 \( n = 4, X = \text{Br}, 90\% \)

In a similar manner, the \( \omega \)-halo-1-alkynes 157 and 159 were converted into the corresponding \( \omega \)-halo-2-bromo-1-alkenes 161 and 162, respectively. The spectral data of 161 and 162 were in agreement with the assigned structures.

\[
\begin{array}{c}
\equiv \text{Br} \\
161
\text{Cl} \\
\text{NaI, acetone, } \Delta, \\
93\%
\rightarrow \\
\equiv \text{Br} \\
163
\end{array}
\]

(38)

The chloride 161 was transformed into the iodide 163 via a simple Finkelstein reaction.\(^{43}\) Treatment of 161 in acetone with sodium iodide (2.5 equiv)
(reflux, 16 h) afforded, after distillation of the crude reaction product, the iodide 163 in 93% yield (Equation 38). The $^1$H NMR and IR spectral data of 163 were consistent with the assigned structure. Furthermore, 163 was shown to have a molecular formula of $C_5H_8BrI$ by high resolution mass spectrometry.

2.1.2. Preparation of (Z)-1-Bromo-2-iodo-2-butene (174)

$$\text{SnMe}_3 \rightarrow \text{Br} \quad \text{I} \quad \text{172} \quad \text{174} \quad (39)$$

Although the haloboration reaction has been very useful for the preparation of 2-halo-1-alkenes, disubstituted alkynes do not undergo this reaction efficiently. Therefore, it was necessary to use an alternative route for the synthesis of the alkylating agent 174. One possibility would involve iododestannylation of a vinylstannane of general structure 172 (Equation 39).

$$\text{R} \quad \text{CH}_2\text{OH} \rightarrow \text{n-Bu}_3\text{SnH}, \quad \text{AIBN}, \Delta \quad \text{R} \quad \text{OH} \quad \text{Sn-n-Bu}_3 \quad \text{164} \quad \text{171} \quad (40)$$

165 R = H
166 R = CH$_3$(CH$_2$)$_2$
167 R = H, 74%
168 R = CH$_3$(CH$_2$)$_2$, 87%

Ensley, Taddei and co-workers observed that tri-$n$-butyltin hydride adds regioselectively to propargylic alcohols 164 and provides predominantly the (Z)-vinylstannanes 171 (Equation 40).$^{44}$ The selective addition of the $n$-Bu$_3$Sn group to the C-2 carbon is observed only when the substrates are non-terminal propargylic alcohols. When the hydroxy group and the triple bond are separated by more than one carbon, this type of selectivity is no longer observed. A possible
catalytic cycle for the hydrostannylation of the propargylic alcohol 164 is illustrated by Scheme 11. Taddei\textsuperscript{44b} hypothesized that the \textit{n-Bu}_3Sn radical generated is probably coordinated to the oxygen atom in the transition state which thus helps the tin group to transfer efficiently to the C-2 carbon. Also, the radical 170 is destabilized by the inductive effect of the hydroxy moiety. Thus, this might explain the preferential formation of the intermediate 169. Reaction of the intermediate 169 with \textit{n-Bu}_3SnH gives predominantly the (Z)-isomer 171 under kinetically controlled conditions and regenerates a \textit{n-Bu}_3Sn radical. Thus, the (Z)-vinylstannane 167 was readily obtained by the hydrostannylation of 2-butyn-1-ol (165).

The (Z)-vinylstannane 167 was converted into the (Z)-vinyl iodide 173 via an iododestannylation reaction. Thus, addition of a dichloromethane solution of 167
to a solution of iodine (1 equiv) in dichloromethane (0°C, 15 min) afforded, after chromatography and distillation of the crude reaction product, the (Z)-vinyl iodide 173 in a 92% yield (Equation 41). The $^1$H NMR spectrum of 173 displayed the expected signals for a vinylic methyl group (a 3-proton doublet of triplets at δ 1.81, $J = 7$, 1 Hz), a hydroxy proton (a 1-proton broad singlet at δ 1.88 which exchanged with D$_2$O), a methylene group (a 2-proton broad singlet at δ 4.26) and an olefinic proton (a 1-proton quartet of triplets at δ 5.98, $J = 7$, 1 Hz). The IR spectrum of 173 exhibited a weak absorption band at 1649 cm$^{-1}$ for the C=C stretch and a strong absorption band at 3310 cm$^{-1}$ for the OH stretch. The high resolution mass spectrum showed that 173 had a molecular formula of C$_4$H$_7$OI.

$$\text{Sn-n-Bu}_3 \overset{\text{I}_2, \text{CH}_2\text{Cl}_2, 92\%}{\rightarrow} \text{OH} \quad (41)$$

Finally, the (Z)-vinyl iodide (173) was readily converted into the required alkylating agent (174) via the triphenylphosphine dibromide reaction (Equation 42). The spectral data of 174 was consistent with the assigned structure. Compound 174 was shown to have a molecular formula of C$_4$H$_6$BrI by high resolution mass spectrometry.

$$\text{OH} \quad (42)$$
2.1.3. Preparation of (E)-3,5-Diiodo-2-pentene (176)

A generous sample of the chloride 175 was provided by B.A. Story. The chloride 175 was readily converted into the iodide 176 via a simple Finkelstein reaction (Equation 43). The $^1$H NMR spectrum of 176 showed the presence of a vinylic methyl group (a 3-proton doublet at $\delta$ 1.66, $J = 7$ Hz), two different methylene groups (two 2-proton triplets at $\delta$ 2.92 and $\delta$ 3.26, $J = 7$ Hz each) and an olefinic proton (a 1-proton quartet at $\delta$ 6.39, $J = 7$ Hz). Furthermore, the high resolution mass spectrum showed that 176 had a molecular formula of C$_5$H$_8$I$_2$.

2.2. Deconjugation-Alkylation of the Trimethylstannyl Esters 1 and 2

With the availability of the ethyl 3-trimethylstannyl-2-alkenoates, 1 and 2, and the necessary alkylating agents, the deconjugation-alkylation reactions could now be investigated.

Reports on deconjugation-alkylation of $\alpha$,\,$\beta$-unsaturated esters have been numerous in the last decade because of the recognition of the synthetic potential of this type of transformation. One of the earliest reports was published by Rathke and Sullivan in 1972. They observed that treatment of $\alpha$,\,$\beta$-unsaturated esters with an excess of a sterically hindered amide base provided the corresponding dienolate anions which could react with electrophiles, such as protons, alkyl halides and
Michael acceptors, predominantly at the α-position of the esters. For example, deprotonation of ethyl (E)-2-butenoate (177) with lithium N-isopropylcyclohexylamide (LiICA) in THF/HMPA at -78°C, followed by quenching with methyl iodide (Equation 44) or with benzyl bromide (Equation 45) provided the corresponding alkylated unconjugated esters, 178 and 179, respectively.

\[ \text{HMPA/THF, b) Mel 178 (87\%)} \]

\[ \text{HMPA/THF, b) PhCH}_2\text{Br 179 (62\%)} \]

The preference for alkylation at the α-carbon after formation of the dienolate anions derived from α,β-unsaturated esters was also observed by Schlessinger and co-workers. They used an essentially non-nucleophilic form of LDA, consisting of an apparent 1:1 complex of the nitrogenous base with HMPA which acted only as a base and permitted alkylation at the α-carbon. Thus, addition of HMPA (1.1 equiv) to a THF solution of LDA (1 equiv) (30 min, -78°C) resulted in the formation of the presumed LDA complex. Sequential addition of ethyl (E)-2-butenoate (177) (1 equiv) (10 min, -78°C) and iodoethane to the solution of the LDA complex afforded the α-alkylated adduct 180 in 96% yield (Equation 46). Furthermore, their simple molecular orbital calculations on the lithium enolate of ethyl (E)-2-butenoate (177) indicated that the maximum negative charge resides on the α-carbon atom.

\[ \text{THF, b) CH}_3\text{CH}_2\text{I 180 (96\%)} \]
These studies established that the alkylation occurred mainly at the \(\alpha\)-carbon of the \(\alpha,\beta\)-unsaturated esters but did not present any information regarding the stereochemical outcome of the double bond geometry in the product. However, Koyama and co-workers reported that the alkylation of methyl \((E)\)-2-pentenoate (181) with \(\text{NaNH}_2\) and 1-iodobutane gave a 33\% yield of a single unconjugated ester 182 (Equation 47).\(^7\) Zimmerman reported that the lithium enolate anion of methyl \((E)\)-4-methoxy-2-butenoate (183) gave a good yield of the alkylated product 184 in which the new double bond stereochemistry was exclusively \(\text{cis}\) (Equation 48).\(^8\)

![Chemical Structures](image)

Subsequently, Kende and Toder systematically examined the stereochemical outcome of the deconjugation-alkylation of a series of \(\alpha,\beta\)-unsaturated esters (Tables 8 and 9).\(^9\) For example, addition of ethyl \((Z)\)-2-pentenoate (189) to a solution of 1.1 equivalents of LDA/HMPA (30 min, -78°C), followed by addition of methyl iodide, provided the alkylated \((E)\)-3-pentenoate 195 (Entry 1, Table 8). Similarly, the alkylated \((Z)\)-3-pentenoate 198 was obtained via the same procedure from ethyl \((E)\)-2-pentenoate 192 (Entry 1, Table 9). It was observed that the deconjugation-alkylation of ethyl \((Z)\)-2-alkenoates 185 stereoselectively produced the alkylated \((E)\)-3-alkenoates 187 (Table 8). In contrast, it was found that the stereoselectivity associated with the deconjugation-alkylation of ethyl \((E)\)-2-alkenoates (186) decreases
Table 8: Deconjugation-Alkylation of Ethyl (Z)-2-Alkenoates 185

\[
\begin{array}{cccc}
\text{Entry} & 185 & \text{R} & 187 & \text{Yield (\%)} \\
1 & 189 & \text{CH}_3 & 195 & 90 \\
2 & 190 & \text{CH}_3(\text{CH}_2)_2 & 196 & 90 \\
3 & 191 & (\text{CH}_3)_2\text{CH} & 197 & 88 \\
\end{array}
\]

Table 9: Deconjugation-Alkylation of Ethyl (E)-2-Alkenoates 186

\[
\begin{array}{cccc}
\text{Entry} & 186 & \text{R} & 187 & 188 \\
1 & 192 & \text{CH}_3 & 195 (0\%) & 198 (90\%) \\
2 & 193 & \text{CH}_3(\text{CH}_2)_2 & 196 (14\%) & 199 (78\%) \\
3 & 194 & (\text{CH}_3)_2\text{CH} & 197 (35\%) & 200 (62\%) \\
\end{array}
\]
as the size of R group increases (Table 9).

The stereoselectivity associated with the double bond isomerization in the deconjugation-alkylation reaction is suggested to arise in the deprotonation step. A mechanistic argument employed by Kende and Toder to rationalize the inversion of the stereochemistry of the double bond in the reaction is based on stereo-electronic control (orbital overlap) in the formation of the conformationally stable intermediate carbanions and the relative stabilities of the transition states leading to these carbanions.

The observed inversion of stereochemistry in the conversion of the 2-(Z)-precursor 185 to the 3-(E)-unsaturated ester 187 or the 2-(E)-precursor 186 to 3-(Z)-unsaturated ester 188 can be rationalized by the formulations shown in Schemes 13 and 14. In the formation of the transition states leading to dienolates, the stereoelectronic control argument requires that in both of the two possible ground state conformations a C-H bond be aligned perpendicular to the plane of the conjugated π system. Thus, in the case of the 2-(Z)-precursor 185 (Scheme 13), deprotonation from the conformation 202 leading to the extended enolate 206 would be unfavorable because of the severe 1,3-allylic strain between the R and the CO₂Et groups in the transition state 204. In contrast, deprotonation from the other conformation 201 would occur via a transition state 203 in which no severe steric interaction would be involved. Thus, in this case, the minimum energy pathway is that involving the conversion of 201 to 205. Subsequent alkylation of 205 would provide the 3-(E)-product 187.

In the case of the 2-(E)-precursor 186 (Scheme 14), there are no major steric interactions observed in the two possible conformations, 207 and 208, and

* These are modified versions of Kende and Toder's formulations.
Scheme 13
Scheme 14
therefore, deprotonation from both of the conformations is feasible. However, the transition state 210 derived from conformation 208 is favored due to stabilization by the cis-alkyl substituent R. The stabilizing effect of an alkyl group in a cisoid allylic anion structure is well established theoretically and experimentally. For example, the crotyl anion system in cis-form 213 is more stable than its trans-form 214 (Equation 49). Therefore for the (E)-2-alkenoates 186, preferential deprotonation from conformation 208 would be anticipated and would result in formation of the 3-(Z)-product 188 after alkylation. However, when R is large, the A₁,₃ interaction between the R and the olefinic proton in the conformation 208 would be significant. Then, the rotamer resembling the conformation 207 would begin to compete with 208. This would lead to the generation of a significant amount of the extended enolate 211 which would provide the 3-(E)-product 187.

![Chemical structures](image)

Protonation-deconjugations of ethyl (Z)- and (E)-3-trimethylstannyl-2-alkenoates 1 and 2 were achieved readily with stereospecificity. Thus, it was not surprising to find that deconjugation-alkylation of ethyl (Z)-3-trimethylstannyl-2-alkenoates 1 with 2,3-dibromopropene (147) was also accomplished readily. For example, addition of a THF solution of ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) to a solution of LDA/HMPA complex (1.3 equiv) in THF (-78°C, 0.5 h; 0°C, 0.5 h) afforded a bright yellow solution of the corresponding lithium dienolate. Cooling of the solution to -78°C and subsequent addition of 2,3-dibromopropene (147) (1.5 equiv) (-78°C, 1 h) provided, after chromatography and distillation of the crude reaction product, a 74% yield of the (E)-diene ester 216.
Table 10
Deconjugation-Alkylation of Ethyl (Z)-3-Trimethylstannyl-2-alkenoates with 2,3-Dibromopropene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>R</th>
<th>Product</th>
<th>Yield (%) II</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>CH₃</td>
<td>215</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>135</td>
<td>CH₃OCH₂O</td>
<td>216</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>136</td>
<td>CH₃OCH₂O(CH₂)₂</td>
<td>217</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>137</td>
<td>t-BuMe₂SiO(CH₂)₃</td>
<td>218</td>
<td>86</td>
</tr>
</tbody>
</table>

- a) LDA/HMPA (1.3 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
  b) 2,3-Dibromopropene (147) (1.5 equiv), -78°C, 1 h.

II Yield of purified, distilled product.

III This product was purified by column chromatography, but was not distilled.
Table 11
Deconjugation-Alkylation of Ethyl (E)-3-Trimethylstannyl-2-alkenoates with 2,3-Dibromopropene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)\textsuperscript{II}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>H</td>
<td>221</td>
<td>69\textsuperscript{III}</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>CH\textsubscript{3}</td>
<td>222</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>142</td>
<td>CH\textsubscript{3}OCH\textsubscript{2}O</td>
<td>223</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>143</td>
<td>CH\textsubscript{3}OCH\textsubscript{2}O(CH\textsubscript{2})\textsubscript{2}</td>
<td>224</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>144</td>
<td>t-BuMe\textsubscript{2}SiO(CH\textsubscript{2})\textsubscript{3}</td>
<td>225</td>
<td>78\textsuperscript{IV}</td>
</tr>
</tbody>
</table>

\textsuperscript{I} a) LDA/HMPA (1.3 equiv), THF, -78\textdegree C, 0.5 h; 0\textdegree C, 0.5 h;  
b) 2,3-Dibromopropene (147) (1.5 equiv), -78\textdegree C, 1 h.  
\textsuperscript{II} Yield of purified, distilled product.  
\textsuperscript{III} In addition, the diene ester 226 (17\%) was produced.  
\textsuperscript{IV} This product was purified by column chromatography, but was not distilled.
In a similar manner, the other (Z)-trimethylstannyl esters 1 were converted into the corresponding (E)-diene esters 215 (Table 10). In each case, careful analysis of the crude product by GLC showed that none of the (Z)-diene ester 220 was produced, but small amounts of other impurities (<5%) were observed in the crude product.

The (E)-trimethylstannyl esters 2 were also converted into the corresponding (Z)-diene esters 220 via a procedure similar to that for the (Z)-trimethylstannyl esters 1. The results are summarized in Table 11. In each case, careful analysis of the crude product by GLC showed that none of the (E)-diene ester 215 was produced. However, in the case of 25, a substantial amount of the γ-alkylated product was obtained from the alkylation reaction.

The reaction of ethyl (E)-3-trimethylstannyl-2-butenoate (25) with 2,3-dibromopropene (147), according to the normal procedure, provided a mixture of the diene esters 221 and 226 with yields of 69% and 17%, respectively (Entry 1, Table 11). The diene ester 226 is the result of an alkylation by 2,3-dibromopropene (147) on the γ-carbon. Rathke and co-workers reported a similar result for their deconjugation of ethyl (E)-2-butenoate (177). Addition of ethyl (E)-2-butenoate (177) to a 0.5 M solution of LiIICA in THF/HMPA produced, after quenching with water, an 87% yield of the unconjugated ester 227 and a 13% yield of the starting material ethyl (E)-2-butenoate (177) (Equation 50). Quenching of the reaction with D₂O produced a similar ratio of the corresponding deuterated products.

\[
\text{CO}_2\text{Et} \quad \begin{array}{c}\text{177} \\
\text{CO}_2\text{Et} \quad \text{227} \\
\text{THF,} \\
\text{H}_2\text{O}
\end{array} \\
a) \text{LDA/HMPA,} \\
b) \text{H}_2\text{O}
\]
Deconjugation-alkylation of the 3-trimethylstannyl-2-alkenoates 1 and 2 were also performed with other alkylating agents via a procedure identical with that employed earlier (Table 12). In each case, except for that summarized in entry 2, careful analysis of the crude product by GLC showed that a single product was obtained. For the experiment given in entry 2, GLC analysis of the crude product showed the presence of the (Z)-diene ester 229 and small amounts of other products (<5%), but none of the (E)-diene ester 228.

Deconjugation-alkylation of the (E)-trimethylstannyl ester 25 with 2-bromo-5-chloro-1-pentene (161) failed under the normal reaction conditions (Equation 51). Apparently, the chloride 161 is not sufficiently reactive for the alkylation to proceed. Therefore, the chloride 161 was converted into the iodide 163 (vide supra), which then alkylated the dienolate anion of the (E)-trimethylstannyl ester (25) in a satisfactory manner (Entry 7, Table 12).

\[
\begin{align*}
\text{Me}_3\text{Sn} & \quad \text{CO}_2\text{Et} \\
\text{25} & \quad \text{a) LDA, HMPA, THF,} \\
 & \quad \text{b) Cl} \\
\text{Br} & \quad \text{Me}_3\text{Sn} \\
\text{161} & \quad \text{CO}_2\text{Et} \\
\text{25} & \quad + \\
\text{Me}_3\text{Sn} & \quad \text{CO}_2\text{Et} \\
\text{238} & \quad \text{Br} \\
\end{align*}
\]

The structural assignments of all the diene esters were supported by their \textsuperscript{1}H NMR spectral data. Three notable differences in the \textsuperscript{1}H NMR spectra of the (E)-diene esters 215 and (Z)-diene esters 220 (except for 221) were the chemical shifts of the methine proton, the chemical shifts of the vinyl proton vicinal to the trimethylstannyl group and the tin-proton coupling constant ($^3J_{\text{Sn-H}}$) associated with coupling between the olefinic proton and the $^{117}$Sn and $^{119}$Sn isotopes (Table 13).
Table 12
Deconjugation-alkylation of Ethyl (Z)- and (E)-3-Trimethylstannyl-2-alkenoates with Other Alkylating Agents

\[
\begin{align*}
R - & \quad CO_2Et \\
Me_3Sn \quad & \quad H \\
1 \ or \ 2
\end{align*}
\]

\[
\begin{align*}
a) \ \text{Base} & \quad \rightarrow \quad R' \quad CO_2Et \\
b) \ \text{R'X} & \quad \rightarrow \quad SnMe_3
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Procedure</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(1) or (2)</td>
<td>A</td>
<td>(5) or (6)</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>(35)</td>
<td></td>
<td>(228)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>(36)</td>
<td>A</td>
<td>(229)</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>(25)</td>
<td>B</td>
<td>(230)</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>(35)</td>
<td>B</td>
<td>(231)</td>
<td>75</td>
</tr>
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Table 12. Continued

<table>
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<th>Entry</th>
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<th>Procedure</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>$\text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>B</td>
<td>$\text{Br} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>232</td>
</tr>
<tr>
<td>6</td>
<td>$\text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>C</td>
<td>$\text{I} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>233</td>
</tr>
<tr>
<td>7</td>
<td>$\text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>D</td>
<td>$\text{Br} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>234</td>
</tr>
<tr>
<td>8</td>
<td>$\text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>D</td>
<td>$\text{Br} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>235</td>
</tr>
<tr>
<td>9</td>
<td>$\text{MOMO(CH}_2)_3 \quad \text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>D</td>
<td>$\text{O} \quad \text{O} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>236</td>
</tr>
<tr>
<td>10</td>
<td>$\text{Me}_3\text{Sn} = \text{CO}_2\text{Et}$</td>
<td>E</td>
<td>$\text{Br} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3$</td>
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<td>237</td>
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</table>
Table 12. Continued

I Procedure A  a) LDA/HMPA (1.1 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
              \[
              \begin{align*}
              &\text{b)} \quad \text{Br} & \quad (174) & \quad (1.3 \text{ equiv}), -78^\circ \text{C}, 1 \text{ h}. \\
              \end{align*}
              \]

I Procedure B  a) LDA/HMPA (1.1 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
              \[
              \begin{align*}
              &\text{b)} \quad \text{Br} & \quad (160) & \quad (1.3 \text{ equiv}), -78^\circ \text{C}, 1 \text{ h}. \\
              \end{align*}
              \]

I Procedure C  a) LDA/HMPA (1.2 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
              \[
              \begin{align*}
              &\text{b)} \quad \text{Br} & \quad (176) & \quad (1.2 \text{ equiv}), -78^\circ \text{C}, 1 \text{ h}. \\
              \end{align*}
              \]

I Procedure D  a) LDA/HMPA (1.2 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
              \[
              \begin{align*}
              &\text{b)} \quad \text{Br} & \quad (163) & \quad (1.3 \text{ equiv}), -78^\circ \text{C}, 1 \text{ h}. \\
              \end{align*}
              \]

I Procedure E  a) LDA/HMPA (1.1 equiv), THF, -78°C, 0.5 h; 0°C, 0.5 h;
              \[
              \begin{align*}
              &\text{b)} \quad \text{Br} & \quad (162) & \quad (1.3 \text{ equiv}), -78^\circ \text{C}, 1 \text{ h}. \\
              \end{align*}
              \]

II Yield of purified, distilled product.
Table 13

The Partial $^1$H NMR Spectral Data of the Diene Esters 215 and 220

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compounds 215</th>
<th>Compounds 220</th>
<th>R</th>
<th>$\delta$ of the methine proton</th>
<th>$\delta$ of the olefinic proton vicinal to SnMe$_3$ group</th>
<th>$^3J_{Sn-H}$ of the olefinic proton (Hz)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>216</td>
<td>CH$_3$</td>
<td>4.06-4.20</td>
<td>5.86</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>222</td>
<td>CH$_3$</td>
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<td>6.20</td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>217</td>
<td>MOMO</td>
<td>4.27</td>
<td>6.05</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>223</td>
<td>MOMO</td>
<td>3.46</td>
<td>6.73</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>218</td>
<td>MOMO(CH$_2$)$_2$</td>
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<td>5.79</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>224</td>
<td>MOMO(CH$_2$)$_2$</td>
<td>3.52</td>
<td>6.13</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>219</td>
<td>TBDMSO(CH$_2$)$_3$</td>
<td>4.05</td>
<td>5.75</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>225</td>
<td>TBDMSO(CH$_2$)$_3$</td>
<td>3.48</td>
<td>6.12</td>
<td>131</td>
<td></td>
</tr>
</tbody>
</table>
For example, the $^1$H NMR spectrum of the (E)-diene ester 216 (Figure 1) displayed the expected signals for a trimethylstannyl group (a 9-proton singlet at $\delta$ 0.12, with satellite peaks due to tin-proton coupling, $^2J_{\text{Sn-H}} = 54$ Hz), a vinylic methyl group (a 3-proton doublet at $\delta$ 1.81, $J = 6.5$ Hz) and a 2-bromopropenyl moiety (two 1-proton doublets of doublets of doublets at $\delta$ 2.44 and $\delta$ 2.94, $J = 14$, 6.5, 1 Hz and $J = 14$, 8, 1 Hz, respectively, and two 1-proton broad doublets at $\delta$ 5.42 and $\delta$ 5.56, $J = 2$ Hz, each). In addition, a 3-proton triplet at $\delta$ 1.24 ($J = 7$ Hz) and a 3-proton multiplet at $\delta$ 4.06-4.20 indicated the presence of an ethyl ester moiety and a methine proton. More importantly, a 1-proton quartet of doublets ($J = 6.5$, 1 Hz) at $\delta$ 5.86 with satellite peaks due to tin-proton coupling ($^3J_{\text{Sn-H}} = 73$ Hz) accounted for the presence of a vicinal vinyl proton that is cis to the trimethylstannyl group.$^{37,38}$ The $^1$H NMR spectrum of the corresponding (Z)-diene ester 222 (Figure 2) was very similar to that of 216 except in the three above-mentioned differences. Firstly, the position of the methine proton was now observed upfield at $\delta$ 3.51. Secondly, the position of the vinyl proton vicinal to the trimethylstannyl group was further downfield at $\delta$ 6.20. Thirdly, the corresponding tin-proton coupling constant ($^3J_{\text{Sn-H}}$) associated with the coupling of the olefinic proton with the $^{117}\text{Sn}$ and $^{119}\text{Sn}$ isotopes was 128 Hz. These data were consistent with a compound having a vicinal vinyl proton trans to a trimethylstannyl group.

The $^1$H NMR spectrum of the diene ester 221, which has two terminal double bonds, exhibited four olefinic proton signals (two 1-proton doublets at $\delta$ 5.44 and $\delta$ 5.57, $J = 2$ Hz in each case; a 1-proton doublet at $\delta$ 5.36, $J = 2$
Figure 1: The 400 MHz $^1$H NMR Spectrum of the Diene Ester 216

Figure 2: The 400 MHz $^1$H NMR Spectrum of the Diene Ester 222
Hz, with satellite peaks due to cis tin-proton coupling, $^3J_{Sn-H} = 66$ Hz; and a 1-proton doublet of doublets at $\delta$ 5.84, $J = 2$, 1 Hz, with satellite peaks due to trans tin-proton coupling, $^3J_{Sn-H} = 137$ Hz).

\[
\begin{align*}
\text{Br} & \quad \text{SnMe}_3 \\
\text{CO}_2\text{Et}
\end{align*}
\]

The $^1$H NMR spectra of the diene esters obtained from the deconjugation-alkylation of ethyl 3-trimethylstannyl-2-alkenoates with the other alkylating agents exhibited $^1$H NMR signals similar to those of the corresponding diene esters 215 and 220 except that the signals for 2-bromopropenyl moiety were replaced by signals due to the side chains from the other alkylating agents. For example, the $^1$H NMR spectrum of 230 exhibited the expected signals for a 3-bromo-3-butenyl moiety (two 1-proton doublets of quartets at $\delta$ 1.75 and $\delta$ 2.07, $J = 14$, 7 Hz in each case, a 2-proton multiplet at $\delta$ 2.33-2.47 and two 1-proton doublets at $\delta$ 5.43 and $\delta$ 5.58, $J = 1.5$ Hz in each case).

The IR spectra of all the diene esters except 226 showed absorption bands at 1727-1731 cm$^{-1}$, consistent in each case with the unconjugated nature of the ester moiety. In addition, the Sn-CH$_3$ rocking vibrations (absorption bands at 768-775 cm$^{-1}$) were observed in each case.

\[
\begin{align*}
\text{Br} & \quad \text{SnMe}_3 \\
\text{CO}_2\text{Et}
\end{align*}
\]

The diene ester 226 was assigned as the $\gamma$-alkylated product because its spectral properties were very different from those of the other diene esters. The $^1$H NMR spectrum of 226 showed the presence of a trimethylstannyl group (a
9-proton singlet at δ 0.20 with satellite peaks, $2J_{Sn-H} = 54$ Hz), an ethyl ester group (a 3-proton triplet at δ 1.30 and a 2-proton quartet at δ 4.19, $J = 7$ Hz, each) and two allylic methylene moieties (two 2-proton broad triplets at δ 2.52 and δ 2.70, $J = 8$ Hz, each). It also displayed signals for three olefinic protons (two 1-proton broad doublets at δ 4.42 and δ 4.56, $J \approx 2$ Hz, each, and a 1-proton triplet at δ 6.40, $J \approx 2$ Hz, with satellite peaks due to trans tin-proton coupling, $3J_{Sn-H} = 116$ Hz). Furthermore, the IR spectrum of 226 exhibited an absorption band at 1703 cm$^{-1}$ for the C=O stretching vibration which indicated the presence of a conjugated ester moiety.

In accordance with previous observations, all the diene esters did not exhibit molecular ion peaks in their mass spectra. Thus, satisfactory high resolution mass spectrometric measurements were carried out on the z/e M$^+$.15 fragment in each case.

The results of deconjugation-alkylation and the previously reported protonation-deconjugation of (Z)- and (E)-3-trimethylstannyl-2-alkenoates 1 and 2 are shown to be highly stereoselective and occur with an inversion of the double bond geometry. These results can be rationalized on the basis of stereoelectronic and product development control (Schemes 15 and 16).

For the kinetically controlled deprotonation of the (E)-trimethylstannyl esters 2, two ground state conformations 239 and 240 must be considered. The highly stereoselective conversion of the (E)-trimethylstannyl esters 2 to the (Z)-products 6 is due mainly to the preference for the ground state conformation 240 (Scheme 15). In the transition state 242 arising from conformation 240, the severe A$^{1,3}$ strain between the R and the CO$_2$Et moieties found in the disfavored transition state 241, is not observed. Although 242 has a steric interaction (A$^{1,2}$ strain$^{45}$) between the R and SnMe$_3$ groups, this interaction is considerably smaller than the A$^{1,3}$ interaction of 241. For example, the A$^{1,2}$ strain between two methyl groups
Scheme 15
Scheme 16
is suggested to be \(-0.9\) kcal/mol, while an \(A^{1,3}\) methyl-methyl interaction is given as \(7.6\) kcal/mol.\(^{45}\) Thus, the deprotonation of 2 proceeds from the conformer 240 through the lower energy pathway involving the transition state 242. Subsequent alkylation or protonation of the dienolate anion 244 yields the (Z)-product 6.

On the other hand, in similar reactions involving transformation of the (Z)-trimethylstannyl esters 1 into the (E)-products 5, there are no major \(A^{1,3}\) interactions in the transition states arising from the two possible ground state conformations 245 and 246 (Scheme 16). Hence, the \(A^{1,2}\) interaction between the \(R\) and the \(\text{SnMe}_3\) groups has a significant influence on the stereochemistry of the reaction. The presence of an \(A^{1,2}\) interaction between the \(R\) and \(\text{SnMe}_3\) in the transition state 248 disfavors deprotonation from the conformer 246. The transition state 247 derived from the conformer 245 is favorable due to the absence of an \(A^{1,2}\) interaction as well as the stabilization by the presence a \(cisoid\) \(R\) group. Thus, the lower energy pathway is through the transition state 247, and eventually, the (E)-product 5 is produced.

2.3. Preparation of Ethyl (E)-2-(2-Bromo-2-propenyl)-7-hydroxy-3-trimethylstannyl-3-heptenoate (251)
The tert-butyldimethylsilyloxy group of the (E)-diene ester 219 was removed via a standard procedure utilizing tetra-n-butylammonium fluoride. In accordance with the procedure, addition of a THF solution of tetra-n-butyl-ammonium fluoride to a solution of the diene ester 219 in THF (0°C, 5 min; room temperature, 2 h) afforded, after chromatography and distillation of the crude reaction product, a 65% yield of the diene ester 251 (Equation 52). The spectral data of 251 were consistent with the assigned structure. Thus, the 1H NMR spectrum of 251 showed the presence of a hydroxy group (a 1-proton broad singlet at δ 1.55-1.62 which exchanged with D2O). A strong absorption band observed at 3368 cm⁻¹ in the IR spectrum of 251 was due to the OH stretching vibration. The high resolution mass spectrometric measurement was performed on the z/e M⁺-15 peak, which was shown to have a molecular formula of C₁₄H₂₄O₃BrSn.

In summary, the requisite alkylating agents with a vinyl halide functionality were readily prepared. Deconjugation-alkylation of ethyl 3-trimethylstannyl-2-alkenoates 1 and 2 with various alkylating agents was shown to be highly stereospecific and resulted in the formation of the various diene esters described. The stereochemistries of these diene esters were assigned mainly on the basis of their 1H NMR spectral data.
3. Synthesis of the Cyclobutanecarboxylates 9 and the Larger Ring Homologs

3.1. Synthesis of the Cyclobutanecarboxylates 9 via Palladium(0)-catalyzed Coupling Reactions

Stille and co-workers have shown that the intermolecular palladium(0)-catalyzed coupling of vinyl halides with vinylstannanes occurs efficiently to provide 1,3-dienes. With the availability of the various diene esters 252 containing a vinylstannane and a vinyl halide group, attempts to cyclize these substrates were made via an intramolecular palladium(0) catalyzed coupling reaction (Equation 53). The choice of the solvent and catalyst were N,N-dimethylformamide (DMF) and tetrakis(triphenylphosphine)palladium (Pd(PPh₃)₄), as they were shown to be very effective by Stille and co-workers.

GLC monitoring of a 0.1 M DMF solution of the diene ester 221 containing 0.05 equivalents of Pd(PPh₃)₄ indicated that the diene ester 221 was
Figure 3: The 400 MHz $^1$H NMR Spectrum of the Cyclobutanecarboxylate 253

cleanly converted into a single compound in 1 h at 80°C. In addition, TLC analysis of the crude product showed a single spot. Isolation and spectral analysis of this product showed that the four-membered cyclic compound 253 had been formed in 82% yield (Equation 54 and Entry 1, Table 14). Explicitly, the $^1$H NMR spectrum of 253 (Figure 3) showed the expected signals for an ethyl ester moiety (a 3-proton triplet at $\delta$ 1.28, $J = 7$ Hz, and a 2-proton multiplet at $\delta$ 4.12-4.26), a methylene group (Hb, a 1-proton doublet of doublets of doublets of doublets of doublets at $\delta$ 2.81, $J_{bc} = 15$ Hz, $J_{ba} = 9$ Hz, $J_{bd} = 3$ Hz, $J_{be} = 2$ Hz; and Hc, a 1-proton doublet of doublets of doublets of doublets of doublets at $\delta$ 3.04, $J_{cb} = 15$ Hz, $J_{ca} = 6$ Hz, $J_{cd} = 3$ Hz, $J_{ce} = 2$ Hz), and a methine proton (Ha, a 1-proton multiplet at $\delta$ 3.69-3.78). It must be noted that the signal for the methylene group of the ethyl ester moiety is a multiplet because the geminal
protons are diastereotopic. There were also the expected signals for four olefinic protons (H_d, a 1-proton broad singlet at δ 4.81; H_g, a 1-proton broad doublet at δ 5.00, J_{gα} = ~ 2 Hz; H_e, a 1-proton triplet at δ 5.23, J_{eb} = J_{ec} = 2 Hz; and H_f, a 1-proton doublet at δ 5.26, J_{fa} = 3 Hz). The assignment of the protons H_a-H_g was based on decoupling experiments. Irradiation at δ 2.81 (H_b) simplified the signal at δ 3.04 (H_c), sharpened the singlet at δ 4.81 (H_d) and converted the multiplet at δ 3.69-3.78 (H_a) to a doublet of doublets of doublets (J_{ac} = 6 Hz, J_{af} = 3 Hz and J_{ag} = 2 Hz) and the triplet at δ 5.23 (H_e) to a doublet (J_{ec} = 2 Hz). Irradiation at δ 3.74 (H_a) simplified the signals at δ 2.81 (H_b) and δ 3.04 (H_c), and converted both doublets at δ 5.00 (H_g) and δ 5.26 (H_f) to singlets. The IR spectrum of 253 exhibited an absorption band at 1736 cm⁻¹ for the C=O stretching vibration of the ester moiety. Compound 253 was shown to have a molecular formula of C₉H₁₂O₂ by high resolution mass spectrometry.

In the literature, the intermolecular palladium(0)-catalyzed coupling of vinyl halides with vinylstannanes is reported to occur in a stereospecific manner; the product retains the double bond stereochemistry of the starting materials.²⁰ For example, the coupling reaction of (Z)-6-iodo-5-hexen-1-ol (266) with (E)-1-trimethylstannyl-1-hexene (265), catalyzed by bis(acetonitrile)dichloropalladium(II) ((CH₃CN)₂PdCl₂) in DMF, afforded (5Z,7E)-5,7-dodecadien-1-ol (267) in 80% yield (Equation 55).

\[ \text{n-Bu} \quad \text{SnMe}_3 \quad 265 \quad + \quad (\text{CH}_3\text{CN})_2\text{PdCl}_2, \quad \text{DMF, 25°C, 16 h, 80%} \quad 267 \]
Not surprisingly, the intramolecular coupling of diene esters containing either one or two stereodefined vinyl partners was also found to be stereospecific. Addition of Pd(PPh₃)₄ (0.05 equiv) to a solution of the diene ester 216 in DMF provided a yellowish solution. The initial yellowish solution was converted into a dark brown solution with deposition of a fine black powder (palladium black) upon heating at 80°C for 1 h. After workup, analysis of the crude reaction product by GLC and TLC indicated that only one coupled product had been formed. Chromatography of the crude reaction product, followed by distillation, afforded ethyl (E)-2-ethylidene-3-methylenecyclobutanecarboxylate (254) in 89% yield (Entry 2, Table 14). In a similar manner, the intramolecular palladium(0)-catalyzed crossing coupling of the diene ester 222 afforded, after chromatography of the crude reaction product, a 96% yield of ethyl (Z)-2-ethylidene-3-methylenecyclobutane-carboxylate (255) (Entry 3, Table 14).

The generality and stereospecificity of this novel method for preparing unusually functionalized cyclobutane systems was further demonstrated by converting the other diene esters 252 into the cyclobutanecarboxylates 9 (Table 14). The procedure employed for the preparation of these cyclobutanecarboxylates, except for 256 and 257, was similar to that outlined in the preparation of 254. In each case, analysis of the crude product by GLC showed that one product was obtained exclusively. It must be noted that even the conversion of the (Z,Z)-diene ester 229 into the cis,cisoid,cis-cyclobutanecarboxylate 264 was accomplished without any isomerization of the double bonds (Entry 12, Table 14).

Cyclization of the diene esters 217 and 223 under the conditions given above yielded none of the desired products but rather caused decomposition of the diene esters 217 and 223. One might speculate that this was mainly due to the instability, under the reaction conditions, of the enol ether functions present in the products. Indeed, when the cyclizations were carried out using Pd(PPh₃)₄ (0.1
Table 14

Synthesis of the Cyclobutanecarboxylates 9

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 252</th>
<th>Product 9</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[\text{Br}C\text{O}_2\text{Et}] \text{SnMe}_3]</td>
<td>[\text{CO}_2\text{Et}]</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>[\text{Br}C\text{O}_2\text{Et}] \text{SnMe}_3]</td>
<td>[\text{CO}_2\text{Et}]</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>[\text{Br}C\text{O}_2\text{Et}] \text{SnMe}_3]</td>
<td>[\text{CO}_2\text{Et}]</td>
<td>96</td>
</tr>
<tr>
<td>4III</td>
<td>[\text{MOMOM}C\text{O}_2\text{Et}] \text{SnMe}_3]</td>
<td>[\text{CO}_2\text{Et}]</td>
<td>68</td>
</tr>
<tr>
<td>5III</td>
<td>[\text{OMOM}C\text{O}_2\text{Et}] \text{SnMe}_3]</td>
<td>[\text{CO}_2\text{Et}]</td>
<td>70</td>
</tr>
<tr>
<td>Entry</td>
<td>Substrate</td>
<td>Product</td>
<td>Yield (%)</td>
</tr>
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<td><img src="image" alt="Substrate 229" /></td>
<td><img src="image" alt="Product 264" /></td>
<td>93</td>
</tr>
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</table>
equiv) in the presence of triethylamine (Et₃N) (1 equiv) for 1 h at 80°C, workup and purification of the crude products by chromatography on silica gel (elution with 8:1 petroleum ether-diethyl ether containing 1% Et₃N) gave the desired products 256 and 257 in yields of 68% and 70%, respectively (Entries 4 and 5, Table 14). The larger amounts of Pd(PPh₃)₄ were required because triethylamine can deactivate the catalyst. Structurally, these cyclobutanecarboxylates are particularly interesting, since they contain, at C-2, a "hidden" aldehyde (enol ether) function.

The intramolecular palladium(0) catalyzed coupling of vinylstannane and vinyl halide moieties constitutes a novel method for the preparation of the cyclobutanecarboxylates 9. All of the structurally interesting cyclobutanecarboxylates 9 gave spectra in accord with the assigned structures. The assignments of the stereochemistries of the cyclobutanecarboxylates 9 were based on the ¹H NMR NOE difference experiments. The ¹H NMR spectrum of the cisoid,trans-cyclobutanecarboxylate 254 (Figure 4) is typical and includes the signals for a vinylic methyl group (a 3-proton doublet at δ 1.68, J = 7 Hz), a methylene group (Hb, a 1-proton doublet of doublets of triplets at δ 2.80, Jbc = 15 Hz, Jba = 9 Hz, Jbd = Jbc = 2 Hz; and Hc, a 1-proton doublet of doublets of triplets at
\( \delta 2.90, J_{cb} = 15 \text{ Hz}, J_{ca} = 6 \text{ Hz}, J_{cd} = J_{cc} = 2 \text{ Hz} \) and a methine proton (\( H_a \), a 1-proton multiplet at \( \delta 3.68-3.78 \)). In addition, there were the expected signals for three olefinic protons (\( H_d \), a 1-proton broad singlet at \( \delta 4.66 \); \( H_e \), a 1-proton broad singlet at \( \delta 5.07 \); and \( H_f \), a 1-proton quartet of doublets at \( \delta 5.78, J \text{ of } H_f-Me = 7 \text{ Hz}, J_{fa} = 2.5 \text{ Hz} \)). In \(^1\)H NMR NOE difference experiments, irradiation at \( \delta 1.68 \) (Me) caused enhancement of the signals at \( \delta 3.68-3.78 \) (\( H_a \)) and \( \delta 5.78 \) (\( H_f \)), while irradiation at \( \delta 5.78 \) (\( H_f \)) caused enhancement of the signals at \( \delta 1.68 \) (Me) and \( \delta 5.07 \) (\( H_e \)).

The \(^1\)H NMR spectrum of the cisoid,cis-cyclobutanecarboxylate 255 (Figure 5) was very similar to that of 254 except for the separation between the signals for \( H_b \) and \( H_c \) In compound 255, this separation was observed to be 0.24 ppm while that in 254 was 0.10 ppm. More importantly, in a \(^1\)H NMR NOE difference experiment, irradiation at the signal for the vinylic methyl group (\( \delta 1.80 \)) caused enhancement of the signals for \( H_e \) (\( \delta 5.14 \)) and \( H_f \) (\( \delta 5.53 \)). This result showed that 255 has a cisoid,cis-diene unit. Similar analyses were performed on the other cyclobutanecarboxylates 9.

All the cyclobutanecarboxylates exhibited absorption bands at 1734-1738 cm\(^{-1}\) for the C=O stretching vibration of the ester moiety in their IR spectra. The high resolution mass spectrometric measurement was performed on the z/e M\(^+\) peak in each case.

It was a surprise to observe the ease of stereospecific formation of the highly strained cyclobutanecarboxylates. A possible rationalization may be illustrated by the working model catalytic cycle of the palladium(0)-catalyzed coupling reaction shown in Scheme 17. Initially, oxidative addition of the vinyl halide to Pd(PPh\(_3\))\(_4\) provides the organopalladium(II) intermediate 268. Then, intramolecular transmetalation of the vinylstannane moiety provides a highly favorable five-membered ring intermediate 269. The transmetalation step is suggested to occur via an
Figure 4: The 400 MHz $^1$H NMR Spectrum of the Cyclobutanecarboxylate 254

Figure 5: The 400 MHz $^1$H NMR Spectrum of the Cyclobutanecarboxylate 255
Scheme 17
electrophilic attack of the organopalladium(II) species on the carbon bonded to tin.\textsuperscript{16c,48} Finally, reductive elimination from the intermediate 269 produces the cyclobutanecarboxylate 9 and regenerates the palladium(0) catalyst. As the oxidative addition,\textsuperscript{49} transmetalation\textsuperscript{14} and reductive elimination\textsuperscript{50} steps are known to occur with retention of configuration, an overall retention of the configuration in the coupling reaction is expected. Thus, this annulation sequence represents a unique method for the stereospecific preparation of the four-membered ring compounds 9.

3.2 X-Ray Analysis of the Cyclobutanecarboxylate Derivatives 270-272

It was of some interest to determine whether or not the \textit{cisoid} diene units in the highly strained compounds 254, 255 and 264 are planar. It might be expected that, particularly in compound 264, the severe steric repulsion between the two vinylic methyl groups would force the diene to be non-planar. An obvious way to determine the molecular conformations of the dienes 254, 255 and 264 (at least in the solid state) would be to convert these substances into crystalline derivatives that would be suitable for single crystal X-ray analyses. To that end, the crystalline amide derivatives 270-272* were prepared from 254, 255, and 264, respectively.

* Although other derivatives were prepared, they were not suitable for single crystal X-ray analysis.
The cyclobutanecarboxamide 270 was prepared via the following procedure, which had been developed previously by Weinreb and co-workers. Thus, a solution of p-chloroaniline (1.5 equiv) was treated with a solution of trimethylaluminum (1.5 equiv) in toluene (room temperature, 20 min) to produce a yellowish solution of the corresponding dimethylaluminum amide reagent. Subsequent addition of a benzene solution of the cyclobutanecarboxylate 254 (1 equiv) to this yellowish solution, followed by refluxing (4 h), provided, after acidic workup, an 87% yield of the cyclobutanecarboxamide 270 (Equation 56). Recrystallization of the compound 270 from dichloromethane-hexane yielded colorless needle-like crystals (melting point 133.5-135°C). Single crystal X-ray analysis of 270 (Appendix 1) indicated that the torsional angle between the C-5 - C-1 and C-2 - C-6 bonds is 3.9° (Figure 6). The bond lengths between the carbon atoms in the four-membered ring are the following: C-1 - C-2, 1.455(4) Å; C-2 - C-3, 1.540(5) Å; C-3 - C-4, 1.565(5) Å; and C-4 - C-1, 1.494(5) Å (Figure 6).

# It should be noted that, for the purposes of this discussion, the numbering system used for the cyclobutanecarboxamides is that shown in their single crystal X-ray structures.
The cyclobutanecarboxamide 271 was prepared via a procedure utilizing \( p \)-bromoaniline hydrochloride.\(^{53} \) A solution of trimethylaluminum (2 equiv) in toluene was added to a solution of \( p \)-bromoaniline hydrochloride (2 equiv) in benzene (room temperature, 1 h) to produce a methylchloroaluminum amide species. Subsequent addition of a benzene solution of the cyclobutanecarboxylate 255 to the amide reagent, followed by refluxing (3 h), afforded, after acidic work-up, a 94% yield of the cyclobutanecarboxamide 271 (Equation 57). Recrystallization of the product 271 from diethyl ether-hexane provided colorless needle-like crystals (melting point 155-156.5°C). Single crystal X-ray analysis\(^{52} \) of this compound (Appendix 1) showed that the torsional angle between the C-5 - C-1 and C-2 - C-6 bonds is 4.8° (Figure 7). The bond lengths between the carbon atoms in the four-membered ring are the following: C-1 - C-2, 1.451(7) Å; C-2 - C-3, 1.495(7) Å; C-3 - C-4, 1.612(7) Å; and C-4 - C-1, 1.495(7) Å (Figure 7).
Figure 7: Stereo view of the Cyclobutanecarboxamide 271

The cyclobutanecarboxamide 272 was prepared via a procedure identical with that used for the synthesis of 270 (Equation 58). Recrystallization of this product from diethyl ether-pentane yielded colorless needle-like crystals (melting point 144-146 °C). Single crystal X-ray analysis of 272 (Appendix 1) indicated that the torsional angle between the C-5 - C-1 and C-2 - C-7 bonds is 25.4° (Figure 8). The bond lengths between the carbon atoms in the four-membered ring are the following: C-1 - C-2, 1.481(3) Å; C-2 - C-3, 1.538(2) Å; C-3 - C-4, 1.544(3) Å; and C-4 - C-1, 1.528(3) Å (Figure 8).
Not unexpectedly, the X-ray analyses showed that the four-membered rings in 270, 271 and 272 are not prefect squares. In each of these substances, the C-1 - C-2 bond is shorter than the other three cyclobutane bonds. More interestingly, although the diene units of the cyclobutanecarboxamides 270 and 271 were found to be nearly planar, the planarity of the diene unit of the cyclobutanecarboxamide 272 is severely disrupted (25.4°). This distortion from planarity is undoubtedly due to the steric repulsion between the two vinylic methyl groups, which are in close proximity to each other (Figure 8). Thus, one would
expect that the diene unit of the cyclobutanecarboxylate 264 would also be twisted away from planarity. Therefore, this substance would undoubtedly be much less reactive than 254 and 255 in, for example, Diels-Alder cycloaddition reactions. This expectation turned out to be correct (vide infra).

3.3. Synthesis of the Larger Ring Homologs of the Cyclobutanecarboxylates 9

As described above, the intramolecular palladium(0)-catalyzed coupling of vinylstannane and vinyl halide moieties was found to be very effective in the syntheses of the cyclobutanecarboxylates 9. It was expected that this methodology could be extended to synthesize larger ring homologs (Equation 59).

\[
\begin{align*}
\text{R'}_n \text{X} \text{SnMe}_3 \text{CO}_2 \text{Et} & \xrightarrow{\text{Pd}(0)} \text{R'}_n \text{CO}_2 \text{Et} \\
\text{Br} \text{SnMe}_3 \text{CO}_2 \text{Et} & \text{230}
\end{align*}
\]

The diene ester 230, which was obtained from the deconjugation-alkylation of ethyl (E)-3-trimethylstannyl-2-butenoate (25) with 2-bromo-4-iodo-1-butene (160), was first cyclized via a procedure identical with that used for the synthesis of the cyclobutanecarboxylates 9. GLC analysis of the crude reaction mixture showed the presence of the desired coupled product, but other uncharacterized compounds were
also present. Therefore, a slightly modified procedure was employed to cyclize the diene ester 230. A solution of 230 in DMF was heated at 80°C for 1 h in the presence of Pd(PPh₃)₄ (0.05 equiv) and LiCl (2 equiv). Workup and chromatography of the crude reaction product afforded an 85% yield of a mixture of the cyclopentanecarboxylates 274 and 278 in the ratio of 13:1, respectively (¹H NMR and GLC analyses) (Entry 1, Table 15). This mixture was separated by preparative thin layer chromatography on silica gel (elution with petroleum ether-diethyl ether, 40:1). The cyclopentanecarboxylate 274 did not isomerize to 278 upon heating at 80°C in DMF. Thus, the isomerization of the double bond is caused by some component (palladium(O)?) of the reaction mixture.

The diene esters 231-233 were also converted into the corresponding cyclopentanecarboxylates 275-277 (Table 15). In each case, except for the experiment summarized in Entry 4, GLC analysis of the crude product showed that a single product was obtained. The intramolecular palladium(0)-catalyzed coupling of the diene ester 233 afforded a mixture of the cyclopentanecarboxylates 277 and 279 in the ratio of 12:1, respectively (GLC analysis) (Entry 4, Table 15).

The cyclopentanecarboxylates 10 exhibited spectra in full accord with the assigned structures. For example, the ¹H NMR spectrum of cyclopentanecarboxylate 274 (Figure 9) showed the signals for a methylene group (Hᵇ, a 2-proton multiplet at δ 1.88-2.10), an allylic methylene group (Hᶜ, a 1-proton doublet of triplets of triplets at δ 2.42, J = 16, 8, 2.5 Hz, and a 1-proton multiplet at δ 2.58-2.68) and a methine proton (Hᵃ, a 1-proton multiplet at δ 3.44-3.51). In addition, there were four olefinic signals (Hᵈ, a 1-proton triplet at δ 4.95, Jᵈᶜ = 2.5 Hz; Hᵍ, a 1-proton doublet at δ 5.11, Jᵍᵃ = 2.5 Hz; Hᵉ, a 1-proton triplet at δ 5.39, Jᵉᶜ = 2.5 Hz; and Hᶠ, a 1-proton doublet at δ 5.52, Jᶠᵃ = 2.5 Hz). The assignment of protons Hᵃ-Hᵍ was based on a decoupling experiment (see Experimental section for details). The compound 274 was shown to have a molecular formula of C₁₀H₁₄O₂
Table 15

Synthesis of the Cyclopentanecarboxylates 10I

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 273</th>
<th>Product 10</th>
<th>YieldII (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="230" alt="" />BrCO_2Et</td>
<td><img src="274" alt="" />CO_2Et</td>
<td>85III</td>
</tr>
<tr>
<td>2</td>
<td><img src="231" alt="" />BrCO_2Et</td>
<td><img src="275" alt="" />CO_2Et</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td><img src="232" alt="" />BrCO_2Et</td>
<td><img src="276" alt="" />CO_2Et</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td><img src="233" alt="" />ICO_2Et</td>
<td><img src="277" alt="" />CO_2Et</td>
<td>83IV</td>
</tr>
</tbody>
</table>
Table 15. Continued

I  Pd(PPh$_3$)$_4$ (0.05 equiv), LiCl (2 equiv), DMF, 80°C, 1 h.

II Yield of purified, distilled product.

III The product included a small amount of the cyclopentanecarboxylate 278. The ratio of 274 : 278 was 13 : 1, respectively.

\[
\begin{align*}
\text{278} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

IV The product included a small amount of the cyclopentanecarboxylate 279. The ratio of 277 : 279 was 12 : 1, respectively.

\[
\begin{align*}
\text{279} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]
Figure 9: The 400 MHz $^1$H NMR Spectrum of the Cyclopentanecarboxylate 274

by high resolution mass spectrometry.

Similar spectral characteristics were observed for the other cyclopentane-
carboxylates 10. The stereochemistries of the double bonds were assigned on the
basis of $^1$H NMR NOE difference experiments. Details can be found in the
Experimental section. All of the cyclopentanecarboxylates 10 showed a z/e M$^+$ peak
in their high resolution mass spectra.

The cyclopentanecarboxylates 278 and 279 exhibited spectral data consistent
with the assigned structures. The IR spectra of 278 and 279 showed the C=O
stretching vibration at 1708-1709 cm$^{-1}$, which is characteristic of a conjugated ester
moiety. The $^1$H NMR spectrum of 278 exhibited the expected signal for a vinylic
methyl group (a 3-proton broad triplet at $\delta$ 2.13, $J = 1$ Hz) and the $^1$H NMR
spectrum of 279 exhibited the expected signals for two vinylic methyl groups (a 3-proton doublet at $\delta$ 1.75, $J = 7$ Hz, and a 3-proton broad triplet at $\delta$ 2.12, $J = 1$ Hz). Furthermore, in each case, $^1$H NMR spectra of 278 and 279 exhibited no signal for the methine proton $\alpha$ to the ester moiety.

The cyclohexanecarboxylates 11 were obtained via a procedure similar to that used in the syntheses of the cyclopentanecarboxylates 10 (Table 16). The yields ranged from 54-74% and, in each case, GLC analysis of the crude product showed that the substrate 280 was cleanly converted into the corresponding cyclohexanecarboxylate 11. It must be noted that when the reaction was done in the absence of LiCl, none of the desired coupled product was obtained.

The cyclohexanecarboxylates 11 exhibited spectra in full accord with the assigned structures. An example is shown by the spectral data for cyclohexanecarboxylate 281. The $^1$H NMR spectrum of 281 (Figure 10) showed the signals for three methylene groups (two 1-proton multiplets at $\delta$ 1.55-1.67 and $\delta$ 1.99-2.09, and two 2-proton multiplets at $\delta$ 1.71-1.87 and $\delta$ 2.18-2.35) and a methine proton (H$_a$, a 1-proton broad doublet of doublets at $\delta$ 3.25, $J \sim 8, 4$ Hz). In addition, there were four olefinic signals (H$_b$ and H$_e$, a 2-proton broad singlet at $\delta$ 4.73; H$_c$, a 1-proton broad singlet at $\delta$ 4.99; and H$_d$, a 1-proton broad singlet at $\delta$ 5.13). The assignment of the protons H$_a$-H$_e$ was based on decoupling and NOE difference experiments (see Experimental section for details).
Table 16
Synthesis of the Cyclohexanecarboxylates 11

![Chemical structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 280</th>
<th>Product 11</th>
<th>Yield(^\text{II}) (%)</th>
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<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Substrate 234" /></td>
<td><img src="image" alt="Product 281" /></td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Substrate 235" /></td>
<td><img src="image" alt="Product 282" /></td>
<td>68</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Substrate 236" /></td>
<td><img src="image" alt="Product 283" /></td>
<td>54</td>
</tr>
</tbody>
</table>

\(^{\text{I}}\) Pd(PPh\(_3\))_4 (0.05 equiv), LiCl (2 equiv), DMF, 80°C, 1 h.

\(^{\text{II}}\) Yield of purified, distilled product.
Figure 10: The 400 MHz $^1$H NMR Spectrum of the Cyclohexanecarboxylate 281

Similar spectral characteristics were observed for the other cyclohexanecarboxylates 11. The stereochemistries of the double bonds were assigned on the basis of $^1$H NMR NOE difference experiments (see Experimental section for details). The high resolution mass spectrometric measurements for all of the cyclohexanecarboxylates 11 were performed on the $z/e$ M$^+$ peaks.

Finally, an attempt to obtain a seven-membered ring via the palladium(0)-catalyzed coupling reaction of the diene ester 237 in the presence of LiCl (2 equiv) was performed (Equation 60). However, none of the expected coupled product was obtained from this reaction, although disappearance of the diene ester 237 was observed.
From our results, it is evident that LiCl is required to achieve successful cyclization of the appropriate diene esters to the cyclopentanecarboxylates 10 and cyclohexanecarboxylates 11. Therefore, LiCl must participate in the coupling reaction. As illustrated in a working model catalytic cycle (Scheme 18), the initial oxidative addition of the vinyl bromide or vinyl iodide to the Pd(0) catalyst, in the presence of LiCl, provides the palladium(II) complex 284. Intramolecular transmetalation of 284, followed by reductive elimination of Pd(0) from 285 yields the coupled product.

Stille and Scott had proposed an oxidative addition intermediate analogous to 284 for the intermolecular coupling reaction of 53 and 54 in the presence of LiCl (Equation 9). However, when LiBr or LiI was used instead of LiCl, they observed a faster rate of decomposition for the initial oxidative addition intermediate. Thus, in our cases, the initial oxidative addition intermediates would be either 286 or 287 when the reactions were done in the absence of LiCl. However, these intermediates are, apparently, more unstable than 284. As the ring size of the palladium metallocycle intermediate 285 increases, the rate of the transmetalation process to produce 285 decreases. Thus, in the absence of LiCl, the rate of the transmetalation step is presumably slower than the rate of the decomposition of 286 or 287 and hence, the coupled product would not be produced efficiently. However, in the presence of LiCl, the rate of the transmetalation step is faster than the rate of decomposition of 284. Therefore, the cyclopentanecarboxylates 10 and cyclohexanecarboxylates 11 were produced readily. However, in the case where \( n = 3 \), the rate of decomposition of 284 is, apparently, faster than the rate of the transmetalation step to produce the eight-membered palladium metallocycle 285 (\( n = 3 \)). Therefore, even when the reaction
Scheme 18

\[ \text{R}^\prime \quad \text{R} \quad \text{L} \quad \text{Pd} \quad \text{L} \quad \text{L} \quad \text{L} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3 \quad \text{PdL}_4 \quad \text{ClSnMe}_3 \quad 2L + \text{LiX} \quad 2L + \text{LiCl} \]

\[ n = 1, 2, 3 \]

285

\[ \text{L}_2\text{ClPd} \quad \text{CO}_2\text{Et} \quad \text{SnMe}_3 \quad 284 \]

286

\[ n = 1, 2, 3 \]

287
was done in the presence of LiCl, none of the seven-membered ring product was formed.

\[
\begin{align*}
\text{O Tf} & + n\text{-Bu}_3\text{Sn} & \text{Pd(PPh}_3\text{)}_4 (2 \text{ mol%),} \\
\text{53} & & \text{THF (reflux),} \\
\text{54} & & \text{LiCl, 91\%} \\
& & \text{55}
\end{align*}
\]

In summary, the cyclobutancarboxylates 9 were readily prepared from the corresponding diene esters via the palladium(0)-catalyzed coupling reaction. It was found that only the diene unit of the cyclobutanecarboxamide 272 (derivative of 264) had a severe deviation from planarity. The cyclopentancarboxylates 10 and cyclohexancarboxylates 11 were also synthesized via the palladium(0)-catalyzed reaction. However, these reactions had to be done in the presence of LiCl. Finally, as the ring size of the product increases, these palladium(0)-catalyzed coupling reactions become less effective and in the case of 237, the reaction failed completely.
4. Diels-Alder Reactions of the Cyclobutanecarboxylates 9 and Related Compounds

With the availability of the various cyclobutanecarboxylates 9 containing a cisoid diene unit, the Diels-Alder reactions of these compounds with a variety of dienophiles were investigated.

4.1. Diels-Alder Reactions with Symmetrical Dienophiles: Tetracyanoethylene (TCNE) and Dimethyl Acetylenedicarboxylate (DMAD)

The carbon-carbon double bond of tetracyanoethylene (TCNE) is highly electron-deficient because of the presence of the four cyano groups. Thus, this substance is highly reactive and has been used extensively as a dienophile in cycloaddition reactions. As it is symmetrical, it can be used to show the face-selectivity* of the Diels-Alder reactions of the cyclobutanecarboxylates 9.

The parent diene 253 was treated with TCNE (1 equiv) in THF at room temperature. After 30 min, GLC analysis of the reaction mixture showed that no more starting material was present. Removal of the solvent and chromatography of the crude reaction product afforded an 87% yield of the ester 289 (Entry 1, Table 17). Recrystallization of this compound from petroleum ether-diethyl ether provided a white solid (melting point 128-129°C). The spectral data for 289 was in accord

* In this thesis, the β-face refers to the side of the molecule on which the ester moiety is situated, while the α-face refers to the side opposite to the ester moiety.
with the assigned structure. The $^1$H NMR spectrum of 289 exhibited the signals for three methylene groups (Hc and Hb, two 1-proton broad doublets at $\delta$ 2.86 and $\delta$ 3.05, respectively, $J$ = 14 Hz in each case, and Hd, a 4-proton multiplet at $\delta$ 3.09-3.36) and a methine proton (Ha, a 1-proton multiplet at $\delta$ 3.76-3.83). In addition, the IR spectrum of 289 showed a weak absorption band at 2256 cm$^{-1}$ for the C=\text{N} stretching vibration. Furthermore, compound 289 was shown to have a molecular formula of C$_{13}$H$_{12}$N$_4$O$_2$ by high resolution mass spectrometry.

Diels-Alder reactions with TCNE were also performed on the other cyclobutanecarboxylates 9 and the results are summarized in Table 17. The procedures employed were similar to that outlined above for the preparation of 289. The yields were greater than 80% in each case except for the experiment summarized in entry 7, where no Diels-Alder adduct was obtained. The only variable in the various reactions was the length of time required for the complete conversion of 9 into 288. Not unexpectedly, the required reaction times were related to the number and geometry of the substituents on the diene unit. The reaction with TCNE of cyclobutanecarboxylates with no substituent or a trans-substituent on the diene unit were complete within 1 h (Entries 1, 2 and 4, Table 17). However, the cyclobutanecarboxylates 255 and 259, each with a cis-substituent on the diene unit, reacted much more slowly with TCNE (Entries 3 and 5, Table 17). The longer reaction times for these substrates may be rationalized on the basis of steric hindrance by the cis-substituent toward the approaching dienophile. In the case of the cyclobutanecarboxylate 264, the presence of the two cis-methyl groups on the diene unit causes the diene to be severely distorted from planarity (see previous discussion on X-ray analysis of 272). Furthermore, the methyl groups will hinder the approach of the dienophile. Therefore, no reaction of the cyclobutanecarboxylate 264 with TCNE was observed even when the reaction was attempted in refluxing THF (Entry 7, Table 17).
Table 17

Diels-Alder Reactions of the Cyclobutanecarboxylates 9 with Tetracyanoethylenes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 9</th>
<th>Reaction time</th>
<th>Product 288</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="#" alt="Substrate 253" /></td>
<td>30 min</td>
<td><img src="#" alt="Product 289" /></td>
<td>87</td>
</tr>
<tr>
<td>2</td>
<td><img src="#" alt="Substrate 254" /></td>
<td>30 min</td>
<td><img src="#" alt="Product 290" /></td>
<td>83</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="#" alt="Product 291" /></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ratio of 290:291 = 19:1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="#" alt="Substrate 255" /></td>
<td>1.5 days</td>
<td><img src="#" alt="Product 292" /></td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td><img src="#" alt="Substrate 258" /></td>
<td>1 h</td>
<td><img src="#" alt="Product 292" /></td>
<td>88</td>
</tr>
<tr>
<td>Entry</td>
<td>Substrate</td>
<td>Reaction time</td>
<td>Product</td>
<td>Yield (%)</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>---------------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>5</td>
<td>MOMO</td>
<td>1 day</td>
<td><img src="image" alt="Product Image" /></td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>259</td>
<td></td>
<td><img src="image" alt="Product Image" /></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Substrate Image" /></td>
<td>3 h</td>
<td><img src="image" alt="Product Image" /></td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>263</td>
<td></td>
<td><img src="image" alt="Product Image" /></td>
<td></td>
</tr>
</tbody>
</table>

The ratio of 294:295 = 24:1

7III

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Reaction time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>264</td>
<td>3 days</td>
<td>no reaction</td>
</tr>
</tbody>
</table>

I  TCNE (1equiv), THF, room temperature

II Yield of purified product that have been pumped on the vacuum pump for a couple of hours.

III The substrate was also subjected to reflux for 3 h and no reaction was observed.
The cyclobutanecarboxylates 9 can react with TCNE in two ways. That is, the dienophile can approach the diene function from either the α-face or the β-face. The cyclobutanecarboxylate 254 reacted with TCNE to provide a mixture of 290 and 291 in a ratio of 19:1, respectively (Entry 2, Table 17). The ratio was obtained by comparing the integration of the methyl group signals of 290 and 291 (δ 1.57 and δ 1.53, respectively) in the 1H NMR spectrum of the mixture. It is no surprise that the major product from this Diels-Alder reaction is the adduct resulting from approach of the dienophile to the α-face of the diene, because there is relatively little or no steric hindrance on that face (Figure 11). In contrast, the β-face of the cyclobutanecarboxylate 254 is relatively hindered because of the presence of the ester group. The spectral data for 290 and 291 were consistent with the assigned structures (Figures 12 and 13). The stereochemistries of these substances could be assigned on the basis of a series of 1H NMR NOE difference experiments performed on 290. Thus, irradiation at δ 1.57 (methyl group) caused enhancement of the signals at δ 3.31-3.41 (H_e) and at δ 3.76-3.82 (H_a), while irradiation at δ 3.36 (H_e) only caused enhancement of the signal at δ 1.57 (methyl group). In addition, irradiation at δ 3.79 (H_a) enhanced the signal for the methyl group (δ 1.57) and the signal for H_b (δ 2.96-3.01). A similar high α-face selectivity for the Diels-Alders reaction with TCNE was also observed for the other cyclobutanecarboxylates 9 (Table 17). In each case, the spectral data of the products were consistent with the assigned structures.
Figure 11: Diagrammatic view of the two possible directions in which TCNE approaches the diene 254.

Figure 12: The 400 MHz $^1$H NMR Spectrum of the Ester 290
The parent cyclobutanecarboxylate 253 was also subjected to a Diels-Alder reaction with dimethyl acetylenedicarboxylate (DMAD). In the event, the cyclobutanecarboxylate 253 was refluxed for 20 h with 2 equivalents of DMAD in diethyl ether to afford, after chromatography of the crude reaction product, an 85% yield of the triester 299 (Entry 1, Table 18). The spectral data for 299 was consistent with the assigned structure. The $^1$H NMR spectrum of 299 showed the signals for three methylene groups (a 6-proton multiplet at $\delta$ 2.73-3.12), a methine proton ($H_a$, a 1-proton multiplet at $\delta$ 3.66-3.70) and two methyl ester moieties (a 6-proton singlet at $\delta$ 3.77). The IR spectrum of 299 exhibited a strong absorption band for the C=O stretching vibration of the ester moieties at 1728 cm$^{-1}$. High
resolution mass spectrometry showed that compound 299 had a molecular formula of C_{15}H_{18}O_{6}.

The triester 299 was readily aromatized via a procedure utilizing 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). A mixture of the triester 299 and DDQ (1 equiv) in benzene was refluxed for 1 h to provide, after chromatography of the crude reaction product, a 93% yield of the triester 300 (Entry 1, Table 18). The spectral data for 300 was in accord with the assigned structure. The $^1$H NMR spectrum of 300 exhibited signals similar to that of 299. However, the presence of two aromatic protons (two 1-proton singlets at $\delta$ 7.44 and $\delta$ 7.55) was observed. The high resolution mass spectrometric measurement was performed on the z/e M$^+$ peak and showed that 300 had a molecular formula of C_{15}H_{16}O_{6}.

In a similar manner, the cyclobutanecarboxylate 254 was subjected to the Diels-Alder reaction with DMAD (Entry 2, Table 18). The $^1$H NMR spectrum of the crude reaction product showed a mixture of two products 301 and 302 in the ratio of 4 : 1, respectively. These substances were epimers and were not separable by chromatography. The major product 301 presumably arose from approach of DMAD from the $\alpha$-face of the cyclobutanecarboxylate 254. Subsequent aromatization of the mixture of the two products 301 and 302, via a procedure identical with that outlined for 299, afforded a single aromatic compound 303. The assigned structure of 303 was consistent with its $^1$H NMR spectral data (Figure 14).
Table 18
Diels-Alder Reaction of the Cyclobutancarboxylates 296 with Dimethyl Acetylene-
dicarboxylate and Aromatization of the Diels-Alder Adducts

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 296</th>
<th>Procedure</th>
<th>Diels-Alder Adducts 297</th>
<th>Product 298</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1III</td>
<td>253 CO₂Et</td>
<td>A</td>
<td>299 MeO₂C₆H₄CO₂Et</td>
<td>300 MeO₂C₆H₄CO₂Et</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>299 MeO₂C₆H₄CO₂Et</td>
<td>300 MeO₂C₆H₄CO₂Et</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>254 CO₂Et</td>
<td>A</td>
<td>301, 302</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>301 and 302</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>ratio of 301:302</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td></td>
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<tr>
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<td>= 4:1</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>255 CO₂Et</td>
<td>B</td>
<td>301, 302 and 303</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td>50</td>
</tr>
<tr>
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<td></td>
<td>ratio = 3:5:2,</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>respectively</td>
<td>303 MeO₂C₆H₄CO₂Et</td>
<td></td>
</tr>
<tr>
<td>Entry</td>
<td>Substrate</td>
<td>Procedure&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Diels-Alder Adducts</td>
<td>Product</td>
<td>Yield&lt;sup&gt;II&lt;/sup&gt; (%)</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>-----------------------</td>
<td>---------------------</td>
<td>---------</td>
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<td></td>
<td>296</td>
<td></td>
<td>297</td>
<td>298</td>
<td></td>
</tr>
</tbody>
</table>

![Chemical Structures](image)

- Ratio of 304:305 = 4:1

<sup>1</sup> Procedure A
- a) DMAD (2 equiv), Et<sub>2</sub>O, reflux, 20 h.
- b) DDQ (1 equiv), benzene, reflux, 1 h.

Procedure B
- a) DMAD (2 equiv), benzene, reflux, 19 h.
- b) DDQ (1 equiv), benzene, reflux, 1 h.

Procedure C
- a) DMAD (2 equiv), Et<sub>2</sub>O, reflux, 19 h.
- b) DDQ (1 equiv), benzene, reflux, 1 h.

<sup>II</sup> Overall yield of purified product that had been kept under vacuum (vacuum pump) for a couple of hours.

<sup>III</sup> Yields of the formation of 299 and 300 are 85% and 93%, respectively.
expected, an aromatic proton signal (a 1-proton singlet at δ 7.56) was observed. A similar result was obtained for the cyclobutanecarboxylate 258 (Entry 4, Table 18).

The cyclobutanecarboxylate 255 did not undergo the Diels-Alder reaction with DMAD in refluxing diethyl ether. This observation was consistent with the fact that cyclobutanecarboxylates with a cisoid,cis-diene function are less reactive than those with a cisoid,trans-diene, as seen earlier in the reactions with TCNE. Thus, in order for the reaction to proceed, a higher temperature was used. A mixture of the cyclobutanecarboxylate 255 and DMAD (2 equiv) was refluxed in benzene (19 h) to afford a mixture of 301, 302 and 303 in the ratio of 3:5:2, respectively (Entry 3, Table 18). Thus, performing the reaction at a higher temperature also led to partial aromatization of the Diels-Alder adducts. The mixture of products was subsequently aromatized under the normal conditions to afford the triester 303 in an overall yield of 50% (from the cyclobutanecarboxylate 255).
4.2. Diels-Alder Reactions with Unsymmetrical Dienophiles: Methyl Propynoate, Methyl Vinyl Ketone (MVK) and Nitroethylene

The Diels-Alder reactions of the cyclobutanecarboxylates 9 with unsymmetrical dienophiles were of interest to us since they would provide information about the regio- and endo/exo-selectivity in these reactions. However, since it was anticipated that a mixture of products would be obtained in these reactions, a simple case was first investigated.

A solution of the cyclobutanecarboxylate 254 and methyl propynoate (1.5 equiv) in benzene was refluxed for 12 h and then was concentrated. A solution of the product and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.2 equiv) in benzene was refluxed for 1 h to afford, after chromatography, an 81% yield of a mixture of the diesters 307 and 308 (Equation 61). Although the mixture of 307 and 308 was not separable by either column chromatography or preparative thin layer chromatography, the structures of 307 and 308 could be determined on the basis of the signals for the aromatic protons in the $^1$H NMR spectrum. In the $^1$H NMR spectrum of the mixture, the diester 307 exhibited two doublets at $\delta$ 7.01 and
$\delta$ 8.00 ($J = 8$ Hz in each case) for the two aromatic proton signals. In contrast, the diester 308 exhibited two singlets at $\delta$ 7.60 and $\delta$ 7.78 for the signals due to the two aromatic protons. The ratio of 307 and 308 as observed in the $^1$H NMR spectrum was 5:1, respectively (the ratios of the integrals of the signals for the aromatic protons at $\delta$ 7.01 and $\delta$ 7.60, and the methyl groups at $\delta$ 1.49 and $\delta$ 1.31 were 5:1). Thus, the regioselectivity of this Diels-Alder reaction favored the "ortho" adduct. This result is in agreement with the regiochemical outcome predicted using either frontier molecular orbital theory$^{56}$ or a biradical argument.$^{57}$ However, only the biradical argument is presented below.

The reaction of methyl propynoate with cyclobutanecarboxylate 254 can be considered to produce two biradical intermediates 309 and 310 (Scheme 19). The regioselectivity of the reaction is determined by the relative stability of these intermediates. Since the intermediate allylic radical in 309 is stabilized by more alkyl substituents than that in 310 (3 alkyl groups vs 2 alkyl groups), 309 is preferred over 310. Thus, the regioisomer 311 would be favored. This expectation was confirmed by the experimental result.

Diels-Alder reactions were also performed with the cyclobutanecarboxylate 254 and methyl vinyl ketone (MVK). Thus, refluxing a mixture of 254 and MVK (5 equiv) in benzene for 8 h yielded a mixture of four compounds as indicated by $^1$H NMR analysis of the crude product (Equation 62). The ratio of these four compounds, 17:4:4:3, was obtained by integration of the signals for the secondary methyl groups (doublets at $\delta$ 0.80, $\delta$ 0.89, $\delta$ 0.93 and $\delta$ 0.97, respectively, $J = 7$ Hz in each case). The mixture was an oil and the components were not separable by either column chromatography or preparative thin layer chromatography. Therefore, the four compounds could not be characterized but from later experiments, two of these compounds were identified. Thus, the major compound with the doublet at $\delta$ 0.80 was subsequently assigned the structure 314
two other adducts

It is well known that addition of a Lewis acid to the Diels-Alder reaction of an electron-poor dienophile and an electron-rich diene increases the rate as well as the regio- and stereoselectivity of the reaction. Thus, as the thermal Diels-Alder reaction of 254 and MVK was not very selective, the reaction was
performed in the presence of the Lewis acid, boron trifluoride etherate complex (BF$_3$·Et$_2$O). Addition of BF$_3$·Et$_2$O (1 equiv) to a mixture of the cyclobutane-carboxylate 254 and MVK (5 equiv) in dichloromethane (-78°C, 1 h) provided, after chromatography of the crude reaction product, a 99% yield of a single compound 314 (from $^1$H NMR analysis) (Entry 1, Table 19). Not unexpectedly, the reaction occurred via an *endo* transition state, with the dienophile approaching the $\alpha$-face of the diene. The spectral data for 314 was in accord with the assigned structure (Figure 15). As expected, the $^1$H NMR spectrum of 314 exhibited the signals for a secondary methyl group (a 3-proton doublet at $\delta$ 0.80, $J$ = 7 Hz), an ethyl ester moiety (a 3-proton triplet at $\delta$ 1.26, $J$ = 7 Hz and 2-proton quartet at $\delta$ 4.15, $J$ = 7 Hz) and a methyl ketone moiety (a 3-proton singlet at $\delta$ 2.13). The other assigned proton signals were the following: H$_a$, a 1-proton multiplet at $\delta$ 3.57-3.64; H$_b$, a 2-proton multiplet at $\delta$ 2.59-2.70; H$_c$, a 1-proton doublet of doublets of doublets at $\delta$ 2.81, $J$ = 12, 5, 2.5 Hz; and H$_d$, a 1-proton multiplet at $\delta$ 2.70-2.77. There were also signals for the two methylene groups in the six-membered ring (a 1-proton multiplet at $\delta$ 1.61-1.72, a 1-proton doublet of quartets at $\delta$ 1.78, $J$ = 14, 2.5 Hz, and a 2-proton multiplet at $\delta$ 1.93-2.00). The assignments of the protons H$_a$-H$_d$ were based on $^1$H NMR decoupling and NOE difference experiments. In the decoupling experiments, irradiation at $\delta$ 0.80 (methyl group) sharpened the multiplet at $\delta$ 2.70-2.77 (H$_d$), while irradiation at $\delta$ 3.60 (H$_a$) simplified the multiplet at $\delta$ 2.59-2.70 (H$_b$) to two broad doublets ($J$ = 13 Hz). In the $^1$H NMR NOE difference experiments, irradiation at $\delta$ 0.80 (methyl group) caused enhancement of the signals at $\delta$ 1.61-1.72, $\delta$ 2.70-2.77 (H$_d$) and $\delta$ 3.57-3.64 (H$_a$), whereas irradiation at $\delta$ 3.60 (H$_a$) caused enhancement of the signals at $\delta$ 0.80 (methyl group) and $\delta$ 2.59-2.70 (H$_b$). The IR spectrum of 314 showed strong absorption bands at 1709 and 1730 cm$^{-1}$ which are due to the
Table 19

Boron Trifluoride Catalyzed Diels-Alder Reactions of the Cyclobutanecarboxylates 296 with Methyl Vinyl Ketone

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 296</th>
<th>Product 313</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>296</td>
<td>313</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>254</td>
<td>314</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>255</td>
<td>315</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>258</td>
<td>316</td>
<td>93</td>
</tr>
</tbody>
</table>

I MVK (5 equiv), BF₃·Et₂O (1 equiv), CH₂Cl₂, -78°C, 1 h.

II Yield of purified product that had been kept under vacuum (vacuum pump) for a couple of hours.

III MVK (5 equiv), BF₃·Et₂O (1 equiv), CH₂Cl₂, -78°C, 3 h.
Figure 15: The 400 MHz $^1$H NMR Spectrum of the Keto Ester 314

C=O stretching vibrations of the methyl ketone and the ethyl ester moieties, respectively. Compound 314 was shown to have a molecular formula of C$_{14}$H$_{20}$O$_{3}$ by high resolution mass spectrometry.

In a similar fashion, the cyclobutanecarboxylates 255 and 258 were subjected to Lewis acid catalyzed Diels-Alder reactions with MVK to provide a single adduct in each case ($^1$H NMR analysis) (Entries 2 and 3, Table 19). However, the reaction of the cyclobutanecarboxylate 255 with MVK required a longer reaction time (Entry 2, Table 19). This observation was consistent with the fact that cisoid,cis-dienes are less reactive than cisoid,trans-dienes. It must be noted that no Diels-Alder adduct was obtained upon refluxing the cyclobutanecarboxylate 255 with MVK in either benzene or toluene. The stereochemistry of each of the
Figure 16: The effect of Lewis acid on the energies of the HOMO and LUMO of the dienophile in the Diels-Alder reaction

Diels-Alder adducts 315 and 316 was assigned on the basis of a series of $^1$H NMR NOE difference experiments. Details can be found in the Experimental section.

The effect of BF$_3$·Et$_2$O on the Diels-Alder reaction of the various cyclobutancarboxylates with MVK is interesting, and can be readily rationalized using frontier molecular orbital theory.$^{56,71-73}$ In the transition state of the normal# Diels-Alder reaction, the principle interaction is that between the HOMO of the diene and the LUMO of the dienophile (Figure 16). The energy difference between these orbitals governs the feasibility of the Diels-Alder reaction. The presence of a Lewis acid, which, in the reactions under discussion, presumably coordinates with

# This refers to the Diels-Alder reaction of an electron-rich diene with an electron-poor dienophile.
the carbonyl group of MVK, lowers the energy of both frontier orbitals of the dienophile. Thus, the energy difference between the HOMO of the diene in 296 and the LUMO of the dienophile, MVK, becomes smaller. As a result the reaction occurs more readily. As observed in the experiments, the cyclobutane carboxylate 254 reacted with MVK at -78°C in 1 h in the presence of BF₃·Et₂O but in the absence of the catalyst, the reaction took 8 h in refluxing benzene.

The Lewis acid also alters the distribution of the atomic orbital coefficients of the dienophile, MVK. The effect of Lewis acid coordination is that the LUMO of MVK has greater polarization, with the β-carbon and the α-carbon having orbitals with larger and smaller coefficients as compared to those of the uncoordinated MVK (Figure 17). Thus, the increased polarization of the LUMO of the double bond in MVK increases the regioselectivity of the reaction.

![Figure 17: Frontier orbitals showing the increased polarization of the LUMO of the double bond in the dienophile in the Lewis acid catalyzed Diels-Alder reaction.](image)

Figure 17: Frontier orbitals showing the increased polarization of the LUMO of the double bond in the dienophile in the Lewis acid catalyzed Diels-Alder reaction.
Finally, the LUMO coefficient on the carbonyl carbon of MVK is also increased in the presence of the Lewis acid. As a result, the secondary orbital interaction is greatly increased and this accounts for the greater *endo* selectivity (Figure 18). Again, the experimental results of the Diels-Alder reactions of the cyclobutanecarboxylate 254 with MVK illustrate the effectiveness of the Lewis acid catalysis, with a single regio- and stereoisomer being formed in the presence of BF$_3$·Et$_2$O, and four isomeric products formed in its absence.

![Frontier orbitals showing the increased secondary orbital interaction in the Lewis acid catalyzed Diels-Alder reaction.](image)

Figure 18: Frontier orbitals showing the increased secondary orbital interaction in the Lewis acid catalyzed Diels-Alder reaction.

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \text{254} \\
\text{LiAlH}_4, \quad \text{Et}_2\text{O}, 92\% & \quad \text{317} \quad \text{OH}
\end{align*}
\]
The ether 318 was also expected to undergo the Lewis acid catalyzed Diels-Alder reaction with MVK in a regio- and stereoselective manner. The ether 318 was readily obtained from the cyclobutanecarboxylate 254 via a two-step procedure. Treatment of the cyclobutanecarboxylate 254 in diethyl ether with lithium aluminum hydride (0.6 equiv) (0°C, 5 min; room temperature, 5 min) afforded, after workup and distillation of the crude reaction product, a 92% yield of the alcohol 317 (Equation 63). The IR spectrum of 317 showed a strong broad absorption band at 3327 cm⁻¹ indicating the presence of the OH moiety. The ¹H NMR spectrum of 317 showed signals similar to those found in the ¹H NMR spectrum of the cyclobutanecarboxylate 254. However, the signals for the ethyl ester moiety were replaced by resonances due to the CH₂OH group (a 1-proton broad singlet at δ 1.43, exchanged with D₂O, and a pair of doublets of doublets at δ 3.76 and δ 3.85, J = 13, 8 Hz and J = 13, 6 Hz, respectively). Furthermore, the high resolution mass spectrometry indicated that compound 317 had a molecular formula of C₈H₁₂O.

\[
\begin{align*}
317 \text{OH} & \quad \text{t-BuPh}_2\text{SiCl,} \\
& \quad \text{Imidazole, DMF,} \\
& \quad \text{90\%} \\
\rightarrow & \quad \text{318 \ OSi} \text{-BuPh}_2
\end{align*}
\]

(64)

The alcohol 317 was converted into the tert-butylidiphenylsilyl ether 318 under normal conditions(47) (90% yield) (Equation 64). The ¹H NMR spectrum of 318 showed the presence of the tert-butylidiphenylsilyloxy moiety (a 9-proton singlet at δ 1.05, a 6-proton multiplet at δ 7.36-7.47 and a 4-proton multiplet at δ 7.68-7.74).
The ether 318 was subjected to the BF₃·Et₂O catalyzed Diels-Alder reaction with MVK via a procedure identical with that outlined for the cyclobutanecarboxylate 254 (Entry 4, Table 19). As expected, only one Diels-Alder adduct 319 was obtained. The spectral data for the keto ether 319 were in accord with the assigned structure. The assignment of the stereochemistry of 319 was based on ¹H NMR NOE difference experiments. Thus, irradiation at the signal for the methyl group (δ 0.82) caused enhancement of the signals for Hₑ (δ 2.70-2.84) and Hₐ (δ 3.00-3.10), while irradiation at the signal for Hₐ (δ 3.05) caused enhancement of the signals for the methyl group (δ 0.82), Hₐ (δ 2.43) and the methylene group next to the ether moiety (δ 3.72 and δ 3.81).

The cyclobutanecarboxylate 254 was subjected to a Diels-Alder reaction with another unsymmetrical dienophile, nitroethylene. The resultant product would have a secondary nitro group which is of great synthetic potential.⁷⁴ For example, a secondary nitro group can be readily converted into a ketone function.⁷⁵ Thus, addition of an excess of freshly prepared nitroethylene⁷⁶ to a solution of 254 in
dichloromethane (0°C, 3 h) afforded a 79% yield of a mixture of three Diels-Alder adducts in a ratio of 84:9:7 (Equation 65). This ratio was obtained from integration of the signals for the secondary methyl groups (the ratio of the integrals of the doublets at δ 0.96, δ 1.04, δ 1.09 was 84:9:7, respectively). Although preparative thin layer chromatography and column chromatography proved to be fruitless in separating this mixture, recrystallization of the mixture from petroleum ether-diethyl ether yielded the major adduct 320 as a colorless plate-like solid (melting point 68-69°C). The spectral data for 320 was consistent with the assigned structure. Explicitly, the 1H NMR spectrum of 320 showed the signals for a methyl group (a 3-proton doublet at δ 0.96, J = 7 Hz), and two methylene groups in the six-membered ring (a 4-proton multiplet at δ 2.08-2.29). The signals for the protons H_a-H_e were assigned as follows: H_a, a 1-proton multiplet at δ 3.62-3.69; H_b, a 1-proton doublet of doublets at δ 2.75, J = 14, 4.5 Hz; H_c, a 1-proton broad doublet at δ 2.68, J = 14 Hz; H_d, a 1-proton quartet at δ 4.77, J = 6 Hz; and H_e, a 1-proton multiplet at δ 3.00-3.10. The IR spectrum of 320 showed strong absorption bands at 1548 and 1372 cm⁻¹ which indicated the presence of the nitro group. A high resolution mass spectrometric measurement showed that 320 has a molecular formula of C₁₂H₁₇O₄N. The two minor adducts from the Diels-Alder reaction were not characterized.
An interesting result was obtained from the Diels-Alder reaction of the ether 318 with nitroethylene. The procedure used was the same as that employed for the cyclobutanecarboxylate 254 but, in this case, only a single Diels-Alder adduct was obtained in an 81% yield (Equation 66). This adduct was assigned the structure 321 on the basis of its spectral data.

In summary, the dienophiles generally approach the diene unit of the cyclobutanecarboxylates 9 on the side opposite to the ethyl ester moiety (attack on the α-face). Tetracyanoethylene shows more face-selectivity than dimethyl acetylenedicarboxylate because it is a more bulky dienophile. In the Diels-Alder reactions of the cyclobutanecarboxylates 9 with unsymmetrical dienophiles, the "ortho", endo products are favored. When methyl vinyl ketone is utilized as the dienophile, boron trifluoride catalyzed reactions provided the "ortho", endo products highly regio- and stereoselectively.
5. Thermolysis of Functionalized Bicyclic Cyclobutenes and Related Reactions

5.1. Preparation of Keto Aldehydes 324 and 327

\[ \text{314} \xrightarrow{\text{DIBAL, } \text{Et}_2\text{O}, \ -78^\circ\text{C}, \ 1 \text{ h}; \ 0^\circ\text{C}, \ 1 \text{ h}} \text{322 and 323} \quad (67) \]

The keto aldehyde 324 was easily obtained from the keto ester 314 via a reduction-oxidation sequence. Thus, treatment of a solution of the keto ester 314 in diethyl ether with a solution of diisobutylaluminum hydride (3.6 equiv) in toluene (-78°C, 1 h; 0°C, 1 h) afforded, after acidic workup and chromatography of the crude product, an 88% yield of an epimeric mixture of diols 322 (major isomer) and 323 (minor isomer) in the ratio of 4:1, respectively (Equation 67). The ratio was obtained from a \(^1\)H NMR analysis (the ratio of the integration for the methyl groups at \(\delta 0.96\) and \(\delta 0.86\) was 4:1). Recrystallization of this mixture from petroleum ether-diethyl ether yielded the major diol 322 as a white solid (melting point 113-114°C). The spectral data of the diol 322 was in accord with the assigned structure. The minor diol 323 was not obtained pure and, therefore, was not characterized.

\[ \text{322 and 323} \xrightarrow{\text{a) (COCl)}_2, \ DMSO, \ CH_2Cl_2, \ -78^\circ\text{C}, \ 5 \text{ min; r.t., \ 30 min}} \text{324} \quad (68) \]

\[ \text{a) (COCl)}_2, \ DMSO, \ CH_2Cl_2, \ -78^\circ\text{C}, \ 5 \text{ min; r.t., \ 30 min}, \ 85\% \]
The mixture of diols 322 and 323 was subjected to a Swern oxidation\textsuperscript{77} to provide the keto aldehyde 324. A dichloromethane solution of dimethyl sulfoxide (2.5 equiv) was treated with oxalyl chloride (2.2 equiv) (-78°C, 15 min). Then, addition of a dichloromethane solution of a mixture of diols 322 and 323 (-78°C, 15 min) to the reaction mixture, followed by addition of triethylamine (-78°C, 5 min; room temperature, 30 min) afforded, after chromatography of the crude reaction product, an 85\% yield of the keto aldehyde 324 (Equation 68). The spectral data for 324 was consistent with the assigned structure. The IR spectrum of 324 exhibited a strong absorption band at 1708 cm\textsuperscript{-1} for the C=O stretching vibration of the methyl ketone and the aldehyde moieties. In addition, an aldehydic C-H stretching vibration (a weak absorption band at 2707 cm\textsuperscript{-1}) was observed. The \textsuperscript{1}H NMR spectrum of 324 was similar to that of the keto ester 314, except for the presence of a signal for the aldehydic proton (a 1-proton doublet at \(\delta 9.59, J = 4\) Hz) instead of that due to an ethyl ester moiety. The keto aldehyde 324 was shown to have a molecular formula of C\textsubscript{12}H\textsubscript{16}O\textsubscript{2} by high resolution mass spectrometry.

\[
\begin{align*}
1) & \text{DIBAL, } \text{Et}_2\text{O, } -78^\circ\text{C, 1 h,} \\
2a) & (\text{COCl})_2, \text{DMSO, } \text{CH}_2\text{Cl}_2, -78^\circ\text{C,} \\
\text{b) } & \text{Et}_3\text{N, } -78^\circ\text{C,} \\
& 5 \text{ min; r.t., 30 min.}
\end{align*}
\]

In a similar fashion, the keto aldehyde 327 was obtained cleanly and efficiently (70\%) from the keto ester 315 via a reduction and Swern oxidation\textsuperscript{77}
reaction sequence (Equation 69). As expected, the keto aldehyde 327, which is epimeric with 324, exhibited a signal for the aldehydic proton at δ 9.48 (a doublet, J = 6 Hz) in the ¹H NMR spectrum. Furthermore, the IR spectrum of 327 showed the presence of two C=O stretching vibrations (absorption bands at 1719 and 1710 cm⁻¹) and an aldehydic C-H stretching vibration (a weak absorption band at 2708 cm⁻¹).

5.2. Thermolysis Reactions

Theoretical¹⁰ and experimental¹⁰ᵃ,ᶜ,ᵈ,¹³ studies on the thermal conrotatory opening of 3-substituted cyclobutenes 97 (Equation 20) have indicated that the direction of the opening is affected by the nature of the substituent, W. Cyclobutenes with a strongly electron-donating group, W, prefer outward rotation to afford 98, while cyclobutenes with a strongly electron-withdrawing group, W, favor an inward rotation to give 99. Since, from the work described above, a variety of bicyclic cyclobutenes with different C-3 substituents (CH₂OR, CO₂Et, CHO) were readily available, the thermal ring opening reaction of these substances could be investigated.
It is well known that the cyclobutene 97 in which W is a methyl or a substituted methyl substituent undergo thermal ring opening with complete outward rotation of that substituent. These observations can be rationalized on the basis of steric factors.\textsuperscript{11} Thus, the bicyclic substances 319, 321 and 322, each of which contains a cyclobutene moiety with a C-3 CH\textsubscript{2}OR substituent, would be expected to undergo ring opening with outward rotation of the substituent.

A solution of the keto ether 319 in mesitylene was refluxed for 1 h. Analysis of the crude reaction mixture by TLC indicated that only one product had been formed. The \textsuperscript{1}H NMR spectrum of the crude product confirmed this observation. Chromatography of this material provided the thermolysis product 328 in an 83\% yield (Equation 70). The keto ether diene 328 was subjected to the conditions employed for its formation and was found to be stable under these conditions. The spectral data for 328 was in accord with the assigned structure. For example, the \textsuperscript{1}H NMR of 328 (Figure 19) exhibited the expected signals for three olefinic protons (H\textsubscript{a} and H\textsubscript{b}, two 1-proton broad triplets at $\delta$ 4.73 and $\delta$ 4.88, respectively, $J \sim$ 1.5 Hz in each case; and H\textsubscript{c}, a 1-proton doublet of doublets at $\delta$ 5.67, $J = 7.5, 5.5$ Hz). The geometry of the diene unit in 328 was assigned on the basis of a \textsuperscript{1}H NMR NOE difference experiment. Thus, irradiation at $\delta$ 5.67 (H\textsubscript{c}) caused enhancement of the signals at $\delta$ 4.28 (=CHCH\textsubscript{2}O-), $\delta$ 4.39 (=CHCH\textsubscript{2}O-) and $\delta$ 4.88 (H\textsubscript{b}).
Using a procedure similar to that employed for the keto ether 319, a thermolysis reaction was performed on the nitro ether 321 (Equation 71). Analysis of the product by $^1$H NMR spectroscopy showed the presence of two dienes in a ratio of 3:1. These two dienes were identified as 329 (major isomer) and 330 (minor isomer) from the spectral data. The stereochemistry of the dienes was assigned on the basis of $^1$H NMR NOE difference experiments. Thus, in the $^1$H NMR spectrum of the nitro ether diene 329, irradiation at $\delta$ 5.75 (H$_c$) caused enhancement of the signals at $\delta$ 4.26 (=CHCH$_2$O-), $\delta$ 4.37 (=CHCH$_2$O-) and $\delta$ 4.96 (H$_b$). Similarly, for the nitro ether diene 330, irradiation at $\delta$ 5.74 (H$_c$) caused enhancement of the signals at $\delta$ 4.29 (=CHCH$_2$O-), $\delta$ 4.32-4.38 (=CHCH$_2$O-) and $\delta$ 4.95 (H$_b$).
The most stable conformation of 329 is that in which the secondary methyl group is in an axial orientation. The other conformation, in which the methyl group is equatorial, is unfavorable due to the presence of a major A\(^1,3\) interaction between the methyl and CH\(_2\)OR groups. Thus, in 329, H\(_e\) must be axially oriented and, consequently, would be coupled to two vicinal equatorial protons and one vicinal axial proton. This assignment of stereochemistry is consistent with the observed \(^1\)H NMR signal for H\(_e\) (a 1-proton doublet of triplets at \(\delta 4.33, J = 11, 5\) Hz). On the other hand, the signal for H\(_e\) in 330 is obscured by the signal of one of the protons of the CH\(_2\)OR group. However, it is known that a carbon center adjacent to a secondary nitro group undergoes epimerization readily, since the proton on that carbon is relatively acidic.\(^78\) In the thermolysis of the nitro ether 321, it is possible that the heating or a small amount of impurity in the reaction mixture promoted epimerization of the center bearing the nitro group. In any case, it is highly likely that 330 is epimeric with 329 at the nitro-bearing carbon.
The major diol 322 from the reduction of the keto ester 314 was also subjected to a thermal ring opening reaction. A sample of the solid diol 322 in a sealed capillary tube was heated in a preheated oil bath (160°C, 0.5 h) to afford the diol diene 333 as a solid (melting point 72.5-74°C) in an 80% yield (Equation 72). Analysis of the product by 1H NMR spectroscopy showed that only one thermolysis product had been formed. The spectral data for 333 was in accord with the assigned structure. The 1H NMR spectrum of 333 showed the presence of three olefinic protons (H_a and H_b, two 1-proton broad triplets at δ 4.71 and δ 4.88, respectively, J ~ 2 Hz in each case; and H_c, a 1-proton doublet of doublets at δ 5.61, J = 8, 6 Hz). The stereochemistry of the diene unit was assigned by comparison with the same compound obtained via a different route (see reduction of the keto ester diene 331, vide infra).

Thus, thermolysis of the bicyclic cyclobutenes 319, 321 and 322 resulted, in each case, in the exclusive outward rotation of the CH_2OR. These results are in complete accord with previous observations.\textsuperscript{10a,11}

Very recently, calculations by Buda, Wang and Houk\textsuperscript{10e} have predicted that the CO_2Me group on the 3-substituted cyclobutene 97 should prefer outward rotation by about 1.7 kcal/mol. On this basis, the ratio of products with the CO_2Me group rotated outward and inward is calculated to be ~9:1, respectively, at 120°C. The readily available substituted 3-ethoxycarbonylcyclobutenes 314 and 315 could be used as substrates to test this prediction experimentally.
In the event, thermally induced ring opening of 314 in mesitylene (reflux, 1 h) provided cleanly an 85% yield of a mixture of the two geometrically isomeric keto ester dienes 331 and 332, in a ratio of 11:1, respectively (1H NMR analysis) (Equation 73). The two thermolysis products, which could be separated by chromatography on silica gel, were shown in separate experiments to be stable under the conditions of their formation from 314. The spectral data for 331 and 332 were in accord with the assigned structures. The 1H NMR spectrum of 331 (Figure 20) exhibited the signals for three olefinic protons (Hₐ, a 1-proton broad triplet at δ 4.91, J ~ 2 Hz; Hₖ, a 1-proton broad triplet at δ 5.03, J ~ 2 Hz; and Hₜ, a 1-proton singlet at δ 5.84). It must be noted that the signal due to Hₜ (a 1-proton multiplet) was observed at δ 4.57-4.67, which indicated that this proton must be situated in the deshielding cone of the carbonyl of the ethyl ester moiety and, therefore, also indicated that the double bond must have an (E)-geometry. This assignment of the stereochemistry of 331 was consistent with 1H NMR NOE
difference experiments. Thus, irradiation at \( \delta 0.88 \) (methyl group) caused enhancement of the signals at \( \delta 1.73-1.82 \) and \( \delta 4.57-4.67 \) (H\(_d\)), while irradiation at \( \delta 5.84 \) (H\(_c\)) caused enhancement of the signal at \( \delta 5.03 \) (H\(_b\)). A high resolution mass spectrometric measurement performed on 331 showed that it had a molecular formula of C\(_{14}H_{20}O_3\).

The spectral data for the keto ester diene 332 was consistent with the assigned structure but was slightly different from those of 331. In the \(^1\)H NMR spectrum of 332 (Figure 21), the H\(_d\) signal (a 1-proton multiplet) appeared at \( \delta 2.90-2.98 \), which suggested that 332 had a double bond with an (Z)-geometry. \(^1\)H NMR NOE difference experiments on 332 confirmed this assigned stereochemistry. Irradiation at \( \delta 2.94 \) (H\(_d\)) caused enhancement of the signals at \( \delta 0.90 \)

![Diagram of molecular structure](image)

Figure 20: The 400 MHz \(^1\)H NMR Spectrum of the Keto Ester Diene 331
Figure 21: The 400 MHz $^1$H NMR Spectrum of the Keto Ester Diene 332

(methyl group), $\delta$ 2.78 (H$_e$) and $\delta$ 5.72 (H$_c$), while irradiation at $\delta$ 5.72 (H$_c$) caused enhancement of the signal at $\delta$ 2.90-2.98 (H$_d$). A high resolution mass spectrometric measurement showed that 332 had a molecular formula of C$_{14}$H$_{20}$O$_3$.

The reduction of the keto ester diene 331 was carried out to correlate the product with that previously obtained from thermolysis of 322. Thus, treatment of a diethyl ether solution of 331 with a solution of diisobutylaluminum hydride (3.4 equiv) in hexane (-78°C, 1 h; 0°C, 1 h) afforded a 90% yield of an epimeric mixture of the diol dienes 333 and 334, in a ratio of 11 : 1, respectively ($^1$H NMR analysis) (Equation 74). The spectral data for the major diol diene 333 were identical with those of the single thermolysis product obtained from 322.
The keto ester 315 was subjected to a thermolysis reaction via a procedure identical with that outlined for 314. Refluxing (1 h) a solution of 315 in mesitylene produced an 82% yield of a 1:1 mixture of 335 and 336 ($^1$H NMR analysis) (Equation 75). The mixture was separated by column chromatography on silica gel. As usual, in separate experiments, each of the isomers was found to be stable under the conditions used for their formation. The spectral data for 335 and 336 were consistent with the assigned structures. In the $^1$H NMR spectra of 335 and 336, the signals due to $H_d$ appeared at $\delta$ 4.55 (a broad quartet, $J = 7$ Hz)
and δ 2.62-2.71 (a multiplet), respectively. ¹H NMR NOE difference experiments confirmed the stereochemical assignments of the two products. In the ¹H NMR spectrum of 335, irradiation at δ 1.17 (methyl group) caused enhancement of the signals at δ 4.55 (Hd) and δ 2.53-2.59 (He), while irradiation at δ 5.82 (Hc) caused enhancement of the signal at δ 5.03 (Hb). On the other hand, in the ¹H NMR spectrum of 336, irradiation at δ 1.04 (methyl group) caused enhancement of the signals at δ 2.48 (Hc), δ 2.62-2.71 (Hd) and δ 5.62 (Hc).

Interestingly, the thermally induced ring openings of 314 and 315 gave rather different results. In accord with the predictions of Buda, Wang, and Houk¹⁰e, the thermolysis of 314 resulted in preferential outward rotation of the CO₂Et function. However, in the thermolysis of 315, the rates of the inward and outward rotation of the ester group were equal. It must be noted that the theoretical predictions of Buda, Wang, and Houk¹⁰e were related to simple 3-substituted cyclobutenes and did not take into consideration of other effects which could arise in the more complex cyclobutenes such as 314 and 315. For example, in the case of the thermolysis of 315, molecular models indicate that, in the conversion of 315 to 335, it is necessary for the CO₂Et group to slide past the (pseudoequatorial) secondary methyl group on the six-membered ring. The resultant steric strain would cause an increase in the transition state energy for the transformation of 315 into 335 relative to that for the 314 to 331 conversion. As a result, the amount of product 336 arising from inward rotation of the CO₂Et group increases. In the case of the thermally induced ring opening of 314, the above mentioned steric strain is not observed in the conversion 314 to 331. Therefore, substrate 314 undergoes the thermolysis reaction in a "normal" way, as predicted by Buda, Wang, and Houk.¹⁰e

As described in the introduction section, Houk and co-workers¹⁰c found that the CHO group in 3-formylcyclobutene 112 preferentially rotates in an inward
direction during the thermally induced ring opening process. It was, therefore, of interest to investigate whether or not the highly substituted 3-formylcyclobutenes 324 and 327 would behave in a manner similar to the parent compound.

A solution of the substituted 3-formylcyclobutene 324 in benzene was refluxed for 3 h (Equation 76). TLC analysis of the crude reaction product showed the presence of two components. However, in spite of the fact that these two components differed considerably in polarity, they could be only partially separated by column chromatography on silica gel. This inability to obtain pure samples of the products was due to the fact that these substances were interconverting slowly to each other at room temperature. However, the products could be identified as the keto aldehyde 337 and the keto ether 338 from the $^1$H NMR spectra of partially purified materials. For example, the $^1$H NMR spectrum of a sample containing mainly 337 exhibited a secondary methyl group (a 3-proton doublet at $\delta$ 0.97, $J = 7$ Hz), a methyl ketone moiety (a 3-proton singlet at $\delta$ 2.20), three olefinic
protons (H\textsubscript{a} and H\textsubscript{b}, two 1-proton broad triplets at \(\delta\) 5.02 and \(\delta\) 5.31, respectively, \(J \approx 1\) Hz in each case; and H\textsubscript{c}, a 1-proton doublet at \(\delta\) 5.99, \(J = 8\) Hz) and an aldehyde proton (a 1-proton doublet at \(\delta\) 9.83, \(J = 8\) Hz). In addition, there were two other signals that could be assigned to H\textsubscript{d} and H\textsubscript{e} (a 1-proton multiplet at \(\delta\) 3.00-3.08 and a 1-proton doublet of triplets at \(\delta\) 2.84, \(J = 12, 4\) Hz, respectively). On the other hand, the \(^1\text{H}\) NMR spectrum of 338 (obtained from a sample containing mainly 338) showed no aldehyde proton but exhibited two olefinic protons (H\textsubscript{b} and H\textsubscript{a}, two doublets at \(\delta\) 5.10 and \(\delta\) 6.40, \(J = 6\) Hz in each case) and a methylene group \(\alpha\) to an oxygen function (a 2-proton multiplet at \(\delta\) 4.39-4.48). Clearly, the keto ether 338 must be formed by (reversible) electrocyclic ring closure of the initially formed dienal 337.

The thermolysis of 324 was also performed in benzene-\(d_6\) (reflux, 3 h) (Equation 76). The \(^1\text{H}\) NMR spectrum (C\(_6\)D\(_6\)) of the crude reaction mixture showed that the ratio of 337 to 338 was 1:2, respectively (the ratio of the integrals of the olefinic protons, H\textsubscript{a} of 337 to H\textsubscript{b} of 338 was 1:2). Removal of the C\(_6\)D\(_6\) provided the mixture of 337 and 338 in 80\% yield.

\[
\begin{align*}
\text{333} &\xrightarrow{\text{a) (COCl)}_2, \text{DMSO, CH}_2\text{Cl}_2, -78^\circ\text{C,}} \text{339} \\
&\quad \text{b) Et}_3\text{N, -78^\circ\text{C, 5 min, r.t., 30 min,}} \text{78%}
\end{align*}
\]

In order to confirm the stereochemical assignment of the dienal system of 337, the stereoisomer 339 was synthesized. The diol diene 333 was oxidized via the Swern oxidation\textsuperscript{77} procedure (Equation 77). The \(^1\text{H}\) NMR spectrum of 339 was clearly different from that of 337. The most dramatic difference was related to
the chemical shift of the signal for the proton $H_d$. In the $^1$H NMR spectrum of 339, the signal due to $H_d$ (a 1-proton multiplet) was observed at $\delta$ 4.07-4.15, while the analogous proton in the $^1$H NMR spectrum of 337 was observed at $\delta$ 3.00-3.08. Presumably, $H_d$ in compound 339 appeared at such low field because this proton is situated in the deshielding cone of the aldehyde moiety. In a separate experiment, 339 was shown to be stable upon heating for 1 h in mesitylene. Thus, the preparation and characterization of 339 provided additional strong evidence that, in the thermally induced ring opening of 324, the CHO group rotated exclusively in an inward direction.

Further confirmation was obtained from the following experiment. Thermolysis of 324 in toluene (30 min), followed by cooling of the solution to -78°C and addition of a solution of diisobutylaluminum hydride (2.5 equiv) (-78°C, 30 min; 0°C, 30 min; room temperature, 2 h), provided a 78% yield of an
epimeric mixture of 340 and 341 in a ratio of 10:3 (\(^1H\) NMR analysis) (Equation 78). The \(^1H\) NMR spectrum of the mixture of 340 and 341 was clearly different from that of 333. The signals for the geminal olefinic protons of 340 and 341 were at \(\delta 4.62\) (H\(_{a}\), a broad singlet) and \(\delta 5.01\) (H\(_{b}\), a broad singlet). It must be noted that the chemical shifts for these signals in 340 are identical with those in 341. In contrast, the corresponding signals of 333 were at \(\delta 4.71\) (H\(_{a}\), a broad singlet) and \(\delta 4.88\) (H\(_{b}\), a broad singlet). The signals for H\(_c\) of compounds 340 and 341 were at \(\delta 5.50\) (a doublet of doublets, \(J = 8, 6\) Hz) and \(\delta 5.46\) (a doublet of doublets, \(J = 8, 6\) Hz), respectively, while the analogous signal for 333 was at \(\delta 5.61\) (a doublet of doublets, \(J = 8, 6\) Hz). Furthermore, in a \(^1H\) NMR NOE difference experiment on the mixture of 340 and 341, irradiation at \(\delta 5.50\) (H\(_c\)) caused enhancement of the signals at \(\delta 2.76-2.85\) (H\(_d\)), \(\delta 4.12\) (-CH\(_2O\)-) and \(\delta 4.32\) (-CH\(_2O\)-), while no enhancement of the signal for H\(_b\) was observed. Thus, it was clear that compounds 340 and 341 possessed, in each case, a (Z)-cisoid-diene system. Therefore, thermolysis of 324 produces initially the dienal 337 which reversibly interconverts with the keto ether 338. Addition of diisobutylaluminum hydride causes reduction of the dienal 337 and, eventually, the thermolysis product mixture is converted entirely into the mixture of the diene diols 340 and 341.

A reversible electrocyclic ring closure similar to that involving 337 and 338 has been reported by Mair and Wiessler.\(^79\) Thermolysis of 342 in toluene (20 h) produced a 1:2 mixture of 343a and 343b, respectively (Equation 79). The diene 343a was not isolated. However, addition of TCNE produced a Diels-Alder adduct that was derived from the ether diene 344. Therefore, Mair and Wiessler proposed\(^79\) that 343a must be readily interconverting with 344, which is a more reactive diene than 343a.
a) PhMe, reflux, 0.5 h.

b) DIBAL, -78°C, 0.5 h, 0°C, 0.5 h, r.t., 2 h, 74%.

The ratio of 345:346 was 1:2
The thermally induced ring opening was also performed on the keto aldehyde 327, which is an epimer of 324. In the event, refluxing a solution of 327 in benzene-$d_6$ (3 h), produced a mixture of the keto aldehyde 345 and the keto ether 346 in a ratio of 1:2 (1H NMR analysis) (Equation 80). The spectral data for 345 and 346 were consistent with the assigned structures. Furthermore, thermolysis of 327 in toluene, followed by reduction as outlined for 324, afforded (74%) a mixture of the diols 347 and 348 in a ratio of 3:1 (Equation 81). These results, which were essentially identical with those obtained from thermolysis of 324, showed that heating of 327 initially gave 345, via an inward rotation of the formyl group. However, subsequently, the primary product 345 interconverted with the keto ether 346 via a reversible electrocyclic ring closure reaction.

Theoretical and experimental studies on the thermolysis of 3-formylcyclobutene 112 by Houk and co-workers showed that the formyl group rotates inwardly exclusively. Our results, obtained from a study of the thermolysis of the structurally more complex 3-formylcyclobutenes 324 and 327 showed that, in these cases too, the ring opening process occurs with exclusive inward rotation of the CHO group. Thus, these substrates behave in a "normal" manner, as predicted by theoretical calculations.

5.3 Diels-Alder Reactions of the Diene 328

As described in section 5.2, above, thermolysis of a number of bicyclic cyclobutenes had provided various conjugated dienes in which both of the carbon-carbon double bonds are exocyclic to a six-membered carbocyclic ring. At least some of these dienes might be expected to undergo facile Diels-Alder reactions,
which, if successful, would lead to highly substituted bicyclo[4.4.0]dec-1(6)-enes. I have briefly investigated the Diels-Alder reactions of the diene 328 (derived from thermolysis of 319) with three dienophiles, DMAD, MVK, and acrolein. Time constraints precluded a more extensive investigation in this area.

In a "one pot" reaction procedure, thermolysis of 319 in mesitylene (1 h), followed by addition of dimethyl acetylenedicarboxylate (reflux, 1 h), afforded a mixture of the diesters 349 and 350 (ratio 5:4, respectively) in a 74% yield (Equation 82). The epimeric mixture was separated by column chromatography on silica gel. The spectral data of 349 and 350 were in accord with the assigned structures. As expected, the IR spectra of 349 and 350 exhibited strong absorption bands at 1719 and 1723 cm\(^{-1}\), respectively, for the C=O stretching vibration of the
methyl esters and methyl ketone moieties. The $^1$H NMR spectrum of 349 showed the signals for two methyl ester moieties (two 3-proton singlets at $\delta$ 3.74, and $\delta$ 3.82) which were overlapped with the resonances for the -CH$_2$O- group (two 1-proton doublets of doublets at $\delta$ 3.75 and $\delta$ 3.82, $J = 8$, 4 Hz, in each case). The signals for the protons H$_a$-H$_d$ were as follows: H$_a$, a 1-proton doublet of triplets at $\delta$ 2.57, $J = 10$, 5 Hz; H$_b$, a 1-proton multiplet at $\delta$ 2.61-2.69; H$_c$, a 1-proton multiplet at $\delta$ 3.30-3.36; and H$_d$, two 1-proton doublets of doublets at $\delta$ 2.73 and $\delta$ 3.10, $J = 16.5$, 2 Hz in each case). The assignment of these signals was based on $^1$H NMR decoupling and NOE difference experiments. In the decoupling experiments, irradiation at $\delta$ 0.82 (methyl group) sharpened the multiplet at $\delta$ 2.61-2.69 (H$_b$), while irradiation at $\delta$ 3.33 (H$_c$) simplified the doublets of doublets at $\delta$ 2.73 (H$_d$), $\delta$ 3.10 (H$_d$), $\delta$ 3.75 (-CHCH$_2$O-) and $\delta$ 3.82 (-CHCH$_2$O-) to doublets ($J = 16.5$ Hz, $J = 16.5$ Hz, $J = 8$ Hz, $J = 8$ Hz, respectively). In a $^1$H NMR NOE difference experiment, irradiation at $\delta$ 0.82 (methyl group) caused enhancement of the signals at $\delta$ 1.77-1.84, $\delta$ 2.61-2.69 (H$_b$) and $\delta$ 3.30-3.36 (H$_c$).

The $^1$H NMR spectrum of 350 was similar to that of 349 and exhibited all of the expected signals. The assignment of the stereochemistry of 350 was based on $^1$H NMR NOE difference experiments. Thus, irradiation at $\delta$ 3.35 (H$_c$) caused enhancement of the signals at $\delta$ 2.53-2.63 (H$_b$), $\delta$ 3.62 (-CHCH$_2$O-) and $\delta$ 3.80 (-CHCH$_2$O-), while irradiation at $\delta$ 3.62 (-CHCH$_2$O-) caused enhancement of the signals at $\delta$ 0.74 (methyl group), $\delta$ 3.33-3.39 (H$_c$) and $\delta$ 3.80 (-CHCH$_2$O-). In high resolution mass spectrometric measurements, both compounds 349 and 350 showed z/e M$^+$.OCH$_3$ peaks, corresponding, in each case, to a formula of C$_{33}$H$_{39}$O$_5$Si.
The result described above showed that the thermal Diels-Alder reaction of the keto ether diene 328 with DMAD was not face*-selective, since there was only a small preference for attack of the dienophile on the β-face of the diene. This result was not surprising, since the linear dienophile DMAD would not be expected to experience steric hindrance in approaching either face of the diene 328.

The keto ether diene 328 was subjected to Lewis acid catalyzed Diels-Alder reactions. A mixture of 328 and MVK (5 equiv) in dichloromethane containing BF₃·Et₂O (1 equiv) was stirred at -78°C for 1 h. Analysis of the crude reaction product by ¹H NMR spectroscopy showed that only one Diels-Alder adduct had been produced. Chromatography of the crude product afforded an 83% yield of the diketo ether 351. The spectral data of 351 was in accord with the assigned structure. The IR spectrum of 351 showed a strong absorption band at 1708 cm⁻¹ for the C=O stretching vibration of the two methyl ketone functions. The ¹H NMR spectrum of 351 (Figure 22) exhibited the expected signals for a secondary methyl group (a 3-proton doublet at δ 0.84, J = 7 Hz), a tert-butylidiphenylsilyl group (a 9-proton singlet at δ 1.02, a 6-proton multiplet at δ 7.37-7.48 and a 4-proton multiplet at δ 7.67-7.75), two methyl ketone moieties (-CH₃COCH₃ and

* In this section, the α-face refers to the side of the diene on which the secondary methyl group is situated, while the β-face refers to the side opposite to the secondary methyl group.
Figure 22: The 400 MHz $^1$H NMR Spectrum of the Diketo Ether 351

-CH$_3$COCH$_3$, two 3-proton singlets at $\delta$ 1.91 and $\delta$ 2.32, respectively) and a methylene group $\alpha$ to an ether function (two 1-proton doublets of doublets at $\delta$ 3.43 and $\delta$ 3.66, $J = 11$, 2 Hz and $J = 11$, 8 Hz, respectively). The other assigned signals, based on decoupling experiments (see Experimental section for details), were the following: H$_a$, a 1-proton doublet of triplets at $\delta$ 2.36, $J = 15$, 5 Hz; H$_b$, a 1-proton multiplet at $\delta$ 2.25-2.31; H$_c$, a 1-proton multiplet at $\delta$ 2.83-2.90; and H$_d$, a 1-proton doublet of triplets at $\delta$ 2.60, $J = 10.5$, 4 Hz. The assignment of the stereochemistry for 351 was based on $^1$H NMR NOE difference experiments. The results of these experiments were as follows: irradiation at $\delta$ 0.84 (methyl group) caused enhancement of the signals at $\delta$ 1.61-1.71, $\delta$ 1.91 (-CH$_3$COCH$_3$), $\delta$ 2.25-2.31 (H$_b$) and $\delta$ 2.83-2.90 (H$_c$); irradiation at $\delta$ 2.60 (H$_d$)
caused enhancement of the signals at $\delta$ 1.78-1.95, $\delta$ 2.32 (-CH$_3$COCH$_3$) and $\delta$ 2.83-2.90 (H$_c$); irradiation at $\delta$ 2.87 (H$_c$) caused enhancement of the signals at $\delta$ 0.82 (methyl group), $\delta$ 2.32 (-CH$_3$COCH$_3$), $\delta$ 2.60 (H$_d$), $\delta$ 3.43 (-CHCH$_2$O-) and $\delta$ 3.66 (-CHCH$_2$O-); irradiation at $\delta$ 3.43 (-CHCH$_2$O-) caused enhancement of the signals at $\delta$ 2.25-2.31 (H$_b$), $\delta$ 2.83-2.90 (H$_c$) and $\delta$ 3.66 (-CHCH$_2$O-). A high resolution mass spectrometric measurement showed that 351 has a molecular formula of C$_{32}$H$_{42}$O$_3$Si. Interestingly, the cycloaddition occurred selectively via an "ortho," endo transition state, with the dienophile approaching the diene from the side opposite the secondary methyl group.

![Chemical structure](image)

The Lewis acid catalyzed Diels-Alder reaction was also performed on 328 with acrolein. The procedure employed was identical with that outlined above except that acrolein was used instead of MVK (Equation 84). Not surprisingly, only one Diels-Alder adduct 352 was obtained in an 86% yield. The IR spectrum of 352 showed two absorption bands at 1725 and 1709 cm$^{-1}$ for the C=O stretching vibration of the aldehyde and methyl ketone moieties. In addition, an aldehydic C-H stretching vibration (a weak absorption band at 2728 cm$^{-1}$) was observed. The $^1$H NMR spectrum of 352 showed signals similar to that of 351 except for the presence of an aldehyde moiety (a 1-proton broad singlet at $\delta$ 10.04) instead of the methyl ketone group. The stereochemistry of 352 was confirmed by $^1$H NMR NOE difference experiments (see Experimental section for details). Thus, the BF$_3$·Et$_2$O catalyzed Diels-Alder reaction of 328 with acrolein also occurs via an
"ortho," endo transition state, with the dienophile approaching the β-face of the diene.

In summary, all of the highly substituted cyclobutenes investigated except for the keto ester 315, underwent thermolytic ring opening with stereochemistries in accord with those predicted by Houk and co-workers. The thermally induced ring opening of the compounds 319, 321 and 322 provided exclusively the products where the CH2OR group had rotated outward. For the thermolysis of the keto ester 314, the ratio of the products resulting from outward and inward rotation of the CO2Et group was 11:1. In the case of the 3-formylcyclobutenes 324 and 327, the thermal ring opening process took place with exclusive inward rotation of the formyl group.

The thermolysis of the keto ester 315 provided a 1:1 ratio of the thermolysis products 335 and 336. Thus, in this case, there was no preference for the direction of rotation of the CO2Et group in the ring opening process. This result, which is somewhat different from that predicted by theoretical calculations, can be rationalized on the basis of a steric effect.

The diene 328, obtained from the thermolysis of 319, readily undergoes Diels-Alder reactions. The thermal Diels-Alder reaction of the 328 with dimethyl acetylenedicarboxylate affords a 5:4 epimeric mixture of 349 and 350. Thus, this reaction exhibited very little face-selectivity. However, the BF3-Et2O catalyzed Diels-Alder reactions of 328 with MVK and acrolein were highly stereo- and regioselective. In each case, a single adduct was obtained.
III. EXPERIMENTAL

1. General

Melting points were determined using a Fisher-Johns melting point apparatus and are uncorrected. Boiling points are also uncorrected and those indicated as air-bath temperatures refer to bulb-to-bulb (Kugelrohr) distillations. Infrared (IR) spectra were recorded either on a Perkin-Elmer model 710B infrared spectrophotometer using the 1601 cm\(^{-1}\) band of polystyrene film for calibration or on a Perkin-Elmer model 1710 Fourier Transform Infrared (FTIR) spectrometer (internal calibration). Proton nuclear magnetic resonance (\(^1\)H NMR) spectra were recorded on deuteriochloroform solutions or hexadeuteriobenzene solutions using Bruker Models WP-80, HXS-270, or WH-400 spectrometers or a Varian model XL-300 instrument. Carbon nuclear magnetic resonance (\(^{13}\)C NMR) were recorded on deuteriochloroform solutions using a Varian model XL-300 instrument. Signal positions are given in \(\delta\) units and for \(^1\)H NMR were measured relative to tetramethylsilane (TMS) as the internal standard or to the chloroform signal (\(\delta\ 7.25\)\(^80\)). The multiplicity, number of protons, coupling constants, and assignments (where possible) are indicated in parentheses. The tin-proton coupling constants (\(J_{\text{Sn-H}}\)) are given as an average of the \(^{117}\)Sn and \(^{119}\)Sn values (unless stated otherwise). For \(^{13}\)C NMR \(\delta\) was measured relative to the deuteriochloroform signal (\(\delta\ 77.0\)\(^80\)). Low and high resolution mass spectra were recorded with AEI MS9 and/or MS50 mass spectrometers. In cases of compounds with trimethylstannyl groups or tri-\(n\)-butylstannyl groups the molecular weight determinations (high resolution mass spectrometry) were based on \(^{120}\)Sn and were made on the (\(M^+-\text{CH}_3\)) or (\(M^+-\text{C}_4\text{H}_9\)) peaks, respectively.
Gas-liquid chromatography (GLC) analyses were performed on Hewlett-Packard models 5880 or 5890 capillary gas chromatographs using 25 m x 0.21 mm fused silica columns coated with cross-linked SE-54 and equipped with flame ionization detectors.

Thin-layer chromatography (TLC) analyses were done on commercial aluminum-backed silica gel plates (E. Merck, Type 5554). Preparative thin-layer chromatography was done on 20 cm x 20 cm plates coated with 2 mm of silica gel (E. Merck, Silica Gel 60). Visualization was accomplished with ultraviolet light, iodine, and/or by spraying the plate with 5% ammonium molybdate-10% aqueous sulfuric acid. Conventional column chromatography was done on 70-230 mesh silica gel (E. Merck, Silica Gel 60) while flash chromatography\textsuperscript{81} was done on 230-400 mesh silica gel (E. Merck, Silica Gel 60).

Unless otherwise stated, all reactions were carried out under an atmosphere of dry argon using carefully flame-dried glassware.

Cold temperatures used for various reactions were obtained as follows: 27 g CaCl\textsubscript{2}/100 mL H\textsubscript{2}O-CO\textsubscript{2} (-20°C), 46 g CaCl\textsubscript{2}/100 mL H\textsubscript{2}O-CO\textsubscript{2} (-48°C) and acetone-CO\textsubscript{2} (-78°C).

Solvents and reagents were purified and dried using established procedures.\textsuperscript{82} Diethyl ether and THF were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from P\textsubscript{2}O\textsubscript{5}. Triethylamine, diisopropylethylamine, diisopropylamine, HMPA, DMSO and DMF were distilled from calcium hydride. Petroleum ether refers to the fraction boiling between 30-60°C. All other solvents were used directly.

Hexamethylditin was obtained from Organometallics Inc. and was used without further purification.

Tetrakis(triphenylphosphine)palladium(0) was obtained from Morton Thiokol, Inc. (Alfa Products) and was used without further purification.
Solutions of methylithium (low halide) in ether, n-butyllithium in hexane and diisobutylaluminum hydride in hexane or toluene were obtained from Aldrich Chemical Co., Inc. and the former two reagents were standardized using the procedure of Kofron and Baclawski.\textsuperscript{83}

A solution of trimethylaluminum in toluene was obtained from Aldrich Chemical Co., Inc.

Phenylthiocopper was prepared by the method of Posner.\textsuperscript{84}

Saturated aqueous ammonium chloride (pH 8) was prepared by the addition of 50 mL of aqueous ammonium hydroxide (58\%) to 1 L of saturated aqueous ammonium chloride.

Tri-n-butyltin hydride was prepared by the method of Kuivila.\textsuperscript{85}

Boron trifluoride-etherate was purified by distillation from calcium hydride (1 g per 250 mL of BF\textsubscript{3}·Et\textsubscript{2}O) under reduced pressure (60°C/20 Torr).\textsuperscript{86}

Nitroethylene was prepared by the method of Noland.\textsuperscript{76}

Lithium diisopropylamide (LDA) was prepared by the addition of a solution of n-butyllithium in hexane to a solution of diisopropylamine (1 equiv) in dry THF at -78°C. The resulting colorless solution was then stirred at 0°C for 10 min before being used.

All other reagents were commercially available and were utilized without further purification.
2. Preparation of Stannylcuprates

Preparation of Trimethylstannyllithium (128)

\[ \text{Me}_3\text{SnLi} \]
128

To a cold (-20°C), stirred solution of hexamethylditin in dry THF (~10 mL per mmol of \( \text{Me}_3\text{SnSnMe}_3 \)), under an argon atmosphere, was added a solution of methyllithium in diethyl ether (1 equiv). The resulting pale yellow-green solution was stirred at -20°C for 20 min to afford a solution of trimethylstannyllithium (128).

Preparation of Lithium (Phenylthio)(trimethylstanny)cuprate (26)

\[ [\text{Me}_3\text{SnCuSPh}]\text{Li} \]
26

To a cold (-20°C), stirred solution of trimethylstannyllithium (128) in dry THF was added solid phenylthiocopper (1 equiv). The resulting slurry was stirred at -20°C for 20 min, producing a deep red solution of lithium (phenylthio)(trimethylstanny)cuprate (26).
Preparation of Lithium (Cyano)(trimethylstannyl)cuprate (30)

\[ \text{[Me}_3\text{SnCuCN]}\text{Li} \]

30

To a cold (-78°C), stirred solution of trimethylstannyllithium (128) in dry THF was added copper(I) cyanide (1 equiv). The resulting slurry was stirred at -48°C for 20 min, producing a pale yellow solution of lithium (cyano)(trimethylstannyl)cuprate (30).

Preparation of Dilithium (Trimethylstannyl)(2-thienyl)(cyano)cuprate (141)

\[ \text{[Me}_3\text{SnCu(2-Th)(CN)}]\text{Li}_2 \]

141

To a cold (-20°C), stirred solution of hexamethylditin in dry THF (~10 mL per mmol of Me\(_3\)SnSnMe\(_3\)) under an argon atmosphere, was added, successively, thiophene (1 equiv) and a solution of methyllithium (2 equiv) in diethyl ether. After the pale yellow solution had been stirred at -20°C for 50 min, it was cooled to -78°C and copper(I) cyanide (1 equiv) was added. The resulting suspension was stirred for 5 min at -78°C and for 20 min at -48°C to provide a bright yellow solution of dilithium (trimethylstannyl)(2-thienyl)(cyano)cuprate (141). The solution was cooled to -78°C and used immediately.
3. Preparation of \(\alpha,\beta\)-Acetylenic Esters

Preparation of 5-Methoxymethoxy-1-pentyne (125)

![Structure of 5-Methoxymethoxy-1-pentyne](image)

To a cold (0°C) solution of 4-pentyn-1-ol (123) (commercially available) (3.05 g, 36.4 mmol) and diisopropylethylamine (7.05 g, 54.6 mmol) in dry dichloromethane (70 mL) was added chloromethylmethyl ether (4.39 g, 54.5 mmol). The resultant solution was stirred at 0°C for 1.5 h. Hydrochloric acid (2N, 30 mL) was added and the mixture was extracted thoroughly with dichloromethane. The combined organic extracts were washed with brine, dried (MgSO4), and dichloromethane was removed by distillation at atmospheric pressure. The residual oil was distilled at reduced pressure (boiling point, 85°C/50 Torr) to yield 4.42 g (95%) of 5-methoxymethoxy-1-pentyne (125) as a colorless oil. Analysis of this oil by GLC and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3292, 2119, 1150, 1113, 1041, 920 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 1.83 (quintet, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_2\text{CH}_2\)-), 1.97 (t, 1H, \(J = 2\) Hz, \(-\text{HC}≡\text{C}\)-), 2.33 (td, 2H, \(J = 7, 2\) Hz, \(≡\text{CH}_2\text{CH}_2\)-), 3.39 (s, 3H, \(-\text{OCH}_3\)), 3.64 (t, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_2\text{O}\)-), 4.63 (s, 2H, \(-\text{OCH}_2\text{O}\)-). Exact Mass calcd. for C\(_7\)H\(_{11}\)O\(_2\) (M\(^+\)-H): 127.0759; found: 127.0758.
General Procedure 1

Preparation of the $\alpha,\beta$-Acetylenic esters 121

\[ \text{EtO}_2\text{C} \equiv \equiv \text{R} \]

To a cold (-78°C), stirred solution of the 1-alkyne (1 equiv) in dry THF (~2 mL per mmol of alkyne), under an argon atmosphere, was added a solution of methyllithium (1 equiv) in diethyl ether. The resulting clear solution was stirred at -78°C for 15 min, warmed to -20°C, and stirred at this temperature for 1 h. Ethyl chloroformate (1 equiv) was added and the resulting mixture was stirred at -20°C for 1 h and at room temperature for 1 h. Saturated aqueous sodium bicarbonate was added and the mixture was extracted thoroughly with diethyl ether. The combined organic extracts were washed (water, brine) and dried (MgSO$_4$). Solvent removal, followed by distillation of the residue, afforded the $\alpha,\beta$-acetylenic ester 121.

Preparation of Ethyl 2-Pentynoate (131)

\[ \text{EtO}_2\text{C} \equiv \equiv \text{R} \]

131

Following general procedure 1 outlined above, 1-butyne (130) was converted into the $\alpha,\beta$-acetylenic ester 131. The following amounts of reagents and solvents were used: 1-butyne (130) (4.20 g, 77.8 mmol) in 155 mL of dry THF; methyllithium (55.0 mL, 77.0 mmol) in diethyl ether; ethyl chloroformate (8.36 g, 77.0 mmol). Normal workup, followed by distillation (air-bath temperature 95-
100°C/45 Torr) of the material thus obtained, afforded 9.00 g (93%) of ethyl 2-pentynoate (131) as a colorless oil. Analysis of this oil by GLC and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2239, 1713, 1251 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 1.21 (t, 3H, $J = 7$ Hz, $\equiv$CCH$_2$CH$_3$), 1.32 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 2.35 (q, 2H, $J = 7$ Hz, $\equiv$CCH$_2$CH$_3$), 4.22 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$). Exact Mass calcd. for C$_7$H$_{10}$O$_2$ (M$^+$): 126.0681; found: 126.0674.

Preparation of Ethyl 4-Methoxymethoxy-2-butyroate (132)

Following general procedure 1 outlined above, 3-methoxymethoxy-1-propyne (124)$^{33}$ was converted into the $\alpha,\beta$-acetylenic ester 132. The following amounts of reagents and solvents were used: 3-methoxymethoxy-1-propyne (124) (1.96 g, 19.6 mmol) in 40 mL of dry THF; methyllithium (14.0 mL, 19.6 mmol) in diethyl ether; ethyl chloroformate (2.13 g, 19.6 mmol). Normal workup, followed by distillation (air-bath temperature 54-62°C/0.15 Torr) of the material thus obtained, afforded 2.84 g (84%) of ethyl 4-methoxymethoxy-2-butyroate (132) as a colorless oil. Analysis of this oil by GLC and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2238, 1718, 1251, 1078 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 80 MHz): $\delta$ 1.30 (t, 3H $J = 7$ Hz, -OCH$_2$CH$_3$), 3.40 (s, 3H, -OCH$_3$), 4.27 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.35 (s, 2H, $\equiv$CCH$_2$O-), 4.62 (s, 2H, -OCH$_2$O-). Exact mass calcd. for C$_8$H$_{11}$O$_4$ (M$^+$-H): 171.0657; found: 171.0657.
Preparation of Ethyl 6-Methoxymethoxy-2-hexynoate (133)

\[
\text{EtO}_2\text{C} \equiv \text{C} \equiv \text{O} \equiv \text{O} \quad 133
\]

Following general procedure 1 outlined above, 5-methoxymethoxy-1-pentyne (125) was converted into the \(\alpha,\beta\)-acetylenic ester 133. The following amounts of reagents and solvents were used: 5-methoxymethoxy-1-pentyne (125) (4.13 g, 32.3 mmol) in 64 mL of dry THF; methyl lithium (23.0 mL, 32.3 mmol) in diethyl ether; ethyl chloroformate (3.50 g, 32.3 mmol). Normal workup, followed by distillation (air-bath temperature 72-80\(^\circ\)C/0.15 Torr) of the material thus obtained, afforded 5.34 g (83%) of ethyl 6-methoxymethoxy-2-hexynoate (133) as a colorless oil. Analysis of this oil by GLC and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2235, 1713, 1254, 1040 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 80 MHz): \(\delta\) 1.30 (t, 3H, \(J = 7\) Hz, \(-\text{OCH}_2\text{CH}_3\)), 1.85 (quintet, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_2\text{CH}_2\)\(\text{-}\)), 2.45 (t, 2H, \(J = 7\) Hz, \(=\text{CCH}_2\text{CH}_2\)\(\text{-}\)), 3.35 (s, 3H, \(-\text{OCH}_3\)), 3.60 (t, 2H, \(J = 7\) Hz, \(-\text{OCH}_2\text{CH}_2\)\(\text{-}\)), 4.18 (q, 2H, \(J = 7\) Hz, \(-\text{OCH}_2\text{CH}_3\)), 4.62 (s, 2H, \(-\text{OCH}_2\text{O}\)\(\text{-}\)). Exact Mass calcd. for C\(_{10}\)H\(_{15}\)O\(_4\) (M\(^+\)-H): 199.0971; found: 199.0979.

Preparation of Ethyl 7-tert-Butyldimethylsilyloxy-2-heptynoate (134)

\[
\text{EtO}_2\text{C} \equiv \text{C} \equiv \text{O} \equiv \text{SiMe}_2\text{-}\text{Bu} \quad 134
\]

Following general procedure 1 outlined above, 6-tert-butyldimethylsilyloxy-1-hexyne (127)\(^3\)\(^4\) was converted into the \(\alpha,\beta\)-acetylenic ester 134. The following amounts of reagents and solvents were used: 6-tert-butyldimethylsilyloxy-1-hexyne
(127) (9.45 g, 44.6 mmol) in 90 mL of dry THF; methyllithium (31.8 mL, 44.6 mmol) in diethyl ether; ethyl chloroformate (4.84 g, 44.6 mmol). Normal workup, followed by distillation (air-bath temperature 110-115°C/0.15 Torr) of the material thus obtained, afforded 9.60 g (76%) of ethyl 7-tert-butyldimethylsilyloxy-2-heptynoate (134) as a colorless oil. Analysis of this oil by GLC and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2236, 1713, 1254, 1078 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz):  δ 0.10 (s, 6H, -SiMe₂), 0.94 (s, 9H, -SiCMe₃), 1.35 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.60-1.76 (m, 4H, -CH₂CH₂CH₂CH₂-), 2.41 (t, 2H, J = 7 Hz, =CCH₂CH₂-), 3.68 (t, 2H, J = 7 Hz, -OCH₂CH₂-), 4.26 (q, 2H, J = 7 Hz, -OCH₂CH₃).

Exact Mass calcd. for C₁₄H₂₅SiO₃ (M⁺-CH₃): 269.1573; found: 269.1575.
4. Preparation of Ethyl (Z)- and (E)-3-Trimethylstannyl-2-alkenoates

General Procedure 2

Preparation of Ethyl (Z)-3-Trimethylstannyl-2-alkenoates (1)

\[
\begin{align*}
R & \quad \equiv \\
\text{Me}_3\text{Sn} & \quad \equiv \\
\text{H} & \quad \equiv \\
\text{CO}_2\text{Et} & \quad \equiv 
\end{align*}
\]

1

To a cold (-78°C), stirred solution of lithium (phenylthio)(trimethylstannyl)-cuprate (26) (1.3 equiv) in dry THF (~10 mL per mmol of cuprate), under an argon atmosphere, was added the appropriate \(\alpha,\beta\)-acetylenic ester (121) (1 equiv) as a solution in dry THF (~1 mL per mmol of ester). The reaction mixture was stirred for 15 min at -78°C, warmed to -48°C and stirred for 4 h. After successive addition of methanol (~2 mL per mmol of cuprate) and petroleum ether (~5 mL per mmol of cuprate), the resulting yellow slurry was filtered through a plug of celite and the collected solid was washed with the same volume of petroleum ether as that used above. The combined filtrates were concentrated and the residue was subjected to flash chromatography on silica gel. Concentration of the appropriate fractions, followed by bulb-to-bulb distillation of the residue, afforded the corresponding ethyl (Z)-3-trimethylstannyl-2-alkenoate 1.
Preparation of Ethyl (Z)-3-Trimethylstannyl-2-pentenoate (35)

\[
\begin{align*}
\text{Me}_3\text{Sn} & \quad \equiv \quad \text{H} \\
\text{CO}_2\text{Et} & 
\end{align*}
\]

35

Following general procedure 2 outlined above, ethyl 2-pentynoate (131) was converted into the ester 35. The following amounts of reagents and solvents and solvents were used: lithium (phenylthio)(trimethylstannyl)cuprate (26) (10.4 mmol) in 80 mL of dry THF; ethyl 2-pentynoate (131) (1.01 g, 8.02 mmol) in 8 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 55-65°C/0.2 Torr) of the material thus obtained, afforded 1.85 g (79%) of ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1703, 1601, 1200, 770 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 0.18 (s, 9H, \(J_{\text{Sn-H}} = 54\) Hz, -SnMe\(_3\)), 1.02 (t, 3H, \(J = 7\) Hz, =C-CH\(_2\)CH\(_3\)), 1.28 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.42 (qd, 2H, \(J = 7\), 1.5 Hz, =C-CH\(_2\)2-), 4.16 (q, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 6.34 (t, 1H, \(J = 1.5\) Hz, \(J_{\text{Sn-H}} = 120\) Hz, olefinic proton). Exact Mass calcd. for C\(_9\)H\(_{17}\)O\(_2\)Sn (M\(^+\)-CH\(_3\)): 277.0250; found: 277.0250.
Preparation of Ethyl (Z)-4-Methoxymethoxy-3-trimethylstannyl-2-butenoate (135)

To a cold (-78°C), stirred solution of dilithium (trimethylstannyl)-(2-thienyl)(cyano)cuprate (141) (0.819 mmol) in 6 mL of dry THF under an argon atmosphere was added ethyl 4-methoxymethoxy-2-butynoate (132) (109 mg, 0.634 mmol) as a solution in 1 mL of dry THF. The reaction mixture was stirred for 4 h at -78°C. Saturated ammonium chloride solution (pH 8) was added and the resultant mixture was allowed to stir with exposure to air until the aqueous phase turned blue. The mixture was then extracted thoroughly with diethyl ether and the combined ether extracts were washed (water, brine), dried (MgSO₄) and concentrated. The remaining oil was subjected to flash chromatography on silica gel (10 g, elution with petroleum ether-diethyl ether, 8:1). Concentration of the appropriate fractions, followed by distillation (air-bath temperature 80-85°C/0.15 Torr) of the residue, afforded 109 mg (51%) of ethyl (Z)-4-methoxymethoxy-3-trimethylstannyl-2-butenoate (135) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1702, 1607, 1197, 1040, 774 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.19 (s, 9H, ²J.Sn-H = 54 Hz, -SnMe₃), 1.29 (t, 3H, J = 7 Hz, -OCH₂CH₃), 3.38 (s, 3H, -OCH₃), 4.20 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.37 (d, 2H, J = 2 Hz, =C-CH₂O-), 4.68 (s, 2H, -OCH₂O-), 6.68 (t, 1H, J = 2 Hz, ³J.Sn-H = 110 Hz, olefinic proton). Exact Mass calcd. for C₁₀H₁₉O₄Sn (M⁺-CH₃): 323.0305; found: 323.0301.
Preparation of Ethyl (Z)-6-Methoxymethoxy-3-trimethylstannyl-2-hexenoate (136)

Following general procedure 2 outlined above, ethyl 6-methoxymethoxy-2-hexynoate (133) was converted into the ester 136. The following amounts of reagents and solvents were used: lithium (phenylthio)(trimethylstannyl)cuprate (26) (9.53 mmol) in 70 mL of dry THF; ethyl 6-methoxymethoxy-2-hexynoate (133) (1.44 g, 7.20 mmol) in 5 mL of dry THF. Flash chromatography of the crude product on silica gel (125 g, elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 84-90°C/0.15 Torr) of the material thus obtained, afforded 1.96 g (74%) of ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (136) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1703, 1600, 1325, 1207, 1042, 774 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.19 (s, 9H, $^2$J$_{Sn-H}$ = 56 Hz, -SnMe$_3$), 1.29 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.71 (quintet, 2H, $J = 7$ Hz, -CH$_2$CH$_2$CH$_2$-), 2.52 (td, 2H, $J = 7$, 1 Hz, =C-CH$_2$-), 3.37 (s, 3H, -OCH$_3$), 3.52 (t, 2H, $J = 7$ Hz, -OCH$_2$CH$_2$-), 4.20 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.63 (s, 2H, -OCH$_2$O-), 6.38 (broad t, 1H, $J = 1$ Hz, $^3$J$_{Sn-H}$ = 120 Hz, olefinic proton). Exact Mass calcd. for C$_{12}$H$_{23}$O$_4$Sn (M$^+$-CH$_3$): 351.0618; found: 351.0617.
Preparation of Ethyl \((Z)-\text{7-tert-Butyldimethylsilyloxy-3-trimethylstannyl}-2\text{-heptenoate}\) (137)

\[
\begin{align*}
\text{t-BuMe}_2\text{SiO} & \quad \text{Me}_3\text{Sn} \\
\quad & \quad \text{H} \\
\quad & \quad \text{CO}_2\text{Et}
\end{align*}
\]

Following general procedure 2 outlined above, ethyl \(7\text{-tert-butyldimethylsilyloxy-2-heptynoate}\) (134) was converted into the ester 137. The following amounts of reagents and solvents were used: lithium (phenylthio)(trimethylstannyl)-cuprate (26) (9.52 mmol) in 70 mL of dry THF; ethyl \(7\text{-tert-butyldimethylsilyloxy-2-heptynoate}\) (134) (2.00 g, 7.04 mmol) in 5 mL of dry THF. Flash chromatography of the crude product on silica gel (125 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 125-130°C/0.15 Torr) of the material thus obtained, afforded 2.25 g (71%) of ethyl \((Z)-7\text{-tert-butyldimethylsilyloxy-3-trimethylstannyl}-2\text{-heptenoate}\) (137) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and \(^1\text{H}\) NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1704, 1600, 1162, 837, 776 cm\(^{-1}\); \(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz): \(\delta\) 0.02 (s, 6H, -SiMe\(_3\)), 0.15 (s, 9H, \(^2\text{J}_{\text{Sn-H}} = 54 \text{ Hz}, -\text{SnMe}_3\)), 0.86 (s, 9H, -SiCMe\(_3\)), 1.26 (t, 3H, \(J = 7 \text{ Hz}, -\text{OCH}_2\text{CH}_3\)), 1.35-1.55 (m, 4H, -CH\(_2\text{CH}_2\text{CH}_2\text{CH}_2\)), 2.41 (broad t, 2H, \(J = 7 \text{ Hz}, -\text{C-CH}_2\text{-}\)), 3.58 (t, 2H, \(J = 7 \text{ Hz}, -\text{OCH}_2\text{CH}_2\)), 4.16 (q, 2H, \(J = 7 \text{ Hz}, -\text{OCH}_2\text{CH}_3\)), 6.33 (broad t, 1H, \(J = 1 \text{ Hz}, ^3\text{J}_{\text{Sn-H}} = 120 \text{ Hz}, \text{olefinic proton}\)). **Exact Mass** calcd. for C\(_{17}\)H\(_{35}\)O\(_3\)SiSn (M\(^+\)-CH\(_3\)): 435.1376; found: 435.1375.
General Procedure 3

Preparation of Ethyl (E)-3-Trimethylstannyl-2-alkenoates (2)

To a cold (-78°C), stirred solution of lithium (cyano)(trimethylstannyl)cuprate (30) (1.3 equiv) in dry THF (~10 mL per mmol of cuprate), under an argon atmosphere, was added the appropriate α,β-acetylenic ester (121) (1 equiv) as a solution in dry THF (~1 mL per mmol of ester). The reaction mixture was stirred for 4 h at -78°C. Saturated ammonium chloride solution (pH 8) was added and the resultant mixture was allowed to stir with exposure to air until the aqueous phase turned blue. The mixture was then extracted thoroughly with diethyl ether and the combined ether extracts were washed (water, brine), dried (MgSO4) and concentrated. The remaining oil was subjected to flash chromatography on silica gel. Concentration of the appropriate fractions, followed by bulb-to-bulb distillation of the residue, afforded the corresponding ethyl (E)-3-trimethylstannyl-2-alkenoate 2.

Preparation of Ethyl (E)-3-Trimethylstannyl-2-butenoate (25)

Following general procedure 3 outlined above, ethyl 2-butyroate (23) was converted into the ester 25. The following amounts of reagents and solvents were used: lithium (cyano)(trimethylstannyl)cuprate (30) (17.8 mmol) in 140 mL of dry
THF; ethyl 2-butynoate (23) (1.54 g, 13.7 mmol) in 14 mL of dry THF. Flash chromatography of the crude product on silica gel (125 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 50-56°C/0.2 Torr) of the material thus obtained, afforded 2.98 g (78%) of ethyl (E)-3-trimethylstannyl-2-butenoate (25) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1718, 1604, 1177, 768 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 0.18 (s, 9H, ²J_{Sn-H} = 54 Hz, -SnMe₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 2.36 (d, 3H, J = 2 Hz, =C-CH₃), 4.12 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.96 (q, 1H, J = 2 Hz, ³J_{Sn-H} = 72 Hz, olefinic proton). Exact Mass calcd. for C₉H₁₅O₂Sn (M⁺-CH₃): 263.0093; found: 263.0087.

Preparation of Ethyl (E)-3-Trimethylstannyl-2-pentenoate (36)

Following general procedure 3 outlined above, ethyl 2-pentynoate (131) was converted into the ester 36. The following amounts of reagents and solvents were used: lithium (cyano)(trimethylstannyl)cuprate (30) (12.4 mmol) in 95 mL of dry THF; ethyl 2-pentynoate (131) (1.20 g, 9.52 mmol) in 9 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 55-70°C/0.2 Torr) of the material thus obtained, afforded 2.25 g (81%) of ethyl (E)-3-trimethylstannyl-2-pentenoate (36) as a colorless oil. Analysis of this oil by GLC, TLC
(petroleum ether-diethyl ether, 200:3) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1718, 1597, 1176, 770 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 0.20 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 1.04 (t, 3H, $J$ = 7 Hz, =C-CH$_2$CH$_3$), 1.28 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 2.88 (qd, 2H, $J$ = 7, 1.5 Hz, =C-CH$_2$-), 4.14 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 5.91 (t, 1H, $J$ = 1.5 Hz, $^3$J$_{Sn-H}$ = 73 Hz, olefinic proton). **Exact Mass** calcd. for C$_9$H$_{17}$O$_2$Sn (M$^+$ -CH$_3$): 277.0250; found: 277.0254.

**Preparation of Ethyl (E)-4-Methoxymethoxy-3-trimethylstannyl-2-butenoate (142)**

Following general procedure 3 outlined above, ethyl 4-methoxymethoxy-2-butynoate (132) was converted into the ester 142. The following amounts of reagents and solvents were used: lithium (cyano)(trimethylstannyl)cuprate (30) (6.24 mmol) in 50 mL of dry THF; ethyl 4-methoxymethoxy-2-butynoate (132) (828 mg, 4.81 mmol) in 5 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 82-86$^\circ$C/0.15 Torr) of the material thus obtained, afforded 962 mg (59%) of ethyl (E)-4-methoxymethoxy-3-trimethylstannyl-2-butenoate (142) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one
component. This material exhibited IR (film): 1712, 1608, 1185, 1040, 772 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 0.19 (s, 9H, \(^2\)J\(_{\text{Sn-H}}\) = 54 Hz, -SnMe\(_3\)), 1.29 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 3.36 (s, 3H, -OCH\(_3\)), 4.16 (q, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 4.66 (s, 2H, -OCH\(_2\)O-), 4.80 (d, 2H, \(J = 2.5\) Hz, =C-CH\(_2\)O-), 5.95 (t, 1H, \(J = 2.5\) Hz, \(^3\)J\(_{\text{Sn-H}}\) = 71 Hz, olefinic proton). **Exact Mass** calcd. for C\(_{10}\)H\(_{19}\)O\(_4\)Sn (M\(^+\)-CH\(_3\)): 323.0305; found: 323.0303.

**Preparation of Ethyl (E)-6-Methoxymethoxy-3-trimethylstannyl-2-hexenoate (143)**

Following general procedure 3 outlined above, ethyl 6-methoxymethoxy-2-hexynoate (133) was converted into the ester 143. The following amounts of reagents and solvents were used: lithium (cyano)(trimethylstannyl)cuprate (30) (4.05 mmol) in 30 mL of dry THF; ethyl 6-methoxymethoxy-2-hexynoate (133) (628 mg, 3.14 mmol) in 3 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 84-90°C/0.15 Torr) of the material thus obtained, afforded 868 mg (76%) of ethyl (E)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (143) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1714, 1598, 1368, 1176, 1044,
774 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.22 (s, 9H, ²J_{Sn-H} = 52 Hz, -SnMe₃), 1.29 (t, 3H, ³J = 7 Hz, -OCH₂CH₃), 1.73 (quintet, 2H, ³J = 7 Hz, -CH₂CH₂CH₂-), 2.96 (qd, 2H, ³J = 7, 1 Hz, =C-CH₂-), 3.36 (s, 3H, -OCH₃), 3.55 (t, 2H, ³J = 7 Hz, -OCH₂CH₂-), 4.17 (q, 2H, ³J = 7 Hz, -OCH₂CH₃), 4.63 (s, 2H, -OCH₂O-), 5.99 (broad t, 1H, ³J = 1 Hz, ³J_{Sn-H} = 72 Hz, olefinic proton). Exact Mass calcd. for C₁₂H₂₃O₄Sn (M⁺ -CH₃): 351.0618; found: 351.0617.

Preparation of Ethyl (E)-7-tert-Butyldimethylsilyloxy-3-trimethylstannyl-2-heptenoate (144)

Following general procedure 3 outlined above, ethyl 7-tert-butyldimethylsilyloxy-2-heptynoate (134) was converted into the ester 144. The following amounts of reagents and solvents were used: lithium (cyano)(trimethylstannyl)cuprate (30) (9.61 mmol) in 70 mL of dry THF; ethyl 7-tert-butyldimethylsilyloxy-2-heptynoate (134) (2.10 g, 7.39 mmol) in 7 mL of dry THF. Flash chromatography of the crude product on silica gel (125 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 125-132°C/0.15 Torr) of the material thus obtained, afforded 2.33 g (70%) of ethyl (E)-7-tert-butyldimethylsilyloxy-3-trimethylstannyl-2-heptenoate (144) as a colorless oil. Analysis of this oil
by GLC, TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1718, 1598, 1163, 1101, 837, 775 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 270 MHz): $\delta$ 0.02 (s, 6H, -SiMe$_2$), 0.18 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 0.87 (s, 9H, -SiCMe$_3$), 1.28 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.40-1.58 (m, 4H, -CH$_2$CH$_2$CH$_2$CH$_2$-), 2.89 (broad t, 2H, $J$ = 7 Hz, =C-CH$_2$-), 3.60 (t, 2H, $J$ = 7 Hz, -OCH$_2$CH$_2$-), 4.14 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 5.95 (broad t, 1H, $J$ = 1 Hz, $^3$J$_{Sn-H}$ = 75 Hz, olefinic proton). **Exact Mass** calcd. for $C_{17}H_{35}O_3SiSn$ (M$^+$-CH$_3$): 435.1376; found: 435.1383.
5. Preparation of Alkylating Agents

Preparation of 4-Iodo-1-butyne (156)

\[
\text{\begin{tikzpicture}
  \draw (-0.5,0) -- (0.5,0);
  \draw (-1.5,0) -- (-1.5,1) -- (1.5,1) -- (1.5,0) -- cycle;
  \draw (-0.5,0) -- (-0.5,1);
  \draw (0.5,0) -- (0.5,1);
  \draw (-1.5,1) -- (-1.5,0);
  \draw (1.5,1) -- (1.5,0);
  \draw (0,1) -- (0,0);
  \draw (0,0) -- (0,-0.5);
  \draw (-0.5,0) -- (-0.5,-0.5);
  \draw (0.5,0) -- (0.5,-0.5);
  \draw (-1.5,1) -- (-1.5,1.5);
  \draw (1.5,1) -- (1.5,1.5);
  \draw (-0.5,1) -- (-0.5,1.5);
  \draw (0.5,1) -- (0.5,1.5);
\end{tikzpicture}}
\]

156

To a stirred solution of triphenylphosphine (7.60 g, 29.0 mmol) in 130 mL of dry dichloromethane under an argon atmosphere was added iodine (7.37 g, 29.0 mmol). The resulting yellow solution was stirred at room temperature for 10 min. A solution of 3-butyne-1-ol (155) (1.90 g, 27.1 mmol, commercially available) in 13 mL of dry dichloromethane was added slowly and the resulting mixture was stirred at room temperature for 3 h. Pentane was added to the reaction mixture and the resultant solid was removed by filtration through a short column of Florisil (6 g). The column was eluted with pentane. Concentration of the eluate, followed by distillation (air-bath temperature 65-70°C/45 Torr) of the material thus obtained, afforded 4.04 g (83%) of 4-iodo-1-butyne (156) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3295, 2121, 1250, 1175, 642 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 2.16 (t, 1H, \(J = 2\) Hz, \(=\text{CH}\)), 2.78 (td, 2H, \(J = 7, 2\) Hz, \(=\text{CCH}_2\)), 3.24 (t, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{I}\)). **Exact Mass** calcd. for C\(_4\)H\(_5\)I (M\(^+\)): 179.9438; found: 179.9441.
Preparation of 6-Bromo-1-hexyne (159)

To a stirred solution of triphenylphosphine (5.38 g, 20.5 mmol) in 90 mL of dry dichloromethane under an argon atmosphere was added bromine (3.28 g, 20.5 mmol). The resulting pale yellow solution was stirred at room temperature for 10 min. A solution of 5-hexyn-1-ol (126) (1.83 g, 18.7 mmol, commercially available) in 10 mL of dry dichloromethane was added slowly and the resulting mixture was stirred at room temperature for 3 h. Pentane was added to the reaction mixture and the resultant solid was removed by filtration through a short column of Florisil (6 g). The column was eluted with pentane. Concentration of the eluate, followed by distillation (air-bath temperature 75-80°C/0.2 Torr) of the material thus obtained, afforded 2.91 g (97%) of 6-bromo-1-hexyne (159) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3299, 2118, 1252, 641 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 1.70 (quintet, 2H, $J = 7$ Hz, =CCH$_2$CH$_2$-), 1.95-2.06 (m, 3H, -CH$_2$CH$_2$Br and =CH), 2.25 (td, 2H, $J = 7$, 1.5 Hz, =CCH$_2$-), 3.45 (t, 2H, $J = 7$ Hz, -CH$_2$Br). Exact Mass calcd. for C$_4$H$_5^{79}$Br (M$^+$-C$_2$H$_4$): 131.9575; found: 131.9573.
General Procedure 4

Preparation of 2-Bromo-1-alkenes (154)

![Chemical Structure](image)

To a cold (0°C), stirred solution of B-bromo-9-borabicyclo[3.3.1]-nonane (B-Br-9-BBN) (2.2 equiv) in dry dichloromethane (~5 mL per mmol of reagent), under an argon atmosphere, was added dropwise, over a period of 10 min, a solution of the appropriate alkyne (1 equiv) in dry dichloromethane (~2 mL per mmol of alkyne). After the reaction mixture had been stirred at 0°C for 3 h, acetic acid (~10 equiv) was added and the solution was stirred at 0°C for a further 1 h. Aqueous sodium hydroxide (~20 equiv) and aqueous hydrogen peroxide (~10 equiv) were added slowly and the resulting mixture was stirred at room temperature for 30 min. The mixture was extracted thoroughly with petroleum ether and the combined organic extracts were washed successively with water, saturated aqueous sodium bicarbonate, and brine, and dried (MgSO₄). The solution was concentrated and the remaining oil was subjected to flash chromatography on silica gel. Concentration of the appropriate fractions, followed by bulb-to-bulb distillation of the residue, afforded the corresponding vinyl bromide 154.
Preparation of 2-Bromo-4-iodo-1-butene (160)

Following general procedure 4 outlined above, 4-iodo-1-butyne (156) was converted into the vinyl bromide 160. The following amounts of reagents and solvents were used: B-Br-9-BBN (6.49 mmol) in 30 mL of dry CH$_2$Cl$_2$; 4-iodo-1-butyne (156) (531 mg, 2.95 mmol) in 3 mL of dry CH$_2$Cl$_2$. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether), followed by distillation (air-bath temperature 45-50°C/0.15 Torr) of the material thus obtained, afforded 731 mg (95%) of 2-bromo-4-iodo-1-butene (160) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1631, 1255, 1171, 894 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 2.95 (broad t, 2H, $J = 7$ Hz, $-\text{CBrCH}_2-$), 3.34 (t, 2H, $J = 7$ Hz, $-\text{CH}_2\text{I}$), 5.56 (d, 1H, $J = 1$ Hz, olefinic proton), 5.68 (broad d, 1H, $J = 1$ Hz, olefinic proton). *Exact Mass* calcd. for C$_4$H$_6^{79}$BrI ($M^+$): 259.8696; found: 259.8702.

Preparation of 2-Bromo-5-chloro-1-pentene (161)

$\text{Br}$

161
Following general procedure 4 outlined above, 5-chloro-1-pentyne (157) (commercially available) was converted into the vinyl bromide 161. The following amounts of reagents and solvents were used: B-Br-9-BBN (11.2 mmol) in 50 mL of dry CH₂Cl₂; 5-chloro-1-pentyne (157) (524 mg, 5.11 mmol) in 5 mL of dry CH₂Cl₂. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether), followed by distillation (air-bath temperature 35-40°C/0.15 Torr) of the material thus obtained, afforded 860 mg (92%) of 2-bromo-5-chloro-1-pentene (161) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1630, 1200, 1174, 892 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 2.05 (quintet, 2H, J = 7 Hz, -CH₂CH₂CH₂-), 2.62 (broad t, 2H, J = 7 Hz, =CBrCH₂-), 3.57 (t, 2H, J = 7 Hz, -CH₂Cl), 5.47 (d, 1H, J = 1 Hz, olefinic proton), 5.66 (broad d, 1H, J = 1 Hz, olefinic proton). Exact Mass calcd. for C₅H₈³⁵Cl⁷⁹Br (M⁺): 181.9498; found: 181.9496.

Preparation of 2,6-Dibromo-1-hexene (162)

Following general procedure 4 outlined above, 6-bromo-1-hexyne (159) was converted into the vinyl bromide 162. The following amounts of reagents and solvents were used: B-Br-9-BBN (19.4 mmol) in 80 mL of dry CH₂Cl₂; 6-bromo-1-hexyne (159) (1.42 g, 8.82 mmol) in 8 mL of dry CH₂Cl₂. Flash
chromatography of the crude product on silica gel (75 g, elution with petroleum ether), followed by distillation (air-bath temperature 51-56°C/0.15 Torr) of the material thus obtained, afforded 1.92 g (90%) of 2,6-dibromo-1-hexene (162) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1631, 1241, 1184, 889 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 1.73\) (quintet, 2H, \(J = 7\) Hz, \(-\text{CBrCH}_2\text{CH}_2\)-), 1.89 (quintet, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_2\text{Br}\)), 2.48 (broad t, 2H, \(J = 7\) Hz, \(-\text{CBrCH}_2\)-), 3.44 (t, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{Br}\)), 5.44 (d, 1H, \(J = 1\) Hz, olefinic proton), 5.61 (q, 1H, \(J = 1\) Hz, olefinic proton). **Exact Mass** calcd. for \(C_6H_{10}Br_2\) (M\(^+\)): 239.9150; found: 239.9141.

**Preparation of 2-Bromo-5-iodo-1-pentene (163)**

\[
\begin{array}{c}
\text{Br} \\
\text{I}
\end{array}
\]

To a stirred solution of 2-bromo-5-chloro-1-pentene (161) (168 mg, 0.916 mmol) in 5 mL of dry acetone under an argon atmosphere was added sodium iodide (344 mg, 2.29 mmol). The stirred reaction mixture was refluxed for 16 h. Pentane was added to the mixture and the resultant solid was removed by filtration through a short column of Florisil (3 g). The column was eluted with pentane. Concentration of the eluate, followed by distillation (air-bath temperature 50-55°C/0.15 Torr) of the material thus obtained, afforded 235 mg (93%) of 2-bromo-5-iodo-1-pentene (163) as a colorless oil. Analysis of this oil by GLC, TLC
(petroleum ether) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1631, 1222, 1171, 891 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 2.07\) (quintet, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_2\text{CH}_2\)-), 2.56 (broad t, 2H, \(J = 7\) Hz, \(=\text{CBrCH}_2\)-), 3.19 (t, 2H, \(J = 7\) Hz, \(-\text{CH}_2\text{I}\)), 5.47 (d, 1H, \(J = 1\) Hz, olefinic proton), 5.68 (broad d, 1H, \(J = 1\) Hz, olefinic proton).

**Exact Mass** calcd. for \(\text{C}_5\text{H}_9\text{BrI}\) (M\(^+\)): 273.8856; found: 273.8855.

**Preparation of (Z)-2-Tri-\(n\)-butylstannyl-2-buten-1-ol (167)**

\[
\text{Sn-}\text{-Bu}_3
\]

\[
\text{167}
\]

\[
\text{Sn-}\text{-Bu}_3 \quad \text{OH}
\]

\[
\text{129}
\]

To stirred freshly prepared tri-\(n\)-butyltin hydride (10.7 g, 36.8 mmol) under an argon atmosphere was added 2-butyln-1-ol (165) (2.58 g, 36.8 mmol, commercially available) and azobisisobutyronitrile (300 mg, 2.11 mmol). The reaction mixture was heated at 80°C in an oil bath for 2.5 h. The crude product was subjected to flash chromatography on silica gel (300 g, elution with petroleum ether-diethyl ether, 8:1) to obtain the two vinylstannanes 167 and 129.

Concentration of the fractions containing the major more polar product, followed by distillation (air-bath temperature 70-75°C/0.15 Torr), afforded 8.66 g (65%) of (Z)-2-tri-\(n\)-butylstannyl-2-buten-1-ol (167) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3300 (broad), 1627, 1377, 1067 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 0.90\) (t, 9H, \(J = 7\) Hz, \(-\text{CH}_2\text{CH}_3\)), 0.98 (t, 6H, \(J = 7\) Hz, \(2J_{\text{Sn-H}} = 54\) Hz, \(\text{Sn-n-BuOH}\) 167 129
\(-\text{SnCH}_2\text{CH}_2\text{-}), 1.16 (t, 1H, \(J = 6\ \text{Hz}\), exchanged with D\(_2\)O, -OH), 1.33 (sextet, 6H, \(J = 7\ \text{Hz}\), -CH\(_2\)CH\(_2\)CH\(_3\)), 1.51 (quintet, 6H, \(J = 7\ \text{Hz}\), -SnCH\(_2\)CH\(_2\)CH\(_2\)\text{-}), 1.75 (broad d, 3H, \(J = 7\ \text{Hz}\), =CHCH\(_3\)), 4.18 (broad d, 2H, \(J \approx 6\ \text{Hz}\), -CH\(_2\)OH), 6.33 (qt, 1H, \(J = 7, 1\ \text{Hz}\), \(^3J_{\text{Sn-H}} = 124\ \text{Hz}\), olefinic proton). Exact Mass calcd. for C\(_{12}\)H\(_{25}\)OSn (M\(^+\)-CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)): 305.0926; found: 305.0927.

Concentration of the fractions containing the minor less polar product, followed by distillation (air-bath temperature 68-72°C/0.15 Torr), afforded 400 mg (3%) of (E)-2-tri-n-butylstannyl-2-buten-1-ol (129) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1\text{H}\) NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3407 (broad), 1618, 1460, 1034 cm\(^{-1}\); \(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz): \(\delta 0.89\) (broad t, 15H, \(J = 7\ \text{Hz}\), \(^2J_{\text{Sn-H}} = 54\ \text{Hz}\), -SnCH\(_2\)CH\(_2\)- and -CH\(_2\)CH\(_3\)), 1.31 (sextet, 6H, \(J = 7\ \text{Hz}\), -CH\(_2\)CH\(_2\)CH\(_2\)\text{-}), 1.48 (quintet, 6H, \(J = 7\ \text{Hz}\), -SnCH\(_2\)CH\(_2\)CH\(_2\)-), 1.56 (broad s, 1H, exchanged with D\(_2\)O, -OH), 1.69 (broad d, 3H, \(J = 7\ \text{Hz}\), =CHCH\(_3\)), 4.35-4.41 (m, 2H, -CH\(_2\)OH), 5.60-5.72 (m, 1H, \(^3J_{\text{Sn-H}} = 69\ \text{Hz}\), olefinic proton). Addition of D\(_2\)O sharpened the multiplet at \(\delta 4.35-4.41\) and converted the multiplet at \(\delta 5.60-5.72\) to a quartet of triplets \((J = 7, 2\ \text{Hz})\). Exact Mass calcd. for C\(_{12}\)H\(_{25}\)OSn (M\(^+\)-CH\(_2\)CH\(_2\)CH\(_2\)CH\(_3\)): 305.0926; found: 305.0930.
Preparation of (Z)-2-Iodo-2-buten-1-ol (173)

To a cold (0°C), stirred solution of iodine (2.62 g, 10.3 mmol) in 20 mL of dry dichloromethane under an argon atmosphere was added a solution of (Z)-2-tri-n-butyllstannyl-2-buten-1-ol (167) (3.72 g, 10.3 mmol) in 10 mL of dry dichloromethane. The reaction mixture was then stirred at room temperature until a pale yellow color persisted for 15 min. Concentration of the solution, followed by flash chromatography of the residual oil on silica gel (45 g, elution with petroleum ether-diethyl ether, 3:1) and distillation (air-bath temperature 40-46°C/0.15 Torr) of the material thus obtained, afforded 1.88 g (92%) of (Z)-2-iodo-2-buten-1-ol (173) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 3:1) and ^1^H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3310 (broad), 1649, 1078, 1010, 807 cm\(^{-1}\); ^1^H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 1.81 (dt, 3H, \(J = 7, 1\) Hz, =CH\(_3\)), 1.88 (broad s, 1H, exchanged with D\(_2\)O, -OH), 4.26 (broad s, 2H, -CH\(_2\)OH), 5.98 (qt, 1H, \(J = 7, 1\) Hz, olefinic proton). **Exact Mass** calcd. for C\(_4\)H\(_7\)OI (M\(^+\)): 197.9543; found: 197.9538.
Preparation of (Z)-1-Bromo-2-iodo-2-butene (174)

![Chemical Structure](image)

To a stirred solution of triphenylphosphine (1.85 g, 7.05 mmol) in 30 mL of dry dichloromethane under an argon atmosphere was added bromine (1.13 g, 7.05 mmol). The resulting pale yellow solution was stirred at room temperature for 10 min. A solution of (Z)-2-iodo-2-buten-1-ol (173) (1.27 g, 6.41 mmol) in 3 mL of dry dichloromethane was added slowly and the resulting mixture was stirred at room temperature for 3 h. Pentane was added to the mixture and the resultant solid was removed by filtration through a short column of Florisil (3 g). The column was eluted with pentane. Concentration of the eluate, followed by distillation (air-bath temperature 40-45°C/0.15 Torr) of the material thus obtained, afforded 1.65 g (98%) of (Z)-1-bromo-2-iodo-2-butene (174) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1635, 1209, 1153, 944, 617 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.81 (d, 3H, $J = 7$ Hz, =CHCH$_3$), 4.36 (broad s, 2H, -CH$_2$Br), 6.06 (qt, 1H, $J = 7, 1$ Hz, olefinic proton). Exact Mass calcd. for C$_4$H$_6$Br$_2$I (M$^+$): 259.8696; found: 259.8693.
Preparation of (E)-3,5-Diiodo-2-pentene (176)

To a stirred solution of (E)-5-chloro-3-iodo-2-pentene (175)* (250 mg, 1.08 mmol) in 5 mL of dry acetone under an argon atmosphere was added sodium iodide (406 mg, 2.71 mmol). The stirred reaction mixture was refluxed for 3 days. Pentane was added to the mixture and the resultant solid was removed by filtration through a short column of Florisil (3 g). The column was eluted with pentane. Concentration of the eluate, followed by distillation (air-bath temperature 65-72°C/0.15 Torr) of the material thus obtained, afforded 302 mg (87%) of (E)-3,5-diiodo-2-pentene (176) as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1633, 1249, 1138, 818 cm⁻¹; 1H NMR (CDCl₃, 300 MHz): δ 1.66 (d, 3H, J = 7 Hz, =CHCH₃), 2.92 (t, 2H, J = 7 Hz, =CICH₂⁻), 3.26 (t, 2H, J = 7 Hz, -CH₂I), 6.39 (q, 1H, J = 7 Hz, olefinic proton). Exact Mass calcd. for C₅H₈I₂ (M⁺): 321.8719; found: 321.8715.

* The sample was generously provided by B.A. Story.
6. Preparation of the Diene Esters 8

General Procedure 5

Deconjugation-Alkylation of Ethyl 3-Trimethylstannyl-2-alkenoates (1 and 2)

To a cold (-78°C), stirred solution of lithium diisopropylamide (1.1-1.3 equiv) in dry THF (~10 mL per mmol of amide), under an argon atmosphere was added, successively, dry hexamethylphosphoramide (1.1-1.3 equiv) and a solution of the appropriate ethyl 3-trimethylstannyl-2-alkenoate 1 or 2 (1 equiv) in dry THF (~1 mL per mmol of ester). After the solution had been stirred at -78°C for 30 min and at 0°C for 30 min, it was recooled to -78°C and the alkyl halide (1.3-1.5 equiv) was added rapidly. The reaction mixture was stirred at -78°C for 1 h. Aqueous sodium bicarbonate was added and the resultant mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO4) and concentrated. The remaining oil was subjected to flash chromatography on silica gel and/or bulb-to-bulb distillation to afford the corresponding alkylated product 8.
Preparation of Ethyl (E)-2-(2-Bromo-2-propenyl)-3-trimethylstannyl-3-pentenoate (216)

Following general procedure 5 outlined above, ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) was converted into the diene ester 216. The following amounts of reagents and solvents were used: LDA (2.00 mmol) in 15 mL of dry THF; HMPA (350 mg, 1.96 mmol); ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) (444 mg, 1.52 mmol) in 1.5 mL of dry THF; 2,3-dibromopropene (147) (445 mg, 2.23 mmol). Flash chromatography of the crude product on silica gel (50 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 88-92°C/0.15 Torr) of the material thus obtained, afforded 461 mg (74%) of the diene ester 216 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1631, 1180, 769 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.12 (s, 9H, 2J⁻Sn-H = 54 Hz, -SnMe₃), 1.24 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.81 (d, 3H, J = 6.5 Hz, =CH₂CH₃), 2.44 (ddd, 1H, J = 14, 6.5, 1 Hz, =CBrCH₂-), 2.94 (ddd, 1H, J = 14, 8, 1 Hz, =CBrCH₂-), 4.06-4.20 (m, 3H, -OCH₂CH₃ and tertiary proton), 5.42 (d, 1H, J = 2 Hz, =CH₂), 5.56 (broad d, 1H, J = 2 Hz, =CH₂), 5.86 (qd, 1H, J = 6.5, 1 Hz, 3J⁻Sn-H = 73 Hz, =CHCH₃). Exact Mass calcd. for C₁₂H₂₀O₂⁷⁹BrSn (M⁺-CH₃): 394.9667; found: 394.9662.
Preparation of Ethyl \((E)-4\text{-Bromo-2-[(2-methoxymethoxy-1-trimethylstannyl)vinyl]-4-pentenoate (217)}\)

Following general procedure 5 outlined above, ethyl \((Z)-4\text{-methoxymethoxy-3-trimethylstannyl-2-butenoate (135)}\) was converted into the diene ester 217. The following amounts of reagents and solvents were used: LDA (1.14 mmol) in 9 mL of dry THF; HMPA (206 mg, 1.15 mmol); ethyl \((Z)-4\text{-methoxymethoxy-3-trimethylstannyl-2-butenoate (135)}\) (305 mg, 0.902 mmol) in 1 mL of dry THF; 2,3-dibromopropene (147) (251 mg, 1.26 mmol). Distillation (air-bath temperature 115-120°C/0.15 Torr) of the crude product afforded 366 mg (89%) of the diene ester 217 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1727, 1614, 1181, 1159, 1123, 1035, 770 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta 0.17\) (s, 9H, \(2\text{J}_{\text{Sn-H}} = 54\) Hz, -SnMe\(_3\)), 1.26 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.53 (ddd, 1H, \(J = 15, 7, 1\) Hz, =CBrCH\(_2\)-), 2.93 (ddd, 1H, \(J = 15, 9, 1\) Hz, =CBrCH\(_2\)-), 3.42 (s, 3H, -OCH\(_3\)), 4.09-4.15 (m, 2H, -OCH\(_2\)CH\(_3\)), 4.27 (ddd, 1H, \(J = 9, 7, 1\) Hz, tertiary proton), 4.85 (s, 2H, -OCH\(_2\)O-), 5.42 (d, 1H, \(J = 2\) Hz, =CH\(_2\)), 5.58 (broad d, 1H, \(J \sim 2\) Hz, =CH\(_2\)), 6.05 (d, 1H, \(J = 1\) Hz, \(3\text{J}_{\text{Sn-H}} = 36\) Hz, =CHO-). Exact Mass calcd. for C\(_{13}\)H\(_{22}\)O\(_4\)\(^{79}\)BrSn (M\(^{+}\)-CH\(_3\)): 440.9722; found: 440.9716.
Preparation of Ethyl (E)-2-(2-Bromo-2-propenyl)-6-methoxymethoxy-3-trimethylstannyl-3-hexenoate (218)

Following general procedure 5 outlined above, ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (136) was converted into the diene ester 218. The following amounts of reagents and solvents were used: LDA (1.71 mmol) in 13 mL of dry THF; HMPA (309 mg, 1.73 mmol); ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (136) (488 mg, 1.33 mmol) in 1 mL of dry THF; 2,3-dibromopropene (147) (387 mg, 1.94 mmol). Distillation (air-bath temperature 138-142°C/0.15 Torr) of the crude product afforded 556 mg (86%) of the diene ester 218 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1631, 1209, 1179, 1152, 1035, 768 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 0.15 (s, 9H, \(2J_{\text{Sn-H}} = 54\) Hz, -SnMe\(_3\)), 1.26 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.47 (ddd, 1H, \(J = 15, 6.5, 1\) Hz, =CBrCH\(_2\)-), 2.51-2.61 (m, 2H, =CHCH\(_2\)-), 2.96 (ddd, 1H, \(J = 15, 8, 1\) Hz, =CBrCH\(_2\)-), 3.36 (s, 3H, -OCH\(_3\)), 3.60 (t, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_2\)-), 4.05 (ddd, 1H, \(J = 8, 6.5, 1\) Hz, tertiary proton), 4.08-4.18 (m, 2H, -OCH\(_2\)CH\(_3\)), 4.64 (s, 2H, -OCH\(_2\)O-), 5.42 (d, 1H, \(J = 2\) Hz, =CH\(_2\)), 5.56 (dd, 1H, \(J = 2, 1\) Hz, =CH\(_2\)), 5.79 (td, 1H, \(J = 7, 1\) Hz, \(3J_{\text{Sn-H}} = 72\) Hz, =CHCH\(_2\)-). Exact Mass calcd. for C\(_{15}\)H\(_{26}\)O\(_4\)\(^{79}\)BrSn (M\(^+\)-CH\(_3\)): 469.0035; found: 469.0030.
Preparation of Ethyl (E)-2-(2-bromo-2-propenyl)-7-tert-butyldimethylsilyloxy-3-trimethylstannyl-3-heptenoate (219)

Following general procedure 5 outlined above, ethyl (Z)-7-tert-butyldimethylsilyloxy-3-trimethylstannyl-2-heptenoate (137) was converted into the diene ester 219. The following amounts of reagents and solvents were used: LDA (3.35 mmol) in 25 mL of dry THF; HMPA (587 mg, 3.28 mmol); ethyl (Z)-7-tert-butyldimethylsilyloxy-3-trimethylstannyl-2-heptenoate (137) (1.15 g, 2.56 mmol) in 2.5 mL of dry THF; 2,3-dibromopropene (147) (774 mg, 3.87 mmol). The crude product was subjected to flash chromatography on silica gel (90 g, elution with petroleum ether-diethyl ether, 40:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 1.10 g (75%) of the diene ester 219 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1631, 1180, 1100, 837, 775 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.06 (s, 6H, -SiMe$_2$), 0.13 (s, 9H, $^2$J$_{Sn-H}$ = 56 Hz, -SnMe$_3$), 0.90 (s, 9H, -SiCMe$_3$), 1.25 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.63 (quintet, 2H, $J$ = 7 Hz, -CH$_2$CH$_2$CH$_2$-), 2.21-2.37 (m, 2H, =CHCH$_2$-), 2.44 (ddd, 1H, $J$ = 14, 6.5, 1 Hz, =CBrCH$_2$-), 2.95 (ddd, 1H, $J$ = 14, 7.5, 1 Hz, =CBrCH$_2$-), 3.64 (t, 2H, $J$ = 7 Hz, -OCH$_2$CH$_2$-), 4.05 (ddd, 1H, $J$ = 7.5, 6.5, 1 Hz, tertiary proton), 4.08-4.16 (m, 2H, -OCH$_2$CH$_3$), 5.42 (broad d, 1H, $J$ = 2 Hz, =CH$_2$), 5.56 (dd,
Preparation of Ethyl 4-Bromo-2-[1-trimethylstannyl]vinyl]-4-pentenoate (221)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-butenoate (25) was converted into the diene ester 221. The following amounts of reagents and solvents were used: LDA (2.93 mmol) in 20 mL of dry THF; HMPA (523 mg, 2.92 mmol); ethyl (E)-3-trimethylstannyl-2-butenoate (25) (676 mg, 2.43 mmol) in 2 mL of dry THF; 2,3-dibromopropene (147) (735 mg, 3.68 mmol). Flash chromatography of the crude product on silica gel (60 g, elution with petroleum ether-diethyl ether, 40:1), afforded the more polar diene ester 221 (666 mg, 69%, after distillation with air-bath temperature 80-85°C/0.15 Torr), as a colorless oil and the less polar diene ester 226 (170 mg, 17%, after distillation with air-bath temperature 78-86°C/0.15 Torr), also as a colorless oil. Analysis of both oils by GLC, TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that each consisted of one component.

The diene ester 221 exhibited IR (film): 1728, 1631, 1277, 771 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 0.19 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 1.26 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 2.55 (dd, 1H, $J$ = 15, 8 Hz, =CBrCH$_2$-), 2.95 (dd, 1H, $J$ = 15, 8 Hz, =CBrCH$_2$-), 3.60 (t, 1H, $J$ = 8 Hz, tertiary proton), 4.09-
4.21 (m, 2H, -OCH₂CH₃), 5.36 (d, 1H, J = 2 Hz, 3JSn-H = 66 Hz, Hₐ), 5.44 (d, 1H, J = 2 Hz, -BrC=CH₂), 5.57 (d, 1H, J = 2 Hz, -BrC=CH₂), 5.84 (dd, 1H, J = 2, 1 Hz, 3JSn-H = 137 Hz, Hₐ). **Exact Mass** calcd. for C₁₁H₁₈O₂⁷⁹BrSn (M⁺-CH₃): 380.9511; found: 380.9508.

The diene ester 226 exhibited IR (film): 1703, 1630, 1209, 772 cm⁻¹; 
¹H NMR (CDCl₃, 400 MHz): δ 0.20 (s, 9H, 2JSn-H = 54 Hz, -SnMe₃), 1.30 (t, 3H, J = 7 Hz, -OCH₂CH₃), 2.52 (broad t, 2H, J = 8 Hz, =CBrCH₂-), 2.70 (broad t, 2H, J = 8 Hz, =C(SnMe₃)CH₂-), 4.19 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.42, 4.56 (broad d each, 2H, J ~ 2 Hz each, =CH₂), 6.40 (broad t, 1H, J ~ 2 Hz, 3JSn-H = 116 Hz, Hₐ). **Exact Mass** calcd. for C₁₁H₁₈O₂⁷⁹BrSn (M⁺-CH₃): 380.9511; found: 380.9511.

**Preparation of Ethyl (Z)-2-(2-Bromo-2-propenyl)-3-trimethylstannyl-3-pentenoate (222)**

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-pentenoate (36) was converted into the diene ester 222. The following amounts of reagents and solvents were used: LDA (2.07 mmol) in 16 mL of dry THF; HMPA (371 mg, 2.07 mmol); ethyl (E)-3-trimethylstannyl-2-pentenoate (36) (475 mg, 1.63 mmol) in 1.5 mL of dry THF; 2,3-dibromopropene (147) (484 mg, 2.42 mmol). Flash chromatography of the crude product on silica gel (50 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 85-
90°C/0.15 Torr) of the material thus obtained, afforded 485 mg (72%) of the diene ester 222. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1729, 1631, 1178, 771 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.23 (s, 9H, 2JSn-H = 52 Hz, -SnMe₃), 1.25 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.75 (d, 3H, J = 7 Hz, =CHCH₃), 2.56 (dd, 1H, J = 15, 8 Hz, =CBrCH₂-), 2.96 (dd, 1H, J = 15, 6 Hz, =CBrCH₂-), 3.51 (broad t, 1H, J ~ 7 Hz, tertiary proton), 4.13 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.40 (d, 1H, J = 1.5 Hz, =CH₂), 5.53 (broad s, 1H, =CH₂), 6.20 (q, 1H, J = 7 Hz, 3JSn-H = 128 Hz, =CHCH₃). Exact Mass calcd. for C₁₂H₂₀O₂⁷⁹BrSn (M⁺-CH₃); 394.9667; found: 394.9674.

Preparation of Ethyl (Z)-4-Bromo-2-[(2-methoxymethoxy-1-trimethylstannyl)vinyl]-4-pentenoate (223)

Following general procedure 5 outlined above, ethyl (E)-4-methoxymethoxy-3-trimethylstannyl-2-butoenoate (142) was converted into the diene ester 223. The following amounts of reagents and solvents were used: LDA (2.00 mmol) in 15 mL of dry THF; HMPA (350 mg, 1.96 mmol); ethyl (E)-4-methoxymethoxy-3-trimethylstannyl-2-butoenoate (142) (512 mg, 1.51 mmol) in 1.5 mL of dry THF;
2,3-dibromopropene (147) (464 mg, 2.32 mmol). Distillation (air-bath temperature 118-122°C/0.15 torr) of the crude product afforded 624 mg (91%) of the diene ester 223 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and \(^1H\) NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1730, 1626, 1160, 1133, 1049, 771 cm\(^{-1}\); \(^1H\) NMR (CDCl\(_3\), 400 MHz): \(\delta 0.21\) (s, 9H, \(J_{Sn-H} = 54\) Hz, -SnMe\(_3\)), 1.25 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.54 (dd, 1H, \(J = 15, 9\) Hz, =CBrCH\(_2\)-), 2.96 (dd, 1H, \(J = 15, 6\) Hz, =CBrCH\(_2\)-), 3.37 (s, 3H, -OCH\(_3\)), 3.46 (dd, 1H, \(J = 9, 6\) Hz, tertiary proton), 4.13 (q, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 4.80 (s, 2H, -OCH\(_2\)O-), 5.42 (d, 1H, \(J = 1.5\) Hz, =CH\(_2\)), 5.54 (broad s, 1H, =CH\(_2\)), 6.73 (s, 1H, \(J_{Sn-H} = 88\) Hz, =CHO-). \textbf{Exact Mass} calcd. for C\(_{13}\)H\(_{22}\)O\(_4\)BrSn (M+-CH\(_3\)): 440.9724; found: 440.9732.

\textbf{Preparation of Ethyl (Z)-2-(2-Bromo-2-propenyl)-6-methoxymethoxy-3-trimethylstannyl-3-hexenoate (224)}

Following general procedure 5 outlined above, ethyl (E)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (143) was converted into the diene ester 224. The following amounts of reagents and solvents were used: LDA (1.00 mmol) in 7 mL of dry THF; HMPA (175 mg, 0.98 mmol); ethyl (E)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (143) (278 mg, 0.76 mmol) in 1 mL of dry THF;
2,3-dibromopropene (147) (232 mg, 1.16 mmol). Distillation (air-bath temperature 138-144°C/0.15 Torr) of the crude product afforded 350 mg (95%) of the diene ester 224 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1729, 1631, 1179, 1153, 1111, 1040, 772 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.23 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 1.25 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 2.37 (q, 2H, $J$ = 7 Hz, =CHCH$_2$-), 2.57 (dd, 1H, $J$ = 15, 8 Hz, =CBrCH$_2$-), 2.97 (dd, 1H, $J$ = 15, 6 Hz, =CBrCH$_2$-), 3.35 (s, 3H, -OCH$_3$), 3.52 (two broad overlapped triplets, 3H, $J$ ~ 7 Hz, -OCH$_2$CH$_2$- and tertiary proton), 4.13 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 4.62 (s, 2H, -OCH$_2$O-), 5.42 (broad d, 1H, $J$ = 1.5 Hz, =CH$_2$), 5.53 (broad s, 1H, =CH$_2$), 6.13 (t, 1H, $J$ = 7 Hz, $^3$J$_{Sn-H}$ = 128 Hz, =CHCH$_2$-). Irradiation at $\delta$ 2.37 simplified one of the triplets at $\delta$ 3.52 to a singlet and the triplet at $\delta$ 6.13 to a singlet. Exact Mass calcd. for C$_{15}$H$_{26}$O$_4$BrSn (M$^+$-CH$_3$): 469.0035; found: 469.0028.

Preparation of Ethyl (Z)-2-(2-Bromo-2-propenyl)-7-tert-butyldimethylsilyloxy-3-trimethylstanny1-3-heptenoate (225)
Following general procedure 5 outlined above, ethyl (E)-7-tert-butylidimethylsilyloxy-3-trimethylstannyl-2-heptenoate (144) was converted into the diene ester 225. The following amounts of reagents and solvents were used: LDA (2.78 mmol) in 20 mL of dry THF; HMPA (494 mg, 2.76 mmol); ethyl (E)-7-tert-butylidimethylsilyloxy-3-trimethylstannyl-2-heptenoate (144) (959 mg, 2.13 mmol) in 2 mL of dry THF; 2,3-dibromopropene (147) (638 mg, 3.19 mmol). The crude product was subjected to flash chromatography on silica gel (90 g, elution with petroleum ether-diethyl ether, 40:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 945 mg (78%) of the diene ester 225 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1731, 1631, 1103, 836, 775 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.05 (s, 6H, -SiMe₂), 0.19 (s, 9H, 2J_{Sn-H} = 54 Hz, -SnMe₃), 0.88 (s, 9H, -SiCMe₃), 1.23 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.55 (quintet, 2H, J = 7 Hz, -CH₂CH₂CH₂⁻), 2.07-2.15 (m, 2H, =CHCH₂⁻), 2.54 (dd, 1H, J = 15, 9 Hz, =CBrCH₂⁻), 2.94 (dd, 1H, J = 15, 6 Hz, =CBrCH₂⁻), 3.48 (dd, 1H, J = 9, 6 Hz, tertiary proton), 3.58 (t, 2H, J = 7 Hz, -OCH₂CH₂⁻), 4.11 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.49 (d, 1H, J = 1.5 Hz, =CH₂), 5.51 (broad s, 1H, =CH₂), 6.12 (broad t, 1H, J = 7 Hz, 3J_{Sn-H} = 131 Hz, =CHCH₂⁻). Exact Mass calcd. for C₂₀H₃₈O₃Si⁷⁹BrSn (M⁺-CH₃): 553.0794; found: 553.0797.
Preparation of Ethyl (Z)-4-Iodo-2-((E)-1-trimethylstannyl-1-propenyl)-4-hexenoate (228)

Following general procedure 5 outlined above, ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) was converted into the diene ester 228. The following amounts of reagents and solvents were used: LDA (2.35 mmol) in 22 mL of dry THF; HMPA (422 mg, 2.36 mmol); ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) (632 mg, 2.16 mmol) in 2 mL of dry THF; (Z)-1-bromo-2-iodo-2-butene (174) (700 mg, 2.68 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 200:1), followed by distillation (air-bath temperature 112-118°C/0.15 Torr) of the material thus obtained, afforded 710 mg (70%) of the diene ester 228 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1727, 1678, 1648, 1196, 1173, 768 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.13 (s, 9H, -SnMe₃), 1.24 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.71 (d, 3H, J = 7 Hz, =CHCH₃), 1.83 (d, 3H, J = 7 Hz, =CHCH₃), 2.49 (dd, 1H, J = 14, 6 Hz, =ClCH₂-), 3.00 (dd, 1H, J = 14, 9 Hz, =ClCH₂-), 4.04-4.18 (m, 3H, -OCH₂CH₃ and tertiary proton), 5.57 (q, 1H, J = 7 Hz, Hₐ), 5.85 (qd, 1H, J = 7, 1 Hz, 3JSn-H = 74 Hz, Hₐ). Exact Mass calcd. for C₁₃H₂₂O₂I₃Sn (M⁺-CH₃): 456.9685; found: 456.9682.
Preparation of Ethyl (Z)-4-Iodo-2-((Z)-1-trimethylstannyl-1-propenyl)-4-hexenoate (229)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-pentenoate (36) was converted into the diene ester 229. The following amounts of reagents and solvents were used: LDA (0.78 mmol) in 7 mL of dry THF; HMPA (144 mg, 0.804 mmol); ethyl (E)-3-trimethylstannyl-2-pentenoate (36) (203 mg, 0.695 mmol) in 0.5 mL of dry THF; (Z)-1-bromo-2-iodo-2-butene (174) (235 mg, 0.900 mmol) in 0.5 mL of THF. Flash chromatography of the crude product on silica gel (20 g, elution with petroleum ether-diethyl ether, 200:1), followed by distillation (air-bath temperature 110-116°C/0.15 Torr) of the material thus obtained, afforded 203 mg (62%) of the diene ester 229 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1648, 1620, 1167, 769 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.21 (s, 9H, ²J₇Sn-H = 54 Hz, -SnMe₃), 1.23 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.70 (d, 3H, J = 7 Hz, =CHCH₃), 1.73 (d, 3H, J = 7 Hz, =CHCH₃), 2.60 (dd, 1H, J = 14, 8 Hz, =ClCH₂⁻), 2.98 (dd, 1H, J = 14, 6 Hz, =ClCH₂⁻), 3.50 (dd, 1H, J = 8, 6 Hz, tertiary proton), 4.06-4.16 (m, 2H, -OCH₂CH₃), 5.55 (q, 1H, J = 7 Hz, H₄), 6.19 (q, 1H, J = 7 Hz, ³J₇Sn-H = 133 Hz, H₅). Exact Mass calcd. for C₁₃H₂₂O₂Sn (M⁺-CH₃): 456.9685; found: 456.9689.
Preparation of Ethyl 5-Bromo-2-[(1-trimethylstannyl)vinyl]-5-hexenoate (230)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-butenoate (2.1) was converted into the diene ester 230. The following amounts of reagents and solvents were used: LDA (1.60 mmol) in 14 mL of dry THF; HMPA (288 mg, 1.61 mmol); ethyl (E)-3-trimethylstannyl-2-butenoate (25) (391 mg, 1.41 mmol) in 1 mL of dry THF; 2-bromo-4-iodo-1-butene (160) (477 mg, 1.83 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (35 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 85-92°C/0.15 Torr) of the material thus obtained, afforded 472 mg (82%) of the diene ester 230 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1630, 1178, 771 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.19 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 1.27 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.75 (dq, 1H, $J$ = 14, 7 Hz, -CHCH$_2$CH$_2$-), 2.07 (dq, 1H, $J$ = 14, 7 Hz, -CHCH$_2$CH$_2$-), 2.33-2.47 (m, 2H, -CBr=CH$_2$), 3.19 (t, 1H, $J$ = 7 Hz, tertiary proton), 4.14 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 5.36 (d, 1H, $J$ = 2 Hz, $^3$J$_{Sn-H}$ = 65 Hz, H$_a$), 5.43 (d, 1H, $J$ = 1.5 Hz, -CBr=CH$_2$), 5.58 (d, 1H, $J$ = 1.5 Hz, -CBr=CH$_2$), 5.78 (d, 1H, $J$ = 2 Hz, $^3$J$_{Sn-H}$ = 139 Hz, H$_b$). Exact Mass calcd. for C$_{12}$H$_{20}$O$_2$BrSn (M$^+$-CH$_3$): 394.9667; found: 394.9669.
Preparation of Ethyl 5-Bromo-2-((E)-1-trimethylstannyl-1-propenyl)-5-hexenoate (231)

Following general procedure 5 outlined above, ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) was converted into the diene ester 231. The following amounts of reagents and solvents were used: LDA (1.61 mmol) in 14 mL of dry THF; HMPA (288 mg, 1.61 mmol); ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) (410 mg, 1.40 mmol) in 1 mL of dry THF; 2-bromo-4-iodo-1-butene (160) (476 mg, 1.82 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (35 g, elution with petroleum ether-diethyl ether, 200:1), followed by distillation (air-bath temperature 92-96°C/0.15 Torr) of the material thus obtained, afforded 447 mg (75%) of the diene ester 231 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1630, 1177, 768 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.14 (s, 9H, ²J₈₉-H = 54 Hz, -SnMe₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.70 (broad dq, 1H, J = 14, 7 Hz, -CHCH₂CH₂-), 1.77 (d, 3H, J = 7 Hz, -CHCH₃), 2.09 (broad dq, 1H, J = 14, 7 Hz, -CHCH₂CH₂-), 2.33-2.47 (m, 2H, -CH=CHR₂), 3.69 (broad t, 1H, J = 7 Hz, tertiary proton), 4.13 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.44 (d, 1H, J = 1.5 Hz, -CBr=CH₂), 5.58 (d, 1H, J = 1.5 Hz, -CBr=CH₂), 5.87 (qd, 1H, J = 7, 1 Hz, ³J₈₉-H = 74 Hz, -CHCH₃). Exact Mass calcd. for C₁₃H₂₂O₂⁷⁹BrSn (M⁺-CH₃): 408.9826; found: 408.9825.
Preparation of Ethyl 5-Bromo-2-((Z)-1-trimethylstannyl-1-propenyl)-5-hexenoate (232)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-pentenoate (36) was converted into the diene ester 232. The following amounts of reagents and solvents were used: LDA (1.85 mmol) in 16 mL of dry THF; HMPA (330 mg, 1.84 mmol); ethyl (E)-3-trimethylstannyl-2-pentenoate (36) (485 mg, 1.66 mmol) in 1.5 mL of dry THF; 2-bromo-4-iodo-1-butene (160) (560 mg, 2.15 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (35 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 90-95°C/0.15 Torr) of the material thus obtained, afforded 508 mg (72%) of the diene ester 232 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1629, 1177, 771 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.23 (s, 9H, 2J_Sn-H = 54 Hz, -SnMe₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.69-1.80 (m, 1H, -CHCH₂CH₂-), 1.77 (d, 3H, J = 7 Hz, =CHCH₃), 2.07-2.17 (m, 1H, -CHCH₂CH₂-), 2.33-2.47 (m, 2H, =CBrCH₂-), 3.10 (broad t, 1H, J = 7 Hz, tertiary proton), 4.14 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.42 (broad d, 1H, J ~ 1 Hz, -CBr=CH₂), 5.58 (broad d, 1H, J ~ 1 Hz, -CBr=CH₂), 6.14 (q, 1H, J = 7 Hz, 3J_Sn-H = 133 Hz, =CHCH₃) Exact Mass calcd. for C₁₃H₂₂O₂⁷⁹BrSn (M⁺-CH₃): 408.9826; found: 408.9824.
Preparation of Ethyl (E)-5-Iodo-2-[(1-trimethylstannyl)vinyl]-5-heptenoate (233)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-butenoate (25) was converted into the diene ester 233. The following amounts of reagents and solvents were used: LDA (0.78 mmol) in 7 mL of dry THF; HMPA (144 mg, 0.804 mmol); ethyl (E)-3-trimethylstannyl-2-butenoate (25) (191 mg, 0.687 mmol) in 0.5 mL of dry THF; (E)-3,5-diiodo-2-pentene (176) (288 mg, 0.894 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 108-116°C/0.15 Torr) of the material thus obtained, afforded 247 mg (76%) of the diene ester 233 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1634, 1162, 770 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.20 (s, 9H, ²J₈-H = 54 Hz, -SnMe₃), 1.27 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.61 (d, 3H, J = 7 Hz, =CHCH₂), 1.65-1.75 (m, 1H, -CHCH₂CH₂-), 1.96-2.07 (m, 1H, -CHCH₂CH₂-), 2.28-2.45 (m, 2H, =CICH₂), 3.18 (broad t, 1H, tertiary proton), 4.15 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.35 (d, 1H, J = 2 Hz, ³J₈-H = 66 Hz, H_a), 5.78 (dd, 1H, J = 2, 1 Hz, ³J₈-H = 140 Hz, H_b), 6.26 (q, 1H, J = 7 Hz, =CHCH₃). Exact Mass calcd. for C₁₃H₂₂O₂I₃Sn (M⁺-CH₃): 456.9685; found: 456.9687.
Preparation of Ethyl 6-Bromo-2-[(1-trimethylstannyl)vinyl]-6-heptenoate (234)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-butenoate (25) was converted into the diene ester 234. The following amounts of reagents and solvents were used: LDA (1.78 mmol) in 15 mL of dry THF; HMPA (320 mg, 1.78 mmol); ethyl (E)-3-trimethylstannyl-2-butenoate (25) (414 mg, 1.49 mmol) in 1 mL of dry THF; 2-bromo-5-iodo-pentene (163) (533 mg, 1.94 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (35 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 92-96°C/0.15 Torr) of the material thus obtained, afforded 473 mg (75%) of the diene ester 234 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1630, 1162, 771 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.17 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, -SnMe$_3$), 1.26 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.44-1.60 (m, 3H), 1.75-1.85 (m, 1H), 2.43 (broad t, 2H, $J$ = 7 Hz, =CBrCH$_2$-), 3.16 (broad t, 1H, $J$ = 7 Hz, tertiary proton), 4.14 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 5.32 (d, 1H, $J$ = 2 Hz, $^3$J$_{Sn-H}$ = 64 Hz, Ha), 5.40 (d, 1H, $J$ = 1 Hz, -CBr=CH$_2$), 5.57 (d, 1H, $J$ = 1 Hz, -CBr=CH$_2$), 5.77 (d, 1H, $J$ = 2 Hz, $^3$J$_{Sn-H}$ = 144 Hz, Hb). Exact Mass calcd. for C$_{13}$H$_{22}$O$_2$BrSn (M$^+$-CH$_3$): 408.9826; found: 408.9826.
Preparation of Ethyl 6-Bromo-2-((E)-1-trimethylstannyl-1-propenyl)-5-heptenoate (235)

Following general procedure 5 outlined above, ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) was converted into the diene ester 235. The following amounts of reagents and solvents were used: LDA (0.57 mmol) in 5 mL of dry THF; HMPA (103 mg, 0.575 mmol); ethyl (Z)-3-trimethylstannyl-2-pentenoate (35) (128 mg, 0.438 mmol) in 0.5 mL of dry THF; 2-bromo-5-iodo-1-pentene (163) (180 mg, 0.654 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 102-106°C/0.15 Torr) of the material thus obtained, afforded 160 mg (83%) of the diene ester 235 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1630, 1186, 769 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.13 (s, 9H, 2J₄Sn-H = 54 Hz, -SnMe₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.37-1.62 (m, 3H), 1.77 (d, 3H, J = 7 Hz, =CHCH₃), 1.78-1.86 (m, 1H), 2.43 (t, 2H, J = 7 Hz, =CBrCH₂-), 3.65 (td 1H, J = 7, 1 Hz, tertiary proton), 4.13 (q, 2H, J = 7 Hz, -OCH₂CH₃), 5.40 (d, 1H, J = 1.5 Hz, -CBr=CH₂), 5.56 (d, 1H, J = 1.5 Hz, -CBr=CH₂), 5.84 (qd, 1H, J = 7, 1 Hz, 3J₄Sn-H = 74 Hz, =CHCH₃). Exact Mass calcd. for C₁₄H₂₄O₂⁷⁹BrSn (M⁺-CH₃): 422.9982; found: 422.9978.
Preparation of Ethyl 6-Bromo-2-((E)-4-methoxymethoxy-1-trimethylstannyl-1-butenyl)-6-heptenoate (236)

Following general procedure 5 outlined above, ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (136) was converted into the diene ester 236. The following amounts of reagents and solvents were used: LDA (0.33 mmol) in 4 mL of dry THF; HMPA (59 mg, 0.33 mmol); ethyl (Z)-6-methoxymethoxy-3-trimethylstannyl-2-pentenoate (136) (110 mg, 0.30 mmol) in 0.5 mL of dry THF; 2-bromo-5-iodo-pentene (163) (110 mg, 0.40 mmol) in 0.5 mL of dry THF. The crude product was subjected to flash chromatography on silica gel (5 g, elution with petroleum ether-diethyl ether, 8:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 125 mg (81%) of the diene ester 236 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1727, 1631, 1186, 1152, 1111, 770 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.13 (s, 9H, $^2$J$_{\text{Sn-H}}$ = 54 Hz, -SnMe$_3$), 1.25 (t, 3H, $^3$J = 7 Hz, -OCH$_2$CH$_3$), 1.36-1.62 (m, 3H), 1.77-1.87 (m, 1H), 2.39-2.55 (m, 4H, =CHCH$_2$- and =CBrCH$_2$-), 3.37 (s, 3H, -OCH$_3$), 3.55-3.69 (m, 3H, -OCH$_2$CH$_2$- and tertiary proton), 4.12 (q, 2H, $^3$J = 7 Hz, -OCH$_2$CH$_3$), 4.64 (s, 2H, -OCH$_2$O-), 5.40 (d, 1H, $^3$J = 1.5 Hz, -CBr=CH$_2$), 5.56 (d, 1H, $^3$J = 1.5 Hz, -CBr=CH$_2$), 5.76 (broad t, 1H, $^3$J = 7 Hz, $^3$J$_{\text{Sn-H}}$ =
74 Hz, =CHCH2-. Exact Mass calcd. for C17H30O479BrSn (M+ -CH3): 497.0350; found: 497.0356.

Preparation of Ethyl 7-Bromo-2-[(1-trimethylstannyl)vinyl]-7-octenoate (237)

Following general procedure 5 outlined above, ethyl (E)-3-trimethylstannyl-2-butenoate (25) was converted into the diene ester 237. The following amounts of reagents and solvents were used: LDA (2.14 mmol) in 19 mL of dry THF; HMPA (402 mg, 2.24 mmol); ethyl (E)-3-trimethylstannyl-2-butenoate (25) (537 mg, 1.93 mmol) in 2 mL of dry THF; 2,6-dibromo-1-hexene (162) (600 mg, 2.48 mmol) in 1 mL of dry THF. Flash chromatography of the crude product on silica gel (75 g, elution with petroleum ether-diethyl ether, 200:3), followed by distillation (air-bath temperature 102-107°C/0.15 Torr) of the material thus obtained, afforded 620 mg (73%) of the diene ester 237 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 200:3) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1727, 1630, 1185,
771 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 0.17 (s, 9H, \(2J_{\text{Sn-H}} = 54\) Hz, \(-\text{SnMe}_3\)), 1.20-1.37 (m, 2H), 1.26 (t, 3H, \(J = 7\) Hz, \(-\text{OCH}_2\text{CH}_3\)), 1.44-1.62 (m, 3H), 1.77-1.87 (m, 1H), 2.41 (broad t, 2H, \(J = 7\) Hz, \(-\text{CBrCH}_2\)) \(^{-}\), 3.15 (broad t, 1H, \(J = 7\) Hz, tertiary proton), 4.13 (q, 2H, \(J = 7\) Hz, \(-\text{OCH}_2\text{CH}_3\)), 5.31 (d, 1H, \(J = 2\) Hz, \(3J_{\text{Sn-H}} = 67\) Hz, \(H_a\)), 5.39 (broad d, 1H, \(J \sim 1.5\) Hz, \(-\text{CBr=CH}_2\)), 5.55 (broad d, 1H, \(J \sim 1.5\) Hz, \(-\text{CBr=CH}_2\)), 5.76 (dd, 1H, \(J = 2, 1\) Hz, \(3J_{\text{Sn-H}} = 142\) Hz, \(H_b\)). **Exact Mass** calcd. for \(\text{C}_{14}\text{H}_{24}\text{O}_2\text{BrSn} (M^+\text{-CH}_3)\): 422.9982; found: 422.9986.

**Preparation of Ethyl (E)-2-(2-Bromo-2-propenyl)-7-hydroxy-3-trimethylstannyl-3-heptenoate (251)**

![Chemical Structure](image)

To a cold (0°C), stirred solution of the diene ester 219 (793 mg, 1.39 mmol) in 6 mL of dry THF under an argon atmosphere was added a solution of tetra-\(n\)-butylammonium fluoride (732 mg, 2.80 mmol) in 2.8 mL of dry THF. The reaction mixture was warmed to room temperature and stirred for 2 h. Water was added and the resultant mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed (water, brine), dried (MgSO\(_4\)) and concentrated. The residual oil was subjected to flash chromatography on silica gel.
(25 g, elution with petroleum ether-ethyl acetate, 9:2). Concentration of the appropriate fractions, followed by distillation (air-bath temperature 125-132°C/0.15 Torr) of the material thus obtained, afforded 410 mg (65%) of the diene alcohol 251 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-ethyl acetate, 9:2) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3368 (broad), 1729, 1631, 1181, 770 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.15 (s, 9H, $^2$J$_{Sn-H}$ = 54 Hz, $-SnMe_3$), 1.27 (t, 3H, $J$ = 7 Hz, $-OCH_2CH_3$), 1.55-1.62 (broad s, 1H, exchanged with D$_2$O, $-OH$), 1.63-1.79 (m, 2H, $-CH_2CH_2CH_2-$), 2.23-2.33 (m, 1H, $=CHCH_2-$), 2.39-2.51 (m, 2H, $=CHCH_2-$ and $=CBrCH_2-$), 2.97 (dd, 1H, $J$ = 16, 7 Hz, $=CBrCH_2-$), 3.66 (broad t, 2H, $J$ ~ 7 Hz, $-CH_2OH$), 4.07-4.17 (m, 3H, tertiary proton and $-OCH_2CH_3$), 5.43 (broad d, 1H, $J$ = 2 Hz, $=CH_2$), 5.56 (broad s, 1H, $=CH_2$), 5.75 (t, 1H, $J$ = 7 Hz, $^3$J$_{Sn-H}$ = 73 Hz, $=CHCH_2-$). Exact Mass calcd. for C$_{14}$H$_{24}$O$_3$BrSn (M$^+$-CH$_3$): 438.9922; found: 438.9919.
7. Preparation of the Cyclobutanecarboxylates 9 and the Larger Ring Homologs

General Procedure 6

Intramolecular Palladium(0)-Catalyzed Coupling Reactions

A stirred solution of tetrakis(triphenylphosphine)palladium(0) (0.05 equiv) and the diene ester 8 (1 equiv) in dry N,N-dimethylformamide (~10 mL per mmol of ester), under an argon atmosphere, was heated at 80°C for 1 h. The reaction mixture was cooled to room temperature, diluted with water, and then was extracted thoroughly with pentane. The combined organic extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel. Concentration of the appropriate fractions, followed by bulb-to-bulb distillation of the resultant oil, afforded the corresponding cyclized product 9, 10 or 11.
Preparation of Ethyl 2,3-bis(Methylene)cyclobutancarboxylate (253)

Following general procedure 6 outlined above, the diene ester 221 was converted into the cyclobutancarboxylate 253. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (14 mg, 12 μmol); the diene ester 221 (99.0 mg, 0.249 mmol) in 3 mL of dry DMF. Flash chromatography of the crude product on silica gel (4 g, elution with pentane-diethyl ether, 19:1), followed by distillation (air-bath temperature 68-72°C/45 Torr) of the material thus obtained, afforded 31.0 mg (82%) of the cyclobutancarboxylate 253 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 19:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1736, 1657, 1645, 1181, 1041, 888 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.28 (t, 3H, J = 7 Hz, -OCH₂CH₃), 2.81 (dddd, 1H, J = 15, 9, 3, 2 Hz, Hₖ), 3.04 (dddd, 1H, J = 15, 6, 3, 2 Hz, H₇), 3.69-3.78 (m, 1H, Hₐ), 4.12-4.26 (m, 2H, -OCH₂CH₃), 4.81 (broad s, 1H, Hₙ), 5.00 (broad d, 1H, J ~ 2 Hz, H₉), 5.23 (t, 1H, J = 2 Hz, Hₐ), 5.26 (d, 1H, J = 3 Hz, H₉). Irradiation at δ 2.81 simplified the signal at δ 3.04, sharpened the singlet at δ 4.81 and converted the multiplet at δ 3.69-3.78 to a doublet of doublets of doublets (J = 6, 3, 2 Hz) and the triplet at δ 5.23 to a doublet (J = 2 Hz). Irradiation at δ 3.74 simplified the signals at δ 2.81 and δ 3.04, and converted
both doublets at $\delta$ 5.00 and $\delta$ 5.26 to singlets. **Exact Mass** calcd. for C$_9$H$_{12}$O$_2$ (M$^+$): 152.0837; found: 152.0843.

**Preparation of Ethyl (E)-2-Ethyldene-3-methylenecyclobutane carboxylate (254)**

Following general procedure 6 outlined above, the diene ester 216 was converted into the cyclobutane carboxylate 254. The following amounts of reagents and solvents were used: Pd(PPh$_3$)$_4$ (35 mg, 30 $\mu$mol); the diene ester 216 (244 mg, 0.594 mmol) in 6 mL of dry DMF. Flash chromatography of the crude product on silica gel (5 g, elution with petroleum ether-diethyl ether, 19:1), followed by distillation (air-bath temperature 84-90°C/45 Torr) of the material thus obtained, afforded 88.0 mg (89%) of the cyclobutane carboxylate 254 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 19:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1734, 1676, 1179, 1043, 868 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.27 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.68 (d, 3H, $J$ = 7 Hz, =CHCH$_3$), 2.80 (ddt, 1H, $J$ = 15, 9, 2 Hz, H$_b$), 2.90 (ddt, 1H, $J$ = 15, 6, 2 Hz, H$_c$), 3.68-3.78 (m, 1H, H$_d$), 4.10-4.24 (m, 2H, -OCH$_2$CH$_3$), 4.66 (broad s, 1H, H$_e$), 5.07 (broad s, 1H, H$_f$), 5.78 (qd, 1H, $J$ = 7, 2.5 Hz, H$_g$). Upon irradiation at $\delta$ 3.73, both signals at $\delta$ 2.80 and $\delta$ 2.90 were converted to doublets.
of triplets \((J = 15, 2 \text{ Hz, each})\) and the signal at \(\delta 5.78\) was converted to a quartet \((J = 7 \text{ Hz})\). NOE difference experiments: irradiation at \(\delta 1.68\) caused enhancement of the signals at \(\delta 3.68-3.78\) and \(\delta 5.78\); irradiation at \(\delta 5.78\) caused enhancement of the signals at \(\delta 1.68\) and \(\delta 5.07\). \(^{13}\text{C}\) NMR (CDCl\(_3\), 75.3 MHz): \(\delta 12.9\) (-ve, C\(_7\) or C\(_{10}\)), 13.9 (-ve, C\(_7\) or C\(_{10}\)), 31.3 (C\(_9\)), 42.2 (-ve, C\(_1\)), 60.3 (C\(_4\)), 101.8 (C\(_8\)), 117.3 (-ve, C\(_6\)), 138.7 (C\(_2\) or C\(_3\)), 145.7 (C\(_2\) or C\(_3\)), 172.6 (C\(_5\)). Exact Mass calcd. for C\(_{10}H_{14}O_2\) (M\(^+\)): 166.0994; found: 166.0995.

**Preparation of Ethyl (Z)-2-Ethylidene-3-methylene cyclobutanecarboxylate (255)**

Following general procedure 6 outlined above, the diene ester 222 was converted into the cyclobutanecarboxylate 255. The following amounts of reagents and solvents were used: Pd(PPh\(_3\))\(_4\) (97 mg, 84 \(\mu\)mol); the diene ester 222 (689 mg, 1.68 mmol) in 15 mL of dry DMF. Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 19:1), followed by distillation (air-bath temperature 88-92°C/45 Torr) of the material thus obtained, afforded 268 mg (96%) of the cyclobutanecarboxylate 255 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 19:1) and \(^1\text{H}\) NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1736, 1643, 1180, 735 cm\(^{-1}\); \(^1\text{H}\) NMR (CDCl\(_3\), 400 MHz):
δ 1.27 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.80 (dd, 3H, J = 7, 2 Hz, =CHCH₃), 2.74 (dddd, 1H, J = 15, 9, 3, 2.5 Hz, Hₚ), 2.98 (ddt, 1H, J = 15, 6, 2 Hz, Hₜ), 3.56-3.65 (m, 1H, Hₜ), 4.11-4.24 (m, 2H, -OCH₂CH₃), 4.91 (broad s, 1H, Hₜ), 5.14 (broad s, 1H, Hₜ), 5.53 (broad q, 1H, J ~ 7 Hz, Hₜ). Upon irradiation at δ 3.60, the doublet of doublets at δ 1.80 was converted to a doublet (J = 7 Hz), both signals at δ 2.74 and δ 2.98 were converted to doublets of triplets (J = 15, ~2.5 Hz and J = 15, 2 Hz, respectively) and the quartet at δ 5.53 was sharpened. NOE difference experiment: irradiation at δ 1.80 caused enhancement of the signals at δ 5.14 and δ 5.53. ¹³C NMR (CDCl₃, 75.3 MHz): δ 14.0 (-ve, C₇ and C₁₀), 30.7 (C₉), 42.5 (-ve, C₁), 60.3 (C₄), 107.4 (C₈), 120.7 (-ve, C₆), 138.0 (C₂ or C₃), 145.9 (C₂ or C₃), 172.4 (C₅). Exact Mass calcd. for C₁₀H₁₄O₂ (M⁺): 166.0994; found: 166.0988.

Preparation of Ethyl (E)-2-(Methoxymethoxymethylene)-3-methylene cyclobutane-carboxylate (256)

Following general procedure 6 outlined above, the diene ester 217 was converted into the cyclobutanecarboxylate 256 in the presence of dry triethylamine. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (18 mg, 16 μmol); the diene ester 217 (200 mg, 0.438 mmol) in 4 mL of dry DMF; Et₃N
(44 mg, 0.44 mmol). Flash chromatography of the crude product on silica gel (4 g, elution with 8:1 petroleum ether-diethyl ether containing 1% triethylamine), followed by distillation (air-bath temperature 75-80°C/0.15 Torr) of the material thus obtained, afforded 63.0 mg (68%) of the cyclobutanecarboxylate 256 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1733, 1677, 1646, 1228 1163, 1058, 954 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 1.28 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 2.85-2.92 (m, 2H, H$_b$ and H$_c$), 3.39 (s, 3H, -OCH$_3$), 3.73 (ddd, 1H, $J = 9$, 6, 2 Hz, H$_a$), 4.13-4.26 (m, 2H, -OCH$_2$CH$_3$), 4.65 (broad s, 1H, H$_d$), 4.83 (s, 2H, -OCH$_2$O-), 4.96 (t, 1H, $J = 2$ Hz, H$_e$), 6.65 (d, 1H, $J = 2$ Hz, H$_f$). Irradiation at δ 3.73 sharpened the multiplet at δ 2.85-2.92 and converted the doublet at δ 6.65 to a singlet, while irradiation at δ 6.65 converted the signal at δ 3.73 to a doublet of doublets ($J = 9$, 6 Hz). NOE difference experiments: irradiation at δ 4.65 caused enhancement of the signals at δ 2.85-2.92 and δ 4.96; irradiation at δ 4.96 caused enhancement of the signals at δ 4.65 and δ 6.65; irradiation at δ 6.65 caused enhancement of the signals at δ 4.83 and δ 4.96. Exact Mass calcd. for C$_{11}$H$_{16}$O$_4$ (M$^+$): 212.1048; found: 212.1052.
Preparation of Ethyl (Z)-2-(Methoxymethoxymethylene)-3-methylene cyclobutane-carboxylate (257)

Following general procedure 6 outlined above, the diene ester 223 was converted into the cyclobutanecarboxylate 257 in the presence of dry triethylamine. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (14 mg, 12 μmol); the diene ester 223 (111 mg, 0.243 mmol) in 3 mL of dry DMF; Et₃N (24 mg, 0.24 mmol). Flash chromatography of the crude product on silica gel (2 g, elution with 8:1 petroleum ether-diethyl ether containing 1% triethylamine), followed by distillation (air-bath temperature 74-80°C/0.15 Torr) of the material thus obtained, afforded 36.0 mg (70%) of the cyclobutanecarboxylate 257 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1734, 1674, 1645, 1160, 1130, 1057, 963 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 2.80 (dddd, 1H, J = 15, 9, 3, 2 Hz, ḻb), 2.98 (dddd, 1H, J = 15, 6, 3, 2.5 Hz, ḻc), 3.42 (s, 3H, -OCH₃), 3.66 (ddd, 1H, J = 9, 6, 2 Hz, ḻa), 4.11-4.23 (m, 2H, -OCH₂CH₃), 4.86, 4.89 (d each, 2H, J = 7 Hz, -OCH₂O-), 4.92 (broad s, 1H, ḻd), 5.25 (broad t, 1H, J = 3 Hz, ḻe), 6.29 (broad s, 1H, ḻf). Irradiation at δ 4.92 simplified both signals at δ 2.80 and δ 2.90 to doublets of doublets of doublets (J = 15, 9, 3 Hz and J = 15, 6, 3 Hz, respectively). Irradiation at δ 5.25
simplified both signals at $\delta$ 2.80 and $\delta$ 2.98 to doublets of doublets of doublets ($J = 15, 9, 2$ Hz and $J = 15, 6, 2.5$ Hz, respectively). Irradiation at $\delta$ 6.29 simplified the signal at $\delta$ 3.66 to a doublet of doublets ($J = 9, 6$ Hz). **Exact Mass** calcd. for C$_{11}$H$_{16}$O$_4$ (M$^+$): 212.1048; found: 212.1053.

**Preparation of Ethyl (E)-2-(3-Methoxymethoxypropylidene)-3-methylene(cyclobutanecarboxylate (258)**

Following general procedure 6 outlined above, the diene ester 218 was converted into the cyclobutanecarboxylate 258. The following amounts of reagents and solvents were used: Pd(PPh$_3$)$_4$ (16 mg, 14 $\mu$mol); the diene ester 218 (137 mg, 0.282 mmol) in 3 mL of dry DMF. Flash chromatography of the crude product on silica gel (3 g, elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 86-92°C/0.15 Torr) of the material thus obtained, afforded 62.0 mg (92%) of the cyclobutanecarboxylate 258 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1733, 1650, 1260, 1154, 1110, 1041, 917 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.28 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 2.39 (q, 2H, $J = 7$ Hz, =CHCH$_2$-), 2.83 (ddddd, 1H, $J = 15, 9, 3, 2$ Hz, H$_b$), 2.93 (ddddd, 1H,
\[ J = 15, 6, 3, 2 \text{ Hz, } H_c \], 3.36 (s, 3H, -OCH\(_3\)), 3.51-3.62 (m, 2H, -OCH\(_2\)CH\(_2\)-), 3.73-3.79 (m, 1H, \(H_d\)), 4.18 (q, 2H, \(J = 7 \text{ Hz, } -\text{OCH}_2\)CH\(_3\)), 4.62 (s, 2H, -OCH\(_2\)O-), 4.72 (broad s, 1H, \(H_d\)), 5.14 (broad t, 1H, \(J \sim 3 \text{ Hz, } H_e\)), 5.79 (td, 1H, \(J = 7, 3 \text{ Hz, } H_f\)). NOE difference experiments: irradiation at \(\delta 2.39\) caused enhancement of the signals at \(\delta 3.51-3.62\), \(\delta 3.73-3.79\) and \(\delta 5.79\); irradiation at \(\delta 3.76\) caused enhancement of the signals at \(\delta 2.39\) and \(\delta 2.83\); irradiation at \(\delta 5.79\) caused enhancement of the signals at \(\delta 2.39\), \(\delta 3.51-3.62\) and \(\delta 5.14\).

**Exact Mass** calcd. for \(\text{C}_{13}\text{H}_{20}\text{O}_4\) (M\(^+\)): 240.1362; found: 240.1372.

**Preparation of Ethyl (Z)-2-(3-Methoxymethoxypropylidene)-3-methylene cyclobutane-carboxylate (259)**

Following general procedure 6 outlined above, the diene ester 224 was converted into the cyclobutanecarboxylate 259. The following amounts of reagents and solvents were used: Pd(PPh\(_3\))\(_4\) (12 mg, 10 \(\mu\)mol); the diene ester 224 (106 mg, 0.219 mmol) in 2 mL of dry DMF. Flash chromatography of the crude product on silica gel (3 g, elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 86-90\(^\circ\)C/0.15 Torr) of the material thus obtained, afforded 37.0 mg (70%) of the cyclobutanecarboxylate 259 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and
1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1736, 1645, 1153, 1110, 1041 cm\(^{-1}\); 1H NMR (CDCl\(_3\), 400 MHz): δ 1.27 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.45-2.58 (m, 2H, =CHCH\(_2\)-), 2.74 (dddd, 1H, \(J = 15, 9, 3, 2\) Hz, \(H_b\)), 2.98 (ddt, 1H, \(J = 15, 6, 3\) Hz, \(H_c\)), 3.36 (s, 3H, -OCH\(_3\)), 3.57-3.68 (m, 3H, -OCH\(_2\)CH\(_2\)- and \(H_a\)), 4.10-4.23 (m, 2H, -OCH\(_2\)CH\(_3\)), 4.63 (s, 2H, -OCH\(_2\)O-), 4.92 (broad s, 1H, \(H_d\)), 5.16 (broad s, 1H, \(H_e\)), 5.51 (broad t, 1H, \(J = 7\) Hz, \(H_f\)). Irradiation at δ 2.51 simplified the signal at δ 3.57-3.68 and converted the triplet at δ 5.51 to a broad singlet. NOE difference experiment: irradiation at δ 2.51 caused enhancement of the signals at δ 3.57-3.68, δ 5.16 and δ 5.51. Exact Mass calcd. for C\(_{12}\)H\(_{17}\)O\(_3\) (M+OCH\(_3\)): 209.1178; found: 209.1184.

Preparation of Ethyl (E)-2-(4-tert-butyldimethyldisilyloxybutyldiene)-3-methylene-cyclobutanecarboxylate (260)

Following general procedure 6 outlined above, the diene ester 219 was converted into the cyclobutanecarboxylate 260. The following amounts of reagents and solvents were used: Pd(PPh\(_3\))\(_4\) (8 mg, 7 μmol); the diene ester 219 (83.0 mg, 0.146 mmol) in 2 mL of dry DMF. Flash chromatography of the crude product on silica gel (3 g, elution with petroleum ether-diethyl ether, 19:1),
followed by distillation (air-bath temperature 110-114°C/0.15 Torr) of the material thus obtained, afforded 41.0 mg (87%) of the cyclobutanecarboxylate 260 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 19:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1734, 1650, 1256, 1178, 1099, 838, 777 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.05 (s, 6H, -SiMe₂), 0.90 (s, 9H, -SiCH₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.54-1.65 (m, 2H, -CH₂CH₂CH₂⁻), 2.06-2.22 (m, 2H, =CHCH₂⁻), 2.81 (dddd, 1H, J = 15, 9, 3, 2 Hz, Hₗ), 2.91 (dddd, 1H, J = 15, 6, 3, 2 Hz, Hₜ), 3.61 (t, 2H, J = 7 Hz, -OCH₂CH₂⁻), 3.68-3.75 (m, 1H, Hₗ), 4.17 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.68 (broad s, 1H, Hₜ), 5.11 (broad t, 1H, J ~ 3 Hz, Hₜ), 5.75 (td, 1H, J = 7, 2 Hz, Hₗ). Irradiation at δ 3.72 converted both signals at δ 2.81 and δ 2.91 to broad triplets (J = 15, ~2.5 Hz each) and the signal at δ 5.75 to a triplet (J = 7 Hz). Irradiation at δ 4.68 simplified both signals at δ 2.81 and δ 2.91 to doublets of doublets of doublets (J = 15, 9, 3 Hz and J = 15, 6, 3 Hz, respectively). Irradiation at δ 5.11 simplified both signals at δ 2.81 and δ 2.91 to doublets of doublets of doublets (J = 15, 9, 2 Hz and J = 15, 6, 2 Hz, respectively). Irradiation at δ 5.75 sharpened the multiplet at δ 2.06-2.22 and converted the multiplet at δ 3.68-3.75 to a doublet of doublets (J = 9, 6 Hz). NOE difference experiments: irradiation at δ 2.13 caused enhancement of the signals at δ 1.54-1.65, δ 3.61, δ 3.68-3.75 and δ 5.75; irradiation at δ 5.11 caused enhancement of the signals at δ 4.68 and δ 5.75; irradiation at δ 5.75 caused enhancement of the signals at δ 2.06-2.22 and δ 5.11. Exact Mass calcd. for C₁₇H₂₉O₃Si (M⁺-CH₃): 309.1887; found: 309.1887.
Preparation of Ethyl (Z)-2-(4-tert-butyldimethylsilyloxybutylic)-3-methylene-cyclobutanecarboxylate (261)

Following general procedure 6 outlined above, the diene ester 225 was converted into the cyclobutanecarboxylate 261. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (7 mg, 6 µmol); the diene ester 225 (63 mg, 0.111 mmol) in 1 mL of dry DMF. Flash chromatography of the crude product on silica gel (3 g, elution with petroleum ether-diethyl ether, 19:1), followed by distillation (air-bath temperature 110-116°C/0.15 Torr) of the material thus obtained, afforded 33.0 mg (92%) of the cyclobutanecarboxylate 261 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 19:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1738, 1645, 1257, 1178, 1101, 837, 777 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.05 (s, 6H, -SiMe₂), 0.90 (s, 9H, -SiCMe₂), 1.27 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.64 (quintet, 2H, J = 7 Hz, -CH₂CH₂CH₂-), 2.20-2.32 (m, 2H, =CHCH₂-), 2.72 (dddd, 1H, J = 15, 9, 3, 2 Hz, H₈), 2.97 (ddddd, 1H, J = 15, 6.5, 3, 2 Hz, H₉), 3.57-3.66 (m, 3H, -OCH₂CH₂ and H₈), 4.12-4.24 (m, 2H, -OCH₂CH₃), 4.89 (broad s, 1H, H₉), 5.15 (broad s, 1H, H₉), 5.48 (broad t, 1H, J = 7 Hz, H₇). Irradiation at δ 4.89 simplified both signals at δ 2.72 and δ 2.97 to doublets of doublets of doublets (J = 15, 9, 3 Hz and J = 15, 6.5, 3 Hz, respectively). Irradiation at δ 5.15 simplified both
signals at $\delta$ 2.72 and $\delta$ 2.97 to doublets of doublets of doublets ($J = 15, 9, 2$ Hz and $J = 15, 6.5, 2$ Hz, respectively). NOE difference experiments: irradiation at $\delta$ 2.26 caused enhancement of the signals at $\delta$ 1.64, $\delta$ 3.57-3.66, $\delta$ 5.15 and $\delta$ 5.48, while irradiation at $\delta$ 5.15 caused enhancement of the signals at $\delta$ 2.20-2.32 and $\delta$ 4.89. Exact Mass calcd. for C\textsubscript{17}H\textsubscript{29}O\textsubscript{3}Si (M$^+$-CH\textsubscript{3}): 309.1887; found: 309.1879.

Preparation of Ethyl (E)-2-(4-Hydroxybutyldiene)-3-methylenecyclobutanecarboxylate (262)

Following general procedure 6 outlined above, the diene ester 251 was converted into the cyclobutanecarboxylate 262. The following amounts of reagents and solvents were used: Pd(PPh\textsubscript{3})\textsubscript{4} (23 mg, 20 $\mu$mol); the diene ester 251 (293 mg, 0.644 mmol) in 6 mL of dry DMF. Flash chromatography of the crude product on silica gel (5 g, elution with petroleum ether-diethyl ether, 3:2), followed by distillation (air-bath temperature 100-105°C/0.15 Torr) of the material thus obtained, afforded 118 mg (87%) of the cyclobutanecarboxylate 262 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 3:2) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material
exhibited IR (film): 3404 (broad), 1729, 1672, 1181, 1043 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.56-1.72 (m, 2H, -CH₂CH₂CH₂⁻), 1.81 (broad s, 1H, exchanged with D₂O, -OH), 2.06-2.20 (m, 2H, =CHCH₂⁻), 2.80-2.90 (m, 2H, H₅ and H₆), 3.61 (broad t, 2H, J = 7 Hz, -OCH₂CH₂⁻), 3.73 (broad t, 1H, J ~ 8 Hz, H₇), 4.16 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.68 (broad s, 1H, H₈), 5.11 (broad t, 1H, J ~ 3 Hz, H₉), 5.72 (td, 1H, J = 7, 3 Hz, H₁₀). Exact Mass calcd. for C₁₂H₁₈O₃ (M⁺): 210.1256; found: 210.1258.

Preparation of Ethyl (E)-2-Ethylidene-(Z)-3-ethylidencyclobutanecarboxylate (263)

Following general procedure 6 outlined above, the diene ester 228 was converted into the cyclobutanecarboxylate 263. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (37 mg, 32 μmol); the diene ester 228 (301 mg, 0.638 mmol) in 5 mL of dry DMF. Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 50-62°C/0.15 Torr) of the material thus obtained, afforded 111 mg (97%) of the cyclobutanecarboxylate 263 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1735, 1189, 1155, 1037, 831 cm⁻¹; ¹H NMR (CDCl₃, 400
MHz): $\delta$ 1.27 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.70 (d, 3H, $J = 7$ Hz, =CH$_4$CH$_3$), 1.75 (d, 3H, $J = 7$ Hz, =CH$_3$CH$_3$), 2.68-2.84 (m, 2H, $H_b$), 3.63-3.71 (m, 1H, $H_a$), 4.12-4.25 (m, 2H, -OCH$_2$CH$_3$), 5.22 (broad q, 1H, $J = 7$ Hz, $H_c$), 5.75 (qd, 1H, $J = 7$, 3 Hz, $H_d$). Irradiation at $\delta$ 3.67 sharpened the multiplet at $\delta$ 2.68-2.84 and simplified the quartet of doublets at $\delta$ 5.75 to a quartet ($J = 7$ Hz). Irradiation at $\delta$ 5.22 converted the doublet at $\delta$ 1.75 to a singlet. Irradiation at $\delta$ 5.75 converted the doublet at $\delta$ 1.70 to a singlet and sharpened the multiplet at $\delta$ 3.63-3.71. NOE difference experiments: irradiation at $\delta$ 5.22 caused enhancement of the signals at $\delta$ 2.68-2.84 and $\delta$ 1.75; irradiation at $\delta$ 5.75 caused enhancement of the signals at $\delta$ 1.70 and $\delta$ 1.75. Exact Mass calcd. for C$_{11}$H$_{16}$O$_2$ (M$^+$): 180.1150; found: 180.1154.

Preparation of Ethyl (Z)-2-Ethylidene-(Z)-3-ethylidene-cyclobutanecarboxylate (264)

Following general procedure 6 outlined above, the diene ester 229 was converted into the cyclobutanecarboxylate 264. The following amounts of reagents and solvents were used: Pd(PPh$_3$)$_4$ (15 mg, 13 $\mu$mol); the diene ester 229 (122 mg, 0.258 mmol) in 3 mL of dry DMF. Flash chromatography of the crude product on silica gel (5 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 55-60$^\circ$C/0.15 Torr) of the material thus
obtained, afforded 43.0 mg (93%) of the cyclobutanecarboxylate 264 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1734, 1184, 1031, 734 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.28 (t, 3H, \(J = 7\) Hz, \(-OCH_2CH_3\)), 1.82 (d, 3H, \(J = 7\) Hz, \(=CH_2CH_3\)), 1.85 (dd, 3H, \(J = 7, 2\) Hz, \(=CH_2CH_3\)), 2.55-2.65 (m, 1H, \(H_b\)), 2.83-2.93 (m, 1H, \(H_b\)), 3.50-3.58 (m, 1H, \(H_a\)), 4.11-4.25 (m, 2H, \(-OCH_2CH_3\)), 5.18 (broad q, 1H, \(J = 7\) Hz, \(H_e\)), 5.36 (broad q, 1H, \(J = 7\) Hz, \(H_d\)). Irradiation at \(\delta\) 5.36 converted the doublet of doublets at \(\delta\) 1.85 to a doublet (\(J = 2\) Hz), and sharpened the signal at \(\delta\) 3.50-3.58. Exact Mass calcd. for \(C_{11}H_{16}O_2\) (M\(^+\)): 180.1150; found: 180.1147.

Preparation of Ethyl 2,3-bis(Methylene)cyclopentanecarboxylate (274)

Following general procedure 6 outlined above, the diene ester 230 was converted into the cyclopentanecarboxylate 274 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh\(_3\))\(_4\) (40 mg, 35 \(\mu\)mol); the diene ester 230 (280 mg, 0.681 mmol) in 5 mL of dry DMF; LiCl (58 mg, 1.36 mmol). Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 45-55\(^\circ\)C/0.15 Torr) of the material thus obtained, afforded 96.0 mg
(85%) of a mixture of the cyclopentanecarboxylates 274 and 278 in a ratio of 13:1, respectively (\(^1\)H NMR and GLC analyses). The mixture of the esters was separated by preparative thin layer chromatography on silica gel (elution 5 times with petroleum ether-diethyl ether, 40:1) and each product was obtained as a colorless oil. Analysis of both oils by GLC, TLC (petroleum ether-diethyl ether, 40:1) and \(^1\)H NMR spectroscopy indicated that each oil consisted of one component.

The major, more polar cyclopentanecarboxylate 274 exhibited IR (film): 1736, 1639, 1178, 891 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.27 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 1.88-2.10 (m, 2H, \(H_b\)), 2.42 (dt, 1H, \(J = 16, 8, 2.5\) Hz, \(H_e\)), 2.58-2.68 (m, 1H, \(H_c\)), 3.44-3.51 (m, 1H, \(H_a\)), 4.11-4.24 (m, 2H, -OCH\(_2\)CH\(_3\)), 4.95 (t, 1H, \(J = 2.5\) Hz, \(H_d\)), 5.11 (d, 1H, \(J = 2.5\) Hz, \(H_g\)), 5.39 (t, 1H, \(J = 2.5\) Hz, \(H_f\)). Irradiation at \(\delta\) 3.47 sharpened the multiplet at \(\delta\) 1.88-2.10 and converted both doublets at \(\delta\) 5.11 and \(\delta\) 5.52 to singlets. **Exact Mass** calcd. for C\(_{10}\)H\(_{14}\)O\(_2\) (M\(^+\)): 166.0994; found: 166.0993.

The minor, less polar cyclopentanecarboxylate 278 exhibited IR (film): 1709, 1656, 1230, 1061 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.31 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.13 (broad t, 3H, \(J = 1\) Hz, =CCH\(_3\)), 2.56-2.70 (m, 4H), 4.24 (q, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 5.06 (broad s, 1H, olefinic proton), 5.16 (broad s, 1H, olefinic proton). **Exact Mass** calcd. for C\(_{10}\)H\(_{14}\)O\(_2\) (M\(^+\)): 166.0994; found: 166.0994.
Preparation of Ethyl (E)-2-Ethylidene-3-methylene cyclopentanecarboxylate (275)

Following general procedure 6 outlined above, the diene ester 231 was converted into the cyclopentanecarboxylate 275 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh3)4 (29 mg, 25 µmol); the diene ester 231 (210 mg, 0.494 mmol) in 5 mL of dry DMF; LiCl (42 mg, 0.99 mmol). Flash chromatography of the crude product on silica gel (8 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 55-60°C/0.15 Torr) of the material thus obtained, afforded 75.0 mg (84%) of the cyclopentanecarboxylate 275 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1735, 1626, 1367, 1149, 1042, 869 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 1.25 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.77 (d, 3H, J = 7 Hz, =CHCH₃), 1.81-1.91 (m, 1H, Hₙ), 2.02-2.10 (m, 1H, Hₘ), 2.39-2.49 (m, 1H, Hₚ), 2.63-2.74 (m, 1H, Hₚ), 3.61 (broad d, 1H, J ~ 8 Hz, H₁₈), 4.07-4.20 (m, 2H, -OCH₂CH₃), 4.81 (broad s 1H, H₁ₖ), 5.24 (broad s, 1H, H₁ₖ), 6.10 (qd, 1H, J = 7, 1 Hz, H₁₇). NOE difference experiment: irradiation of δ 6.10 caused enhancement of the signals at δ 1.77 and δ 5.24. Exact Mass calcd. for C₁₁H₁₆O₂ (M⁺): 180.1150; found: 180.1159.
Preparation of Ethyl (Z)-2-Ethylidene-3-methylenecyclopentanecarboxylate (276)

Following general procedure 6 outlined above, the diene ester 232 was converted into the cyclopentanecarboxylate 276 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh3)4 (20 mg, 17 μmol); the diene ester 232 (150 mg, 0.353 mmol) in 4 mL of dry DMF; LiCl (30 mg, 0.71 mmol). Flash chromatography of the crude product on silica gel (6 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 58-65°C/0.15 Torr) of the material thus obtained, afforded 50.0 mg (79%) of the cyclopentanecarboxylate 276 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 40:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1735, 1639, 1176, 1148, 1043, 880 cm⁻¹; 1H NMR (CDCl3, 400 MHz): δ 1.24 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.82-1.92 (m, 1H, Hₖ), 1.88 (dd, 3H, J = 7, 1 Hz, =CHCH₃), 1.96-2.05 (m, 1H, Hₖ), 2.37-2.47 (m, 1H, Hₖ), 2.60-2.70 (m, 1H, Hₖ), 3.37-3.44 (m, 1H, Hₕ), 4.07-4.20 (m, 2H, -OCH₂CH₃), 5.16 (broad s, 1H, Hₙ), 5.20 (broad s, 1H, Hₙ), 5.79 (broad q, 1H, J ~ 7 Hz, Hₙ). Irradiation at δ 3.40 sharpened the signals at δ 1.82-1.92, δ 1.96-2.05 and δ 5.79, and converted the doublet of doublets at δ 1.88 to a doublet (J = 7 Hz). Irradiation at δ 5.18 simplified both multiplets at δ 2.37-2.47 and δ 2.60-2.70 to doublets of triplets (J = 15, 7.5 Hz, each). Exact Mass calcd. for C₁₁H₁₆O₂ (M⁺): 180.1150; found: 180.1150.
Preparation of Ethyl 2-Methylene-(E)-3-ethylidene-cyclopentanecarboxylate (277)

Following general procedure 6 outlined above, the diene ester 233 was converted into the cyclopentanecarboxylate 277 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (26 mg, 23 μmol); the diene ester 233 (210 mg, 0.445 mmol) in 5 mL of dry DMF; LiCl (38 mg, 0.89 mmol). Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 55-65°C/0.15 Torr) of the material thus obtained, afforded 66.0 mg (83%) of a mixture of the cyclopentanecarboxylates 277 and 279 in a ratio of 12:1, respectively (GLC analysis). The mixture of the esters was separated by preparative thin layer chromatography on silica gel (elution 5 times with petroleum ether-diethyl ether, 40:1) and each product was obtained as a colorless oil. Analysis of both oils by GLC, TLC (petroleum ether-diethyl ether, 40:1) and ¹H NMR spectroscopy indicated that each consisted of one component.

The major, more polar cyclopentanecarboxylate 277 exhibited IR (film): 1735, 1661, 1623, 1177, 1044, 884 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.27 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.71 (d, 3H, J = 7 Hz, =CHCH₃), 1.88-1.99 (m, 1H, H₆), 2.01-2.11 (m, 1H, H₇), 2.30-2.41 (m, 1H, H₈), 2.53-2.64 (m, 1H, H₉), 3.43-3.49 (m, 1H, H₁₀), 4.11-4.24 (m, 2H, -OCH₂CH₃), 4.94 (broad d, 1H, J ~ 2 Hz, H₉), 5.36 (broad d, 1H, J ~ 2 Hz, H₁₀), 5.91-6.00 (m, 1H, H₁₁). Irradiation at δ 1.71 simplified the multiplet at δ 5.91-6.00 to a triplet (J = 2 Hz).
NOE difference experiments: irradiation at $\delta$ 5.36 caused enhancement of the signals at $\delta$ 4.94 and $\delta$ 5.91-6.00, while irradiation at $\delta$ 5.95 caused enhancement of the signals at $\delta$ 1.71 and $\delta$ 5.36. **Exact Mass** calcd. for C$_{11}$H$_{16}$O$_{2}$ (M$^+$): 180.1150; found: 180.1155.

The minor, less polar cyclopentanecarboxylate 279 exhibited IR (film): 1708, 1649, 1614, 1229, 1063 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.31 (t, 3H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 1.75 (d, 3H, $J$ = 7 Hz, =CHCH$_3$), 2.12 (broad t, 3H, $J$ = 1 Hz, =CCH$_3$), 2.46-2.54 (m, 2H), 2.64-2.71 (m, 2H), 4.24 (q, 2H, $J$ = 7 Hz, -OCH$_2$CH$_3$), 5.65-5.74 (m, 1H, olefinic proton). **Exact Mass** calcd. for C$_{11}$H$_{16}$O$_{2}$ (M$^+$): 180.1150; found: 180.1159.

**Preparation of Ethyl 2,3-bis(Methylene)cyclohexanecarboxylate (281)**

![Chemical structure of 281]

Following general procedure 6 outlined above, the diene ester 234 was converted into the cyclohexanecarboxylate 281 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh$_3$)$_4$ (40 mg, 35 $\mu$mol); the diene ester 234 (160 mg, 0.376 mmol) in 4 mL of dry DMF; LiCl (32 mg, 0.75 mmol). Flash chromatography of the crude product on silica gel (10 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 56-64°C/0.15 Torr) of the material thus obtained, afforded 50.0 mg (74%) of the cyclohexanecarboxylate 281 as a colorless oil. Analysis of this oil
by GLC, TLC (petroleum ether-diethyl ether, 40:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1736, 1637, 1158, 1034, 898 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.55-1.67 (m, 1H), 1.71-1.87 (m, 2H), 1.99-2.09 (m, 1H), 2.18-2.35 (m, 2H), 3.25 (broad dd, 1H, J ~ 8, 4 Hz, Hₐ), 4.06-4.26 (m, 2H, -OCH₂CH₃), 4.73 (broad s, 2H, Hₗ and Hₜ), 4.99 (broad s, 1H, Hᵢ), 5.13 (broad s, 1H, Hₙ). Irradiation at δ 3.25 sharpened the signals at δ 1.71-1.87, δ 1.99-2.09, δ 4.73 and δ 5.13. NOE difference experiment: irradiation at δ 3.25 caused enhancement of the signals at δ 1.71-1.87, δ 1.99-2.09 and δ 4.73. Exact Mass calcd. for C₁₁H₁₆O₂ (M⁺): 180.1150; found: 180.1145.

Preparation of Ethyl (E)-2-Ethylidene-3-methylenecyclohexanecarboxylate (282)

Following general procedure 6 outlined above, the diene ester 235 was converted into the cyclohexanecarboxylate 282 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh₃)₄ (13 mg, 11 μmol); the diene ester 235 (100 mg, 0.228 mmol) in 3 mL of dry DMF; LiCl (19 mg, 0.45 mmol). Flash chromatography of the crude product on silica gel (5 g, elution with petroleum ether-diethyl ether, 40:1), followed by distillation (air-bath temperature 70-78°C/0.15 Torr) of the material thus obtained, afforded 30.0 mg (68%) of the cyclohexanecarboxylate 282 as a colorless oil. Analysis of this oil
by GLC, TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1734, 1627, 1154, 1030, 891 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.22 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.55-1.81 (m, 3H), 1.69 (d, 3H, $J = 7$ Hz, =CHCH$_3$), 2.05-2.15 (m, 1H), 2.20-2.28 (m, 1H), 2.34-2.42 (m, 1H), 3.66 (dd, 1H, $J = 6$, 2 Hz, H$_a$), 4.05-4.18 (m, 2H, -OCH$_2$CH$_3$), 4.64 (t, 1H, $J = 2$ Hz, H$_b$), 4.87 (t, 1H, $J = 2$ Hz, H$_c$), 5.75 (q, 1H, $J = 7$ Hz, H$_d$). Irradiation at $\delta$ 5.75 converted the doublet at $\delta$ 1.69 to a singlet. NOE difference experiments: irradiation at $\delta$ 4.87 caused enhancement of the signals at $\delta$ 4.64 and $\delta$ 5.75; irradiation at $\delta$ 5.75 caused enhancement of the signals at $\delta$ 1.69 and $\delta$ 4.87. Exact Mass calcd. for C$_{12}$H$_{18}$O$_2$ (M$^+$): 194.1307; found: 194.1309.

Preparation of Ethyl (E)-2-(3-Methoxymethoxypropylidene)-3-methylene cyclohexane-
carboxylate (283)

Following general procedure 6 outlined above, the diene ester 236 was converted into the cyclohexanecarboxylate 283 in the presence of lithium chloride. The following amounts of reagents and solvents were used: Pd(PPh$_3$)$_4$ (13 mg, 11 $\mu$mol); the diene ester 236 (110 mg, 0.214 mmol) in 3 mL of dry DMF; LiCl (18 mg, 0.42 mmol). Flash chromatography of the crude product on silica gel (5 g,
elution with petroleum ether-diethyl ether, 8:1), followed by distillation (air-bath temperature 85-95°C/0.15 Torr) of the material thus obtained, afforded 31.0 mg (54%) of the cyclohexanecarboxylate 283 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 8:1) and ^1^H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1733, 1152, 1111, 1034 cm\(^{-1}\); ^1^H NMR (CDCl\(_3\), 400 MHz): δ 1.22 (t, 3H, J = 7 Hz, -OCH\(_2\)CH\(_3\)), 1.55-1.83 (m, 3H), 2.04-2.15 (m, 1H), 2.20-2.28 (m, 1H), 2.30-2.51 (m, 3H), 3.36 (s, 3H, -OCH\(_3\)), 3.52-3.62 (m, 2H, -OCH\(_2\)CH\(_2\)-), 3.63-3.68 (m, 1H, H\(_a\)), 4.05-4.16 (m, 2H, -OCH\(_2\)CH\(_3\)), 4.64 (s, 2H, -OCH\(_2\)O-), 4.66 (broad dd, 1H, J ~ 2, 1 Hz, H\(_b\)), 4.88 (broad dd, 1H, J ~ 2, 1 Hz, H\(_c\)), 5.67 (t, 1H, J = 7 Hz, H\(_d\)). NOE difference experiment: irradiation at δ 5.67 caused enhancement of the signals at δ 2.30-2.51 and δ 4.88. \textbf{Exact Mass} calcd. for C\(_{15}\)H\(_{24}\)O\(_4\) (M\(^+\)): 268.1674; found: 268.1671.
8. Preparation of Cyclobutanecarboxamides

Preparation of \( N-p \)-Chlorophenyl-(E)-2-ethylidene-3-methylene-cyclobutanecarboxamide (270)

\[
\begin{align*}
\text{To a stirred solution of } p\text{-chloroaniline (64.0 mg, 0.502 mmol) in 2 mL of dry benzene under an argon atmosphere was added a solution of trimethylaluminum (0.250 mL, 0.500 mmol) in toluene. The reaction mixture was stirred at room temperature for 20 min until no more bubbling was observed. A solution of the cyclobutanecarboxylate 254 (55.3 mg, 0.333 mmol) in 1 mL of dry benzene was added and the resulting solution was refluxed for 4 h. Dilute hydrochloric acid (5%, 5 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed (water, brine) and dried (\( \text{MgSO}_4 \)). Concentration of the solution, followed by pumping on a vacuum pump to remove traces of solvent, afforded 71.0 mg (87%) of the cyclobutanecarboxamide 270. Recrystallization of this material from dichloromethane-hexane provided the amide 270 as a colorless needle-like solid (melting point 133.5-135°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and \(^1\text{H} \) NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (\( \text{CHCl}_3 \)): 1670, 1590, 1490, 1400, 1100, 820 cm\(^{-1}\); \(^1\text{H} \) NMR (\( \text{CDCl}_3 \), 300 MHz): \( \delta \) 1.74 (d, 3H, \( J = 7 \text{ Hz} \), \( =\text{CHCH}_3 \)), 2.80 (ddt, 1H, \( J = 16.5, 6, 3 \text{ Hz} \), \( H_b \)), 3.10
\end{align*}
\]
(ddt, 1H, J = 16.5, 10.5, 2.5 Hz, H_c), 3.72-3.81 (m, 1H, H_a), 4.79 (broad s, 1H, H_d), 5.20 (broad s, 1H, H_e), 5.96 (qd, 1H, J = 7, 3 Hz, H_f), 7.29 (d, 2H, J = 10 Hz, aromatic protons), 7.49 (d, 2H, J = 10 Hz, aromatic protons), 7.60 (broad s, 1H, -NH). Exact Mass calcd. for C_{14}H_{14}NO_{35}Cl (M^+): 247.0764; found: 247.0764.

Preparation of N-p-Bromophenyl-(Z)-2-ethylen-3-methylenecyclobutanecarboxamide (271)

\[ \text{[Diagram of molecule 271]} \]

To a cold (-5°C), stirred solution of p-bromoaniline hydrochloride (96.0 mg, 0.460 mmol) in 1.5 mL of dry benzene under an argon atmosphere was added a solution of trimethylaluminum (0.230 mL, 0.460 mmol) in toluene. The reaction mixture was stirred at room temperature for 1 h until no more bubbling was observed. A solution of the cyclobutanecarboxylate 255 (38.1 mg, 0.229 mmol) in 0.5 mL of dry benzene was added and the resulting solution was refluxed for 3 h. Dilute hydrochloric acid (5%, 4 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed (water, brine) and dried (MgSO_4). Concentration of the solution, followed by pumping on a vacuum pump to remove traces of solvent, afforded 62.8 mg (94%) of the cyclobutanecarboxamide 271. Recrystallization of this material from diethyl ether-
hexane provided the amide 271 as a colorless needle-like solid (melting point, 155-156.5°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl$_3$): 1670, 1580, 1480, 1390, 1075, 880 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 1.90 (dd, 3H, $J = 8, 2$ Hz, =CHCH$_3$), 2.88 (ddt, 1H, $J = 15.5, 6, 3$ Hz, $H_b$), 3.00 (ddt, 1H, $J = 15.5, 9.5, 2.5$ Hz, $H_c$), 3.64-3.72 (m, 1H, $H_a$), 4.01 (broad s, 1H, $H_d$), 4.26 (broad s, 1H, $H_e$), 4.60 (broad q, 1H, $J \sim 8$ Hz, $H_f$), 7.44 (s, 4H, aromatic protons), 7.52 (broad s, 1H, -NH). **Exact Mass** calcd. for C$_{14}$H$_{14}$NO$_7$Br (M$^+$): 291.0260; found: 291.0263.

Preparation of  \(N\)-\(p\)-Chlorophenyl-(Z),(Z)-2,3-bis(ethylidene)cyclobutanecarboxamide (272)

\[
\begin{array}{c}
\text{H}_b \\
\text{H}_c \\
\text{N} \\
\text{O} \\
\text{H}_a \\
\text{Cl}
\end{array}
\]

To a stirred solution of \(p\)-chloroaniline (35.0 mg, 0.274 mmol) in 1.5 mL of dry benzene under an argon atmosphere was added a solution of trimethylaluminum (0.130 mL, 0.260 mmol) in toluene. The reaction mixture was stirred at room temperature for 20 min until no more bubbling was observed. A solution of the cyclobutanecarboxylate 264 (32.2 mg, 0.179 mmol) in 0.5 mL of dry benzene was added and the resulting solution was refluxed for 4 h. Dilute hydrochloric acid (5%, 4 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed (water, brine) and
dried (MgSO₄). Concentration of the solution, followed by pumping on a vacuum pump to remove traces of solvent, afforded 36.2 mg (77%) of the cyclobutanecarboxamide 272. Recrystallization of this material from diethyl ether-pentane provided the amide 272 as a colorless needle-like solid (melting point, 144-146 °C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl₃): 1680, 1600, 1510, 1210, 1040, 830 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.86 (d, 3H, J = 7 Hz, =CHCH₃), 1.91 (dd, 3H, J = 7, 1 Hz, =CHCH₃), 2.73-2.90 (m, 2H, Hₐ and Hₗ), 3.54-3.61 (m, 1H, Hₐ), 5.26 (broad q, 1H, J = 7 Hz, =CHCH₃), 5.39 (broad q, 1H, J = 7 Hz, =CHCH₃), 7.28 (d, 2H, J = 10 Hz, aromatic protons), 7.50 (d, 2H, J = 10 Hz, aromatic protons), 7.60 (broad s, 1H, -NH). Exact Mass calcd. for C₁₅H₁₆NO₃Cl (M⁺): 261.0920; found: 261.0916.
9. Diels-Alder Reactions

Preparation of the Ester 289

To a stirred solution of the cyclobutanecarboxylate 253 (41.0 mg, 0.270 mmol) in 3 mL of dry THF under an argon atmosphere was added tetracyanoethylene (35.0 mg, 0.273 mmol). The reaction mixture was stirred for 30 min at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (1 g, elution with petroleum ether-diethyl ether, 1:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 66.0 mg (87%) of the ester 289 as a solid. Analysis of this solid by TLC (petroleum ether-diethyl ether, 1:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. Recrystallization of this material from petroleum ether-diethyl ether provided the ester 289 as a white solid (melting point, 128-129°C). This material exhibited IR (KBr pellet): 2256, 1729, 1261, 1200 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.30 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.86 (broad d, 1H, \(J = 14\) Hz, \(H_d\)), 3.05 (broad d, 1H, \(J = 14\) Hz, \(H_b\)), 3.09-3.36 (m, 4H, \(H_d\)), 3.76-3.83 (m, 1H, \(H_a\)), 4.15-4.28 (m, 2H, -OCH\(_2\)CH\(_3\)). Exact Mass calcd. for C\(_{15}\)H\(_{12}\)N\(_4\)O\(_2\) (M\(^+\)): 280.0970; found: 280.0964.
Preparation of the Ester 290

To a stirred solution of the cyclobutanecarboxylate 254 (57.0 mg, 0.343 mmol) in 3.5 mL of dry THF under an argon atmosphere was added tetracyanoethylene (44.0 mg, 0.343 mmol). The reaction mixture was stirred for 0.5 h at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 84.0 mg (83%) of a mixture of the esters 290 and 291 in a ratio of 19:1, respectively (\(^1\)H NMR analysis). Recrystallization of this mixture from petroleum ether-diethyl ether provided the ester 290 as a white solid (melting point, 152-153°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl\(_3\)): 2230, 1720, 1080, 1060 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.29 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 1.57 (d, 3H, \(J = 7\) Hz, -CHCH\(_3\)), 2.83-2.91 (m, 1H, H\(_c\)), 2.96-3.01 (m, 1H, H\(_b\)), 3.09-3.21 (m, 2H, H\(_d\)), 3.31-3.41 (m, 1H, H\(_c\)), 3.76-3.82 (m, 1H, H\(_a\)), 4.20 (q, 2H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)). Irradiation at \(\delta\) 1.57 sharpened the signal at \(\delta\) 3.31-3.41. Irradiation at \(\delta\) 3.36 converted the doublet at \(\delta\) 1.57 to a singlet, the multiplet at \(\delta\) 2.83-2.91 to a broad doublet (\(J \approx 14\) Hz) and the multiplet at \(\delta\) 2.96-3.01 to a broad doublet of doublets (\(J \approx 14, 6\) Hz), and sharpened the multiplet at \(\delta\) 3.76-3.82. Irradiation at \(\delta\) 3.79 converted the signal at \(\delta\) 2.83-2.91 to a doublet of
doublets ($J \sim 14$, 3 Hz) and the signal at $\delta$ 2.96-3.01 to a broad doublet of doublets ($J \sim 14$, 2.5 Hz), and sharpened the multiplet at $\delta$ 3.31-3.41. NOE difference experiment: irradiation at $\delta$ 1.57 caused enhancement of the signals at $\delta$ 3.31-3.41 and $\delta$ 3.76-3.82; irradiation at $\delta$ 3.36 caused enhancement of the signal at $\delta$ 1.57; irradiation at $\delta$ 3.79 caused enhancement of the signals at $\delta$ 1.57 and $\delta$ 2.96-3.01. Exact Mass calcd. for C$_{16}$H$_{14}$N$_{4}$O$_{2}$ (M$^+$): 294.1118; found: 294.1117.

Preparation of the Ester 291

To a stirred solution of the cyclobutanecarboxylate 255 (52.0 mg, 0.313 mmol) in 3.5 mL of dry THF under an argon atmosphere was added tetracyanoethylene (41.0 mg, 0.320 mmol). The reaction mixture was stirred for 1.5 days at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 79.0 mg (86%) of a mixture of the esters 291 and 290 in a ratio of 9:1, respectively ($^1$H NMR analysis). Recrystallization of this mixture from petroleum ether-diethyl ether provided the ester 291 as a white solid (melting point, 110-111°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of
one component. This material exhibited IR (KBr pellet): 2255, 1733, 1255, 1029 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.29 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 1.53 (d, 3H, \(J = 7\) Hz, -CHCH\(_3\)), 2.84 (broad d, 1H, \(J = 14\) Hz, H\(_e\)), 2.92 (broad dt, 1H, \(J = 14, 4\) Hz, H\(_b\)), 3.13 (broad d, 1H, \(J = 16\) Hz, H\(_d\)), 3.22-3.36 (m, 2H, H\(_d\) and H\(_e\)), 3.73-3.79 (m, 1H, H\(_a\)), 4.14-4.27 (m, 2H, -OCH\(_2\)CH\(_3\)). Exact Mass calcd. for C\(_{16}\)H\(_{14}\)N\(_4\)O\(_2\) (M\(^+\)) : 294.1118; found: 294.1123.

**Preparation of the Ester 292**

![Diagram of 292](attachment:diagram.png)

To a stirred solution of the cyclobutanecarboxylate 258 (80.0 mg, 0.333 mmol) in 3 mL of dry THF under an argon atmosphere was added tetracyanoethylene (43.0 mg, 0.336 mmol). The reaction mixture was stirred for 1 h at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-ethyl acetate, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 108 mg (88%) of the ester 292 as a colorless oil. Analysis of this oil by TLC (petroleum ether-ethyl acetate, 3:1) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2255, 1732, 1153, 1113, 1045 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 1.27 (t, 3H, \(J = 7\) Hz, -OCH\(_2\)CH\(_3\)), 2.02-2.21 (m, 2H, -CHCH\(_2\)CH\(_2\)O-),
2.68-2.78 (m, 1H, H_c), 2.95-3.04 (m, 1H, H_b), 3.08-3.22 (m, 2H, H_d), 3.37 (s, 3H, -OCH_3), 3.40-3.50 (m, 1H, H_e), 3.64-3.81 (m, 3H, -CH_2CH_2O- and H_a), 4.17 (q, 2H, J = 7 Hz, -OCH_2CH_3), 4.59 (d, 1H, J = 7.5 Hz, -OCH_2O-), 4.61 (d, 1H, J = 7.5 Hz, -OCH_2O-). Irradiation at δ 2.13 sharpened the signal at δ 3.40-3.50 and converted part of the signal at δ 3.64-3.81 to two doublets (J = 10.5 Hz, each). Irradiation at δ 3.45 sharpened the signal at δ 2.02-2.21, converted the multiplet at δ 2.68-2.78 to a broad doublet (J = 13.5 Hz) and converted the multiplet at δ 2.95-3.04 to doublet of doublets (J = 13.5, 4.5 Hz). NOE difference experiment: irradiation at δ 2.13 caused enhancement of the signals at δ 3.40-3.50 and δ 3.64-3.81; irradiation at δ 3.45 caused enhancement of the signal at δ 2.02-2.21. Exact Mass calcd. for C_{18}H_{17}N_4O_3 (M^+-OCH_3): 337.1300; found: 337.1304.

Preparation of the Ester 293

To a stirred solution of the cyclobutanecarboxylate 259 (42.0 mg, 0.175 mmol) in 2 mL of dry THF under an argon atmosphere was added tetracyanoethylene (22.5 mg, 0.176 mmol). The reaction mixture was stirred for 24 h at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-ethyl acetate,
Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 56.0 mg (87%) of the ester 293 as a colorless oil. Analysis of this oil by TLC (petroleum ether-ethyl acetate, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2255, 1729, 1261, 1201, 1113, 1040 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 1.21 (t, 3H, $-\text{OCH}_2\text{CH}_3$), 1.97-2.10 (m, 1H, -CH$_2$CH$_2$O-), 2.15-2.28 (m, 1H, -CHCH$_2$CH$_2$O-), 2.65 (broad d, 1H, $J = 13.5$ Hz, $\text{H}_c$), 2.89 (broad dt, 1H, $J = 13.5$, 3 Hz, $\text{H}_b$), 3.05 (broad d, 1H, $J = 18$ Hz, $\text{H}_d$), 3.19 (broad d, 1H, $J = 18$ Hz, $\text{H}_d$), 3.31 (broad s, 4H, -OCH$_3$ and $\text{H}_e$), 3.51-3.76 (m, 3H, -CH$_2$CH$_2$O- and $\text{H}_a$), 4.02-4.20 (m, 2H, -OCH$_2$CH$_3$), 4.55 (d, 1H, $J = 6$ Hz, -OCH$_2$O-), 4.58 (d, 1H, $J = 6$ Hz, -OCH$_2$O-). Exact Mass calcd. for C$_{18}$H$_{17}$N$_4$O$_3$ (M$^+$-OCH$_3$): 337.1300; found: 337.1304.

**Preparation of the Ester 294**

![structure 294](image)

![structure 295](image)

To a stirred solution of the cyclobutanecarboxylate 263 (32.0 mg, 0.177 mmol) in 1.5 mL of dry THF under an argon atmosphere was added tetracyanoethylene (25.0 mg, 0.195 mmol). The reaction mixture was stirred for 3 h at room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (1 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump
to remove traces of solvent, afforded 47.0 mg (86%) of a mixture of the esters 294 and 295 in a ratio of ~24:1, respectively (1H NMR analysis). Recrystallization of this mixture from petroleum ether-diethyl ether provided the ester 294 as a white solid (melting point, 111-112°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl₃): 2230, 1720, 1085, 1035, 920 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 1.29 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.54 (d, 3H, J = 7 Hz, -CHCH₃), 1.56 (d, 3H, J = 7 Hz, -CHCH₃), 2.83 (ddt, 1H, J = 14, 4, 2 Hz, H₆), 2.90 (dddd, 1H, J = 14, 4, 3, 2 Hz, H₇b), 3.25-3.33 (m, 1H), 3.33-3.43 (m, 1H), 3.73-3.78 (m, 1H, H₈a), 4.15-4.25 (m, 2H, -OCH₂CH₃). Exact Mass calcd. for C₁₇H₁₆N₄O₂ (M⁺): 308.1273; found: 308.1274.

Preparation of the Triester 299

![Triester 299](image)

To a stirred solution of the cyclobutanecarboxylate 253 (45.0 mg, 0.296 mmol) in 1 mL of dry diethyl ether under an argon atmosphere was added dimethyl acetylenedicarboxylate (84.4 mg, 0.594 mmol). The reaction mixture was refluxed for 20 h and then was concentrated. The crude product was subjected to
chromatography on silica gel (3 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 74.0 mg (85%) of the triester 299 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1728, 1630, 1263 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 1.26 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 2.73-3.12 (m, 6H), 3.66-3.70 (m, 1H, H$_a$), 3.77 (s, 6H, -CO$_2$CH$_3$), 4.14 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$). Exact Mass calcd. for C$_{15}$H$_{18}$O$_6$ (M$^+$): 294.1103; found: 294.1096.

Preparation of the Triester 300

![Diagram of 300]

To a stirred solution of the triester 299 (74.0 mg, 0.250 mmol) in 1 mL of dry benzene under an argon atmosphere was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (57.0 mg, 0.251 mmol). The reaction mixture was refluxed for 1 h and then was concentrated. The crude product was subjected to chromatography on silica gel (3 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 68.0 mg (93%) of the triester 300 as a colorless oil. Analysis
of this oil by TLC (petroleum ether-diethyl ether, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1729, 1590, 1268, 1206, 781 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.28 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 3.49 (dd, 1H, $J = 15$, 6 Hz, H$_b$), 3.54 (dd, 1H, $J = 15$, 3 Hz, H$_b$), 3.89 (s, 6H, -CO$_2$CH$_3$), 4.20 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.34 (dd, 1H, $J = 6$, 3 Hz, H$_a$), 7.44 (s, 1H, aromatic proton), 7.55 (s, 1H, aromatic proton). Exact Mass calcd. for C$_{15}$H$_{16}$O$_6$ (M$^+$): 292.0947; found: 292.0945.

Preparation of the Triester 303

(a) From the Cyclobutanecarboxylate 254

![Chemical Structures]

To a stirred solution of the cyclobutanecarboxylate 254 (56.0 mg, 0.337 mmol) in 1 mL of dry diethyl ether under an argon atmosphere was added dimethyl acetylenedicarboxylate (92.5 mg, 0.651 mmol). The reaction mixture was refluxed for 20 h and then was concentrated. The crude product was subjected to chromatography on silica gel (3 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 85.0 mg (82%) of a colorless oil that consisted of a mixture of the triesters 301 (major isomer) and 302 (minor isomer).
as a colorless oil (ratio of 4:1, respectively, from $^1$H NMR analysis). The
$^1$H NMR (CDCl$_3$, 300 MHz) signals that could be assigned to the major triester 301 were the following: $\delta$ 1.13 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.22 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 3.70 (s, 3H, -CO$_2$CH$_3$), 3.76 (s, 3H, -CO$_2$CH$_3$), 4.11 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$). The only $^1$H NMR (CDCl$_3$, 300 MHz) signal that could be assigned to the minor triester 302 were the following: $\delta$ 1.08 (d, 3H, $J = 7$ Hz, -CHCH$_3$).

A stirred solution of a mixture of the triesters 301 and 302 (85.0 mg, 0.276 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (69.0 mg, 0.304 mmol) in 1 mL of dry benzene under an argon atmosphere was refluxed for 1 h. The solution was then concentrated and the crude product was subjected to chromatography on silica gel (3 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 69.0 mg (82%) of the triester 303 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1732, 1607, 1263, 1206, 796 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 1.28 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 2.25 (s, 3H, -CCH$_3$), 3.39 (dd, 1H, $J = 13.5$, 5 Hz, H$_b$), 3.45 (dd, 1H, $J = 13.5$, 3 Hz, H$_b$), 3.86 (s, 3H, -CO$_2$CH$_3$), 3.92 (s, 3H, -CO$_2$CH$_3$), 4.20 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.31 (dd, 1H, $J = 5$, 3 Hz, H$_b$), 7.56 (s, 1H, aromatic proton). Exact Mass calcd. for C$_{16}$H$_{18}$O$_6$ (M$^+$): 306.1103; found: 306.1103.
(b) From the Cyclobutanecarboxylate 255

To a stirred solution of the cyclobutanecarboxylate 255 (35.0 mg, 0.211 mmol) in 0.5 mL of dry benzene under an argon atmosphere was added dimethyl acetylenedicarboxylate (57.8 mg, 0.407 mmol). The reaction mixture was refluxed for 19 h and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, afforded a mixture of the triesters 301, 302 and 303 in a ratio of 3:5:2, respectively (¹H NMR analysis). A stirred solution of the mixture and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (52.6 mg, 0.232 mmol) in 0.5 mL of dry benzene under an argon atmosphere was refluxed for 1 h. The solution was then concentrated and the crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 32.2 mg (50%) of the triester 303. The ¹H NMR spectrum of this product was identical with that of the same material obtained as described in (a), above.

Preparation of the Triester 306

304 and 305

306
To a stirred solution of the cyclobutanecarboxylate 258 (40.0 mg, 0.162 mmol) in 1 mL of dry diethyl ether under an argon atmosphere was added dimethyl acetylenedicarboxylate (27.7 mg, 0.195 mmol). The reaction mixture was refluxed for 19 h and then was concentrated. The crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 2:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 56.8 mg (89%) of a colorless oil that consisted of a mixture of the triesters 304 (major isomer) and 305 (minor isomer) (ratio of 4:1, respectively, from 1H NMR analysis). The 1H NMR (CDCl₃, 300 MHz) signals that could be assigned to the major triester 304 were the following: δ 1.24 (t, 3H, J = 7 Hz, -OCH₂CH₃), 3.30 (s, 3H, -OCH₃), 3.74 (s, 3H, -CO₂CH₃), 3.78 (s, 3H, -CO₂CH₃), 4.12 (q, 2H, -OCH₂CH₃), 4.53 (s, 2H, -OCH₂O-). The 1H NMR (CDCl₃, 300 MHz) signals that could be assigned to the minor triester 305 were the following: δ 1.25 (t, 3H, J = 7 Hz, -OCH₂CH₃), 3.29 (s, 3H, -OCH₃), 4.51 (s, 2H, -OCH₂O-).

A stirred solution of a mixture of the triesters 304 and 305 (50.8 mg, 0.133 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (33.0 mg, 0.145 mmol) in 1 mL of dry benzene under an argon atmosphere was refluxed for 1 h. The solution was then concentrated and the crude product was subjected to chromatography on silica gel (3 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 45.0 mg (89%) of the triester 306 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1729, 1624, 1264, 1219, 1152, 1037, 768 cm⁻¹; 1H NMR (CDCl₃, 300 MHz): δ 1.29 (t, 3H, J = 7 Hz, -OCH₂CH₃), 2.80 (dt, 1H, J = 15, 7.5 Hz, -CH₂CH₂O-), 3.05 (dt, 1H, J = 15, 7.5 Hz, -CH₂CH₂O-) 3.27 (s,
3H, -OCH₃), 3.38-3.50 (m, 2H, Hₖ), 3.61-3.78 (m, 2H, -CH₂CH₂O-), 3.87 (s, 3H, -CO₂CH₃), 3.90 (s, 3H, -CO₂CH₃), 4.20 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.38 (broad t, 1H, J ~ 4 Hz, Hₐ), 4.56 (s, 2H, -OCH₂O-), 7.59 (s, 1H, aromatic proton). Exact Mass calcd. for C₁₉H₂₄O₈ (M⁺): 380.1471; found: 380.1468.

Preparation of the Diesters 307 and 308

To a stirred solution of the cyclobutanecarboxylate 254 (36.8 mg, 0.222 mmol) in 1 mL of dry benzene under an argon atmosphere was added methyl propynoate (28.0 mg, 0.333 mmol). The reaction mixture was refluxed for 12 h and then concentrated to remove excess methyl propynoate. A stirred solution of the mixture and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (60.0 mg, 0.264 mmol) in 1 mL of dry benzene under an argon atmosphere was refluxed for 1 h. The solution was then concentrated and the crude product was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 8:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 44.0 mg (81%) of a colorless oil that consisted of a mixture of the diesters 307 and 308 in a ratio of 5:1, respectively (¹H NMR analysis). This mixture exhibited IR (film): 1723, 1614, 1266, 1035, 772 cm⁻¹. The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the
major diester 307 were the following: \( \delta \) 1.29 (t, 3H, \( J = 7 \Hz, -\text{OCH}_2\text{CH}_3 \)), 1.49 (s, 3H, -\text{CCH}_3), 3.35-3.49 (m, 2H, \( \text{H}_b \)), 3.88 (s, 3H, -\text{CO}_2\text{CH}_3), 4.12 (q, 2H, \( J = 7 \Hz, -\text{OCH}_2\text{CH}_3 \)), 4.30 (broad t, 1H, \( J \sim 4 \Hz, \text{H}_a \)), 7.01 (d, 1H, \( J = 8 \Hz, \text{aromatic proton} \)), 8.00 (d, 1H, \( J = 8 \Hz, \text{aromatic proton} \)). The \( ^1\text{H} \) NMR (CDCl\(_3\), 400 MHz) signals that could be assigned to the minor diester 308 were the following: \( \delta \) 1.29 (t, 3H, \( J = 7 \Hz, -\text{OCH}_2\text{CH}_3 \)), 1.31 (s, 3H, -\text{CCH}_3), 3.35-3.49 (m, 2H, \( \text{H}_b \)), 3.90 (s, 3H, -\text{CO}_2\text{CH}_3), 4.12 (q, 2H, \( J = 7 \Hz, -\text{OCH}_2\text{CH}_3 \)), 4.30 (broad t, 1H, \( J \sim 4 \Hz, \text{H}_a \)), 7.60 (s, 1H, aromatic proton), 7.78 (s, 1H, aromatic proton). Exact Mass calcd. for C\(_{14}\)H\(_{16}\)O\(_4\) (M\(^+\)): 248.1049; found 248.1046.

General Procedure 7

Preparation of the Ketone 296

![Chemical Structure](image)

To a cold (-78°C), stirred solution of the diene 296 (1 equiv) and methyl vinyl ketone (MVK) (5 equiv) in dry dichloromethane (~10 mL per mmol of ester), under an argon atmosphere, was added boron trifluoride-etherate complex (1 equiv). The reaction mixture was stirred at -78°C for 1-3 h. Saturated aqueous ammonium chloride was added and the mixture was extracted thoroughly with diethyl ether.
The combined ether extracts were washed (water, brine), dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel. Concentration of the appropriate fractions afforded the ketone 313.

**Preparation of the Keto Ester 314**

Following general procedure 7 outlined above, the cyclobutanecarboxylate 254 was converted into the keto ester 314. The following amounts of reagents and solvents were used: the cyclobutanecarboxylate 254 (173 mg, 1.04 mmol) in 10 mL of dry CH₂Cl₂; MVK (362 mg, 5.16 mmol); BF₃·Et₂O (148 mg, 1.04 mmol). The reaction time was 1 h. The crude product was subjected to flash chromatography on silica gel (10 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 245 mg (99%) of the keto ester 314 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1730, 1709, 1179, 1038 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.80 (d, 3H, J = 7 Hz, -CH₃), 1.26 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.61-1.72 (m, 1H), 1.78 (dq, 1H, J = 14, 2.5 Hz), 1.93-2.00 (m, 2H), 2.13 (s, 3H, -COCH₃), 2.59-2.70 (m, 2H, Hb), 2.70-2.77 (m, 1H, Hd), 2.81 (ddd, 1H, J = 12, 5, 2.5 Hz, Hc), 3.57-3.64 (m, 1H, Ha), 4.15 (q, 2H, J = 7 Hz, CO₂Et).
-OCH₂CH₃). Irradiation at δ 0.80 sharpened the multiplet at δ 2.70-2.77. Irradiation at δ 1.97 simplified the multiplet at δ 1.61-1.72 to a doublet of doublets (J = 14, 12 Hz) and the doublet of quartets at δ 1.78 to a doublet of doublets (J = 14, 2.5 Hz), and sharpened the multiplet at δ 2.59-2.70. Irradiation at δ 3.60 simplified the multiplet at δ 2.59-2.70 to two broad doublets (J = 13 Hz). NOE difference experiments: irradiation at δ 0.80 caused enhancement of the signals at δ 1.61-1.72, δ 2.70-2.77 and δ 3.57-3.64; irradiation at δ 3.60 caused enhancement of the signals at δ 0.80 and δ 2.59-2.70. Exact Mass calcd. for C₁₄H₂₀O₃ (M⁺): 236.1412; found: 236.1414.

Preparation of the Keto Ester 315

Following general procedure 7 outlined above, the cyclobutanecarboxylate 255 was converted into the keto ester 315. The following amounts of reagents and solvents were used: the cyclobutanecarboxylate 255 (62.0 mg, 0.373 mmol) in 4 mL of dry CH₂Cl₂; MVK (131 mg, 1.87 mmol); BF₃·Et₂O (53.0 mg, 0.373 mmol). The reaction time was 3 h. The crude product was subjected to flash chromatography on silica gel (5 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 58.0 mg (66%) of the keto ester 315 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and
$^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1731, 1712, 1177, 1033 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): δ 0.89 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.25 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.59-1.70 (m, 1H), 1.89-2.03 (m, 2H), 2.08-2.16 (m, 1H), 2.17 (s, 3H, -COCH$_3$), 2.41 (ddd, 1H, $J = 11$, 8, 3 Hz, H$_c$), 2.50-2.58 (m, 1H, H$_d$), 2.58-2.69 (m, 2H, H$_b$), 3.52-3.57 (m, 1H, H$_a$), 4.12 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$).

Irradiation at δ 0.89 sharpened the multiplet at δ 2.50-2.58, while irradiation at δ 3.54 sharpened the multiplet at δ 2.58-2.69. NOE difference experiment: irradiation at δ 3.54 caused enhancement of the signals at δ 2.50-2.58 and δ 2.58-2.69. Exact Mass calcd. for C$_{14}$H$_{20}$O$_3$ (M$^+$): 236.1412; found: 236.1417.

Preparation of the Keto Ester 316

Following general procedure 7 outlined above, the cyclobutanecarboxylate 258 was converted into the keto ester 316. The following amounts of reagents and solvents were used: the cyclobutanecarboxylate 258 (55.0 mg, 0.229 mmol) in 2.5 mL of dry CH$_2$Cl$_2$; MVK (80.3 mg, 1.15 mmol); BF$_3$·Et$_2$O (32.5 mg, 0.229 mmol). The reaction time was 1 h. The crude product was subjected to flash chromatography on silica gel (2 g, elution with petroleum ether-ethyl acetate, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump
to remove traces of solvent, afforded 57.5 mg (81%) of the keto ester 316 as a colorless oil. Analysis of this oil by TLC (petroleum ether-ethyl acetate, 3:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1729, 1709, 1152, 1112, 1039 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.27 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.40-1.61 (m, 2H, -CH$_2$CH$_2$O-), 1.66-1.78 (m, 1H), 1.83-1.91 (m, 1H), 1.97-2.05 (m, 2H), 2.16 (s, 3H, -COCH$_3$), 2.59 (broad d, 1H, $J = 13$ Hz, H$_b$), 2.71 (broad dd, 1H, $J = 13$, 4 Hz, H$_b$), 2.75-2.85 (m, 2H, H$_c$ and H$_d$), 3.32 (s, 3H, -OCH$_3$), 3.44-3.60 (m, 2H, -CH$_2$CH$_2$O-), 3.60-3.65 (m, 1H, H$_a$), 4.15 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.57 (s, 2H, -OCH$_2$O-). Irradiation at $\delta$ 1.50 sharpened the multiplet at $\delta$ 2.75-2.85 and simplified the multiplet at $\delta$ 3.44-3.60 to two broad doublets ($J = 11$ Hz). Irradiation at $\delta$ 2.00 sharpened the signals at $\delta$ 1.66-1.78, $\delta$ 1.83-1.91, $\delta$ 2.59 and $\delta$ 2.71. Irradiation at $\delta$ 3.62 sharpened the signal at $\delta$ 2.59 and simplified the signal at $\delta$ 2.71 to a broad doublet ($J = 13$ Hz). NOE difference experiment: irradiation at $\delta$ 1.50 caused enhancement of the signals at $\delta$ 2.75-2.85, $\delta$ 3.44-3.60 and $\delta$ 3.60-3.65. **Exact Mass** calcd. for C$_{17}$H$_{26}$O$_5$ (M$^+$): 310.1780; found: 310.1782.

**Preparation of 1-(Hydroxymethyl)-(E)-2-ethylidene-3-methylene cyclobutane (317)**
To a cold (0°C), stirred solution of lithium aluminum hydride (32.0 mg, 0.843 mmol) in 3 mL of dry diethyl ether under an argon atmosphere was added the cyclobutanecarboxylate 254 (232 mg, 1.40 mmol) as a solution in 1 mL of dry diethyl ether. The reaction mixture was stirred at 0°C for 5 min, then at room temperature for 5 min. Sodium sulfate decahydrate (271 mg, 0.842 mmol) was added and the mixture was stirred at room temperature for 10 min. The resulting solid was removed by filtration through a short column of Florisil (2 g) and the column was eluted with diethyl ether. Concentration of the eluate, followed by distillation (air-bath temperature 45-50°C/0.2 Torr) of the material thus obtained, afforded 159 mg (92%) of the alcohol 317 as a colorless oil. Analysis of this oil by GLC, TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 3327 (broad), 1673, 1646, 1439, 1024, 864 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 1.43 (broad s, 1H, exchanged with D₂O, -OH), 1.70 (d, 3H, J = 7 Hz, =CHCH₃), 2.38-2.47 (m, 1H, H₈), 2.72-2.84 (m, 1H, H₇), 3.16-3.27 (m, 1H, H₆), 3.76 (dd, 1H, J = 13, 8 Hz, -CHCH₂OH), 3.85 (dd, 1H, J = 13, 6 Hz, -CHCH₂OH), 4.66 (broad s, 1H, H₅), 5.08 (broad t, 1H, J = 2 Hz, H₄), 5.78 (qd, 1H, J = 7, 2 Hz, H₃). **Exact Mass** calcd. for C₈H₁₂O (M⁺): 124.0888; found: 124.0891.
Preparation of \(1-(\text{tert-Butyldiphenylsilyloxy}-\text{methyl})-(\text{E})-2\text{-ethyldene}-3\text{-methylenecyclobutane} \ (318)\)

\[
\begin{array}{c}
\text{H}_d \\
\text{H}_e \\
\text{H}_f \\
\text{H}_g \\
\text{OSi(BuPh)}_2
\end{array}
\]

318

To a stirred solution of the alcohol 317 (165 mg, 1.33 mmol) in 13 mL of dry \(N,N\)-dimethylformamide under an argon atmosphere was added imidazole (230 mg, 3.38 mmol) and \text{tert}-butylchlorodiphenylsilane (438 mg, 1.59 mmol). The reaction mixture was stirred for 16 h at room temperature. Saturated ammonium chloride solution was added and the mixture was extracted thoroughly with petroleum ether. The combined petroleum ether extracts were washed (water, brine), dried (MgSO\(_4\)) and concentrated. The residual oil was subjected to flash chromatography on silica gel (10 g, elution with petroleum ether). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 435 mg (90\%) of the ether 318 as a colorless oil. Analysis of this oil by TLC (petroleum ether) and \(^1\)H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1673, 1647, 1428, 1112, 1083, 824 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 1.05 (s, 9H, -SiCMe\(_3\)), 1.57 (d, 3H, \(J = 7\) Hz, -CHCH\(_3\)), 2.35-2.43 (m, 1H, \(H_b\)), 2.68-2.76 (m, 1H, \(H_c\)), 3.11-3.20 (m, 1H, \(H_d\)), 3.70 (dd, 1H, \(J = 11, 8\) Hz, -CHCH\(_2\)O-), 3.89 (dd, 1H, \(J = 11, 6\) Hz, -CHCH\(_2\)O-), 4.60 (broad s, 1H, \(H_e\)), 5.03 (broad t, 1H, \(J \sim 2\) Hz, \(H_e\)), 5.67 (qd, 1H, \(J = 7, 2\) Hz, \(H_f\)), 7.36-7.47 (m, 6H, aromatic protons), 7.68-7.74 (m, 4H, aromatic protons). Irradiation at \(\delta\) 5.03 simplified both
multiplets at $\delta$ 2.35-2.43 and $\delta$ 2.68-2.76 to a pair of doublets of doublets of doublets ($J = 16, 5, 2$ Hz and $J = 16, 9, 2$ Hz, respectively). **Exact Mass** calcd. for C$_{20}$H$_{21}$OSi (M$^+$-CMe$_3$): 305.1362; found: 305.1370.

**Preparation of the Keto Ether 319**

Following general procedure 7 outlined above, the ether 318 was converted into the keto ether 319. The following amounts of reagents and solvents were used: the ether 319 (143 mg, 0.395 mmol) in 4 mL of dry CH$_2$Cl$_2$; MVK (135 mg, 1.92 mmol); BF$_3$-Et$_2$O (56.1 mg, 0.395 mmol). The reaction time was 1 h. The crude product was subjected to flash chromatography on silica gel (5 g, elution with petroleum ether-diethyl ether, 40:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 158 mg (93%) of the keto ether 319 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 40:1) and $^1$H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1709, 1429, 1113, 1083, 703 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 0.82 (d, 3H, $J = 7$ Hz, -CH$_3$), 1.08 (s, 9H, -SiCMe$_3$), 1.60-1.82 (m, 2H), 1.82-2.02 (m, 2H), 2.06 (broad d, 1H, $J = 12$ Hz, H$_c$), 2.11 (s, 3H, -COCH$_3$), 2.43 (broad dd, 1H, $J = 12, 4.5$ Hz, H$_b$), 2.70-2.84 (m, 2H, H$_d$ and H$_e$), 3.00-3.10 (m, 1H, H$_d$), 3.72 (dd, 1H, $J = 10.5, 7.6$ Hz, -CH$_2$O), 3.81 (dd, 1H, $J = 10.5, 5.7$ Hz, -COCH$_3$).
-CHCH₂O-), 7.36-7.48 (m, 6H, aromatic protons), 7.67-7.72 (m, 4H, aromatic protons). Irradiation at δ 0.82 sharpened the multiplet at δ 2.70-2.84. Irradiation at δ 2.43 simplified the broad doublet at δ 2.06 to a broad singlet and sharpened the multiplet at δ 3.00-3.10. Irradiation at δ 3.76 sharpened the multiplet at δ 3.00-3.10. NOE difference experiments: irradiation at δ 0.82 caused enhancement of the signals at δ 2.70-2.84 and δ 3.00-3.10; irradiation at δ 3.05 caused enhancement of the signals at δ 0.82, δ 2.43, δ 3.72 and δ 3.81. Exact Mass calcd. for C₂₈H₃₆O₂Si (M⁺): 432.2485; found: 432.2491.

Preparation of the Nitro Ester 320

![Diagram of 320]

To a cold (0°C), stirred solution of the cyclobutanecarboxylate 254 (32.5 mg, 0.195 mmol) in 2 mL of dichloromethane under an argon atmosphere was added freshly prepared nitroethylene (300 mg, 4.11 mmol). The reaction mixture was stirred at 0°C for 3 h and then was concentrated. The crude product was subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 37.0 mg (79%) of a mixture of the nitro ester 320 and two other isomers in a ratio of 84:9:7, respectively (¹H NMR analysis). Recrystallization of this mixture from petroleum ether-diethyl ether provided the nitro ester 320 as a colorless plate-like solid (melting point, 68-
69°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 3:1) and
$^1$H NMR spectroscopy indicated that it consisted of one component. This material
exhibited IR (CCl₄): 1734, 1548, 1372, 1180, 1036 cm⁻¹; $^1$H NMR (CDCl₃, 400
MHz): \( \delta \) 0.96 (d, 3H, \( J = 7 \) Hz, -CHCH₃), 1.28 (t, 3H, \( J = 7 \) Hz,
-OCH₂CH₃), 2.08-2.29 (m, 4H), 2.68 (broad d, 1H, \( J = 14 \) Hz, Hc), 2.75 (dd, 
1H, \( J = 14 \), 4.5 Hz, Hb), 3.00-3.10 (m, 1H, Hc), 3.62-3.69 (m, 1H, Ha), 4.17
(q, 2H, \( J = 7 \) Hz, -OCH₂CH₃), 4.77 (q, 1H, \( J = 6 \) Hz, Hz). Irradiation at
\( \delta \) 2.18 sharpened the signals at \( \delta \) 3.62-3.69 and simplified the quartet at \( \delta \) 4.77 to
a doublet (\( J = 6 \) Hz). Irradiation at \( \delta \) 3.05 simplified the doublet at \( \delta \) 0.96 to a
singlet and the quartet at \( \delta \) 4.77 to a triplet (\( J = 6 \) Hz), and sharpened the signals
at \( \delta \) 2.68 and \( \delta \) 2.75. Irradiation at \( \delta \) 3.64 sharpened the broad doublet at \( \delta \) 2.68
and simplified the doublet of doublets at \( \delta \) 2.75 to a doublet (\( J = 14 \) Hz). NOE
difference experiments: irradiation at \( \delta \) 0.96 caused enhancement of the signals at
\( \delta \) 3.00-3.10 and \( \delta \) 3.62-3.69; irradiation at \( \delta \) 3.05 caused enhancement of the
signals at \( \delta \) 0.96 and \( \delta \) 4.77. **Exact Mass** calcd. for C₁₂H₁₇O₄N (M⁺): 239.1157;
found: 239.1160.

The \(^1\)H NMR signals that could be assigned to the two minor isomers
were \( \delta \) 1.04 (d, 3H, \( J = 7 \) Hz, -CHCH₃) and \( \delta \) 1.09 (d, 3H, \( J = 7 \) Hz,
-CHCH₃), respectively.
Preparation of the Nitro Ether 321

To a cold (0°C), stirred solution of the ether 318 (80.0 mg, 0.221 mmol) in 2 mL of dichloromethane under an argon atmosphere was added freshly prepared nitroethylene (320 mg, 4.40 mmol). The reaction mixture was stirred at 0°C for 3 h and then was concentrated. The crude product was subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 8:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 78.0 mg (81%) of the nitro ether 321 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 8:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1544, 1429, 1377, 1112, 703 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.92 (d, 3H, J = 7 Hz, -CHCH₃), 1.05 (s, 9H, -SiCMe₃), 2.01-2.21 (m, 5H, one of the protons was Hc), 2.45 (broad d, 1H, J = 14 Hz, Hb), 2.98-3.09 (m, 2H, Ha and Hc), 3.18 (dd, 1H, J = 10, 8 Hz, -CHCH₂O⁻), 3.28 (dd, 1H, J = 10, 6 Hz, -CHCH₂O⁻), 4.67 (dt, 1H, J = 10, 5 Hz, Hd), 7.36-7.46 (m, 6H, aromatic protons), 7.64-7.70 (m, 4H, aromatic protons). Exact Mass calcd. for C₂₂H₂₄O₃NSi (M⁺-CMe₃): 378.1525; found: 378.1518.
10. Thermal Ring Opening of Functionalized Bicyclic Cyclobutenes

Preparation of the Diols 322 and 323

![Diagram of molecules 322 and 323]

To a cold (-78°C), stirred solution of the keto ester 314 (247 mg, 1.05 mmol) in 5 mL of dry diethyl ether under an argon atmosphere, was added dropwise, a solution of diisobutylaluminum hydride (3.70 mL, 3.70 mmol) in toluene. The reaction mixture was stirred at -78°C for 1 h and at 0°C for 1 h. Aqueous hydrochloric acid (5%, 10 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel (10 g, elution with petroleum ether-diethyl ether, 2:3). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 181 mg (88%) of a mixture of the diols 322 (major isomer) and 323 (minor isomer) in a ratio of 4:1, respectively (¹H NMR analysis).

Recrystallization of this mixture from petroleum ether-diethyl ether provided the major diol 322 as a white solid (melting point, 113-114°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 2:3) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl₃): 3600, 2900, 1460, 1375, 1015 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.96 (d, 3H, J = 7 Hz, -CHCH₃), 1.27 (d, 3H, J = 6 Hz, -CHOHCH₃), 1.31-1.46 (m,
3H, part of the multiplet exchanged with D$_2$O), 1.49-1.62 (m, 2H), 1.90-2.06 (m, 2H), 2.18 (broad d, 1H, $J = 12$ Hz, H$_c$), 2.44-2.55 (m, 2H, H$_b$ and H$_d$), 3.03-3.11 (m, 1H, H$_a$), 3.61-3.67 (m, 2H, -CHOHCH$_3$ and -CHCH$_2$OH), 3.74 (dd, 1H, $J = 10$, 6 Hz, -CHCH$_2$OH). Irradiation at $\delta$ 0.96 sharpened the multiplet at $\delta$ 2.44-2.55. Irradiation at $\delta$ 1.27 simplified the multiplet at $\delta$ 3.61-3.67. Irradiation at $\delta$ 3.07 simplified the H$_b$ part of the multiplet at $\delta$ 2.44-2.55 to a broad doublet ($J = 12$ Hz), part of the signal at $\delta$ 3.61-3.67 to a doublet ($J = 10$ Hz), and the signal at $\delta$ 3.74 to a doublet ($J = 10$ Hz). **Exact Mass** calcd. for C$_{12}$H$_{20}$O$_2$ (M$^+$): 196.1463; found: 196.1462.

The $^1$H NMR (CDCl$_3$, 400 MHz) signals that could be assigned to the minor diol 323 were the following: $\delta$ 0.86 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.25 (d, 3H, $J = 6$ Hz, -CHOHCH$_3$).

**Preparation of the Keto Aldehyde 324**

![Diagram](image)

To a cold (-78°C), stirred solution of dry dimethyl sulfoxide (73.8 mg, 0.945 mmol) in 3.5 mL of dry dichloromethane under an argon atmosphere, was added oxalyl chloride (105 mg, 0.827 mmol). After the reaction mixture had been stirred at -78°C for 15 min, a solution of the diols 322 and 323 (73.7 mg, 0.376 mmol) in 0.5 mL of dry dichloromethane was added dropwise. The resulting mixture was stirred at -78°C for 15 min. Dry triethylamine (305 mg, 3.01 mmol) was added and the solution was stirred at -78°C for 5 min, and at room
temperature for 30 min. Saturated aqueous ammonium chloride (10 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄), and concentrated. The residual oil was subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 61.5 mg (85%) of the keto aldehyde 324 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2707, 1708, 1366 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.83 (d, 3H, J = 7 Hz, -CHCH₃), 1.63-1.83 (m, 2H), 2.00-2.08 (m, 2H), 2.15 (s, 3H, -COCH₃), 2.61 (broad d, 1H, J = 14 Hz, Hc), 2.66-2.76 (m, 2H, Hb and Hz), 2.84 (ddd, 1H, J = 12, 6, 4 Hz, Hd), 3.58-3.63 (m, 1H, Ha), 9.59 (d, 1H, J = 4 Hz, -CHO). Exact Mass calcd. for C₁₂H₁₆O₂ (M⁺): 192.1150; found: 192.1145.

Preparation of the Diols 325 and 326

To a cold (-78°C), stirred solution of the keto ester 315 (160 mg, 0.678 mmol) in 7 mL of dry diethyl ether under an argon atmosphere was added, dropwise, a solution of diisobutylaluminum hydride (2.40 mL, 2.40 mmol) in toluene. The reaction mixture was stirred at -78°C for 1 h and at 0°C for 1 h.
Aqueous hydrochloric acid (5%, 10 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel (6.5 g, elution with petroleum ether-diethyl ether, 2:3). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 113 mg (85%) of a mixture of the diols 325 (major isomer) and 326 (minor isomer) in a ratio of 5:3, respectively (¹H NMR analysis).

Recrystallization of this mixture from petroleum ether-diethyl ether provided the major diol 325 as a white solid (melting point, 109-110.5°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 2:3) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl₃): 3600, 1500, 1410, 1010 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.04 (d, 3H, J = 7 Hz, -CHCH₃), 1.23 (d, 3H, J = 6 Hz, -CHOHCH₃), 1.32 (broad s, 2H, exchanged with D₂O, -OH), 1.55-1.66 (m, 2H), 1.74-1.83 (m, 1H), 1.95-2.03 (m, 2H), 2.11-2.19 (m, 1H, H₆), 2.20 (broad d, 1H, J ~ 14 Hz, H₇), 2.53 (broad dt, 1H, J ~ 14, 4 Hz, H₈), 2.96-3.04 (m, 1H, H₉), 3.76 (dd, 1H, J = 12, 7 Hz, -CH₂OH), 3.84 (dd, 1H, J = 12, 5 Hz, -CH₂OH), 3.93-4.01 (m, 1H, -CHOHCH₃). Exact Mass calcd. for C₁₂H₂₀O₂ (M⁺): 196.1463; found: 196.1458.

The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the minor diol 326 were the following: δ 1.15 (d, 3H, J = 6 Hz, -CHOHCH₃), 3.88-3.93 (m, 1H, -CHOHCH₃).
Preparation of the Keto Aldehyde 327

To a cold (-78°C), stirred solution of dry dimethylsulfoxide (81.6 mg, 1.04 mmol) in 4 mL of dry dichloromethane under an argon atmosphere, was added oxalyl chloride (126 mg, 0.993 mmol). After the reaction mixture had been stirred at -78°C for 15 min, a solution of the diols 325 and 326 (89.0 mg, 0.454 mmol) in 0.5 mL of dry dichloromethane was added dropwise. The resulting mixture was stirred at -78°C for 15 min. Dry triethylamine (305 mg, 3.01 mmol) was added, and the solution was stirred at -78°C for 5 min and at room temperature for 30 min. Saturated aqueous ammonium chloride (10 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO4) and concentrated. The residual oil was subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 71.1 mg (82%) of the keto aldehyde 327 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2708, 1719, 1710, 1364, 1158 cm⁻¹; 1H NMR (CDCl3, 400 MHz): δ 0.87 (d, 3H, J = 7 Hz, -CHCH3), 1.64-1.76 (m, 1H), 1.98 (d of quintets, 1H, J = 13, 3 Hz), 2.01-2.18 (m, 2H), 2.19 (s, 3H, -COCH3), 2.40 (ddd, 1H, J = 11, 8, 3 Hz, H_d), 2.52-2.64 (m, 2H, H_c and H_e),
2.67-2.75 (m, 1H, H_b), 3.52-3.57 (m, 1H, H_a), 9.48 (d, 1H, J = 6 Hz, -CHO).

Exact Mass calcd. for C_{12}H_{16}O_{2} (M^+): 192.1150; found: 192.1145.

Preparation of the Keto Ether Diene 328

A solution of the keto ether 319 (120 mg, 0.277 mmol) in 3 mL of mesitylene was refluxed for 1 h under an argon atmosphere. The reaction mixture was cooled to room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (6 g, elution first with petroleum ether, then with petroleum ether-diethyl ether, 19:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 100 mg (83%) of the keto ether diene 328 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 19:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1710, 1155, 1060, 705 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.68 (d, 3H, J = 7 Hz, -CHCH₃), 1.06 (s, 9H, -SiCMe₃), 1.69-1.79 (m, 2H), 2.01 (s, 3H, -COCH₃), 2.02-2.13 (m, 1H), 2.38-2.50 (m, 2H, one of the protons was H_c), 3.01-3.09 (m, 1H, H_d), 4.28 (dd, 1H, J = 13.5, 5.5 Hz, =CHCH₂O-), 4.39 (dd, 1H, J = 13.5, 7.5 Hz, =CHCH₂O-), 4.73 (broad t, 1H, J ~ 1.5 Hz, H_a), 4.88 (broad t, 1H, J ~ 1.5 Hz, H_b), 5.67 (dd, 1H, J = 7.5, 5.5 Hz, H_c), 7.37-7.48...
(m, 6H, aromatic protons), 7.70-7.78 (m, 4H, aromatic protons). Irradiation at δ 0.68 simplified the multiplet at δ 3.01-3.09 to a doublet (J = 4 Hz). Irradiation at δ 3.05 converted the doublet at δ 0.68 to a singlet and simplified part of the signal at δ 2.38-2.50. NOE difference experiment: irradiation at δ 5.67 caused enhancement of the signals at δ 4.28, δ 4.39 and δ 4.88. **Exact Mass** calcd. for C_{28}H_{36}O_2Si: 432.2484; found: 432.2475.

This product was refluxed in mesitylene for 1 h under an argon atmosphere and no isomerization of the double bonds was observed.

**Preparation of the Nitro Ether Dienes 329 and 330**

A solution of the nitro ether 321 (45.0 mg, 0.103 mmol) in 1 mL of mesitylene was refluxed for 1 h under an argon atmosphere. The reaction mixture was cooled to room temperature and then was concentrated. The crude product was subjected to chromatography on silica gel (6 g, elution first with petroleum ether, then with diethyl ether). Concentration of the diethyl ether fractions afforded 38 mg (85%) of a mixture of the nitro ether dienes 329 and 330 in a ratio of 3:1, respectively (¹H NMR analysis). This mixture was again subjected to chromatography on silica gel (2 g, elution with petroleum ether-diether ether, 19:1). Concentration of the appropriate fractions, followed by pumping on a vacuum
pump to remove traces of solvent, afforded 25.0 mg (56%) of the nitro ether diene 329, as a colorless oil, and 9.0 mg (20%) of the nitro ether diene 330, also as a colorless oil. Analysis of both oils by TLC (petroleum ether-diethyl ether, 19:1) and $^1$H NMR spectroscopy indicated that each oil consisted of one component.

The major nitro ether diene 329 exhibited IR (film): 1546, 1376, 1112, 703 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.77 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.08 (s, 9H, -SiCMe$_3$), 2.07-2.20 (m, 3H), 2.45-2.52 (m, 1H), 3.36-3.45 (m, 1H, H$_d$), 4.26 (dd, 1H, $J = 14$, 5.5 Hz, =CHCH$_2$O$^-$), 4.33 (dt, 1H, $J = 11$, 5 Hz, H$_e$), 4.37 (dd, 1H, $J = 14$, 7 Hz, =CHCH$_2$O$^-$), 4.81 (broad s, 1H, H$_a$), 4.96 (broad s, 1H, H$_b$), 5.75 (dd, 1H, $J = 7$, 5.5 Hz, H$_c$), 7.38-7.48 (m, 6H, aromatic protons), 7.69-7.76 (m, 4H, aromatic protons). Irradiation at $\delta$ 0.77 simplified the multiplet at $\delta$ 3.36-3.45 to a doublet ($J = 5$ Hz). NOE difference experiment: irradiation at $\delta$ 5.75 caused enhancement of the signals at $\delta$ 4.26, $\delta$ 4.37 and $\delta$ 4.96. Exact Mass calcd. for C$_{26}$H$_{33}$NO$_3$Si (M$^+$): 435.2230; found: 435.2229.

The minor nitro ether diene 330 exhibited IR (film): 1545, 1371, 1112, 703 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.99 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.06 (s, 9H, -SiCMe$_3$), 2.00-2.48 (m, 4H), 3.43-3.52 (m, 1H, H$_d$), 4.29 (dd, 1H, $J = 13$, 6 Hz, =CHCH$_2$O$^-$), 4.32-4.38 (m, 2H, H$_e$ and =CHCH$_2$O$^-$), 4.77 (broad s, 1H, H$_a$), 4.95 (broad t, 1H, $J \sim 1.5$ Hz, H$_b$), 5.74 (t, 1H, $J = 6$ Hz, H$_c$), 7.36-7.47 (m, 6H, aromatic protons), 7.68-7.74 (m, 4H, aromatic protons). NOE difference experiment: irradiation at $\delta$ 5.74 caused enhancement of the signals at $\delta$ 4.29, $\delta$ 4.32-4.38 and $\delta$ 4.95. Exact Mass calcd. for C$_{26}$H$_{33}$NO$_3$Si (M$^+$): 435.2230; found: 435.2223.
Preparation of the Keto Ester Dienes 331 and 332

A solution of the keto ester 314 (150 mg, 0.636 mmol) in 6 mL of mesitylene was refluxed for 1 h under an argon atmosphere. The reaction mixture was cooled to room temperature and then was concentrated. The crude product was subjected to flash chromatography on silica gel (6 g, elution first with petroleum ether, then with diethyl ether). Concentration of the diethyl ether fractions afforded 128 mg (85%) of a mixture of the keto ester dienes 331 and 332 in a ratio of 11:1, respectively (1H NMR analysis). This mixture was again subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 114 mg (76%) of the keto ester diene 331, as a colorless oil, and 11 mg (7%) of the keto ester diene 332, also as a colorless oil. Analysis of both oils by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that each oil consisted of one component.

The keto ester diene 331 exhibited IR (film): 1713, 1635, 1184, 1137 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.88 (d, 3H, J = 7 Hz, -CHCH₃), 1.32 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.73-1.82 (m, 1H), 1.87 (qd, 1H, J = 13, 5.5 Hz), 2.10-2.24 (m, 1H), 2.22 (s, 3H, -COCH₃), 2.53 (ddd, 1H, J = 14, 5, 2 Hz), 2.70 (dt, 1H, J = 13, 4 Hz, Hₖ), 4.20 (q, 2H, J = 7 Hz, -OCH₂CH₃), 4.57-4.67 (m, 1H, Hₜ), 4.91 (broad t, 1H, J ~ 2 Hz, Hₙ), 5.03 (broad t, 1H, J ~ 2 Hz, Hₗ), 5.84 (s, 1H, Hₜ). Irradiation at δ 0.88 simplified the multiplet at δ 4.57-
4.67 to a doublet ($J = 4$ Hz). Irradiation at $\delta$ 2.70 sharpened the signal at $\delta$ 1.73-1.82, and simplified the signal at $\delta$ 1.87 to a triplet of doublets ($J = 13, 5.5$ Hz) and the multiplet at $\delta$ 4.57-4.67 to a quartet ($J = 7$ Hz). Irradiation at $\delta$ 4.63 simplified the doublet at $\delta$ 0.88 to a singlet and the signal at $\delta$ 2.70 to a doublet of doublets ($J = 13, 4$ Hz). NOE difference experiments: irradiation at $\delta$ 0.88 caused enhancement of the signals at $\delta$ 1.73-1.82 and $\delta$ 4.57-4.67; irradiation at $\delta$ 5.84 caused enhancement of the signal at $\delta$ 5.03. **Exact Mass** calcd. for C$_{14}$H$_{20}$O$_{3}$ (M$^+$): 236.1412; found: 236.1411.

The keto ester diene 332 exhibited IR (film): 1724, 1709, 1638, 1181 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 0.90 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.26 (t, 3H, $J = 7$ Hz, -OCH$_2$CH$_3$), 1.77-1.94 (m, 2H), 2.17 (s, 3H, -COCH$_3$), 2.18-2.28 (m, 1H), 2.52 (ddd, 1H, $J = 13, 4.5, 3$ Hz), 2.78 (dt, 1H, $J = 12, 4$ Hz, H$_e$), 2.90-2.98 (m, 1H, H$_d$), 4.14 (q, 2H, $J = 7$ Hz, -OCH$_2$CH$_3$), 4.90 (broad t, 1H, $J \sim 1.5$ Hz, H$_a$), 5.08 (broad t, 1H, $J \sim 1.5$ Hz, H$_b$), 5.72 (s, 1H, H$_c$). NOE difference experiments: irradiation at $\delta$ 2.94 caused enhancement of the signals at $\delta$ 0.90, $\delta$ 2.78 and $\delta$ 5.72; irradiation at $\delta$ 5.72 caused enhancement of the signal at $\delta$ 2.90-2.98. **Exact Mass** calcd. for C$_{14}$H$_{20}$O$_{3}$ (M$^+$): 236.1412; found: 236.1417.

Both materials were refluxed in mesitylene for 1 h under an argon atmosphere and no isomerization of the double bonds was observed in either case.
Preparation of the Diol Diene 333 (major isomer)

(a) By Reduction of the Keto Ester Diene 331

To a cold (-78°C), stirred solution of the keto ester diene 331 (75.3 mg, 0.319 mmol) in 3 mL of dry diethyl ether under an argon atmosphere was added, dropwise, a solution of diisobutylaluminum hydride (1.1 mL, 1.1 mmol) in hexane. The reaction mixture was stirred at -78°C for 1 h and at 0°C for 1 h. Saturated aqueous ammonium chloride (5 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 2:3). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 56.0 mg (90%) of a mixture of the diol dienes 333 (major isomer) and 334 (minor isomer) in a ratio of 11:1, respectively (¹H NMR analysis).

Recrystallization of this mixture from petroleum ether-diethyl ether provided the major diol diene 333 as a white solid (melting point, 72.5-74°C). Analysis of this solid by TLC (petroleum ether-diethyl ether, 2:3) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (CHCl₃): 3600, 1640, 1000, 900 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.90 (d, 3H, J = 7 Hz, -CHCH₃), 1.25 (d, 3H, J = 6 Hz, -CHOHCH₃), 1.32-1.46 (m, 1H), 1.49-
1.61 (m, 2H), 1.71 (broad s, 2H, exchanged with D$_2$O, -OH), 2.10-2.21 (m, 1H), 2.42 (ddd, 1H, $J$ = 14, 4, 2 Hz), 3.20-3.30 (m, 1H, H$_d$), 3.60-3.70 (m, 1H, -CHOHCH$_3$), 4.14 (dd, 1H, $J$ = 12, 6 Hz, =CHCH$_2$OH), 4.30 (dd, 1H, $J$ = 12, 8 Hz, =CHCH$_2$OH), 4.71 (broad t, 1H, $J$ ~ 2 Hz, H$_a$), 4.88 (broad t, 1H, $J$ ~ 2 Hz, H$_b$), 5.61 (dd, 1H, $J$ = 8, 6 Hz, H$_c$). Irradiation at $\delta$ 0.90 simplified the multiplet at $\delta$ 3.20-3.30 to a doublet ($J$ = 4 Hz). Irradiation at $\delta$ 1.25 simplified the multiplet at $\delta$ 3.60-3.70 to a doublet ($J$ = 8 Hz). Exact Mass calcd. for C$_{12}$H$_{20}$O$_2$ (M$^+$): 196.1463; found: 196.1465.

The only $^1$H NMR (CDCl$_3$, 400 MHz) signal that could be assigned to the minor diol diene 334 was the following: $\delta$ 0.85 (d, 3H, $J$ = 7 Hz, -CHCH$_3$).

(b) By Thermolysis of Diol 322

A sample of the major diol 322 (20 mg, 0.10 mmol) in a sealed capillary tube was heated in a preheated oil bath (160°C) for 0.5 h. The tube was cooled to room temperature and the product was extracted with chloroform-$d$. Concentration of the solution, followed by pumping on a vacuum pump to remove traces of solvent, afforded 16 mg (80%) of the major diol diene 333. The $^1$H NMR spectrum of this product was identical with that of the major diol diene 333 obtained from the reduction of keto ester diene 331.

This product was refluxed in mesitylene for 1 h under an argon atmosphere and no isomerization of the double bonds was observed.
Preparation of the Keto Ester Dienes 335 and 336

A solution of the keto ester 315 (75.6 mg, 0.320 mmol) in 3.2 mL of mesitylene was refluxed for 1 h under an argon atmosphere. The reaction mixture was cooled to room temperature and then was concentrated. The crude product was subjected to flash chromatography on silica gel (6 g, elution first with petroleum ether, then with diethyl ether). Concentration of the diethyl ether fractions afforded 62.0 mg (82%) of a mixture of the keto ester dienes 335 and 336 in a ratio of 1:1, respectively (1H NMR analysis). This mixture was subjected to chromatography on silica gel again (2.5 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 30.0 mg (40%) of the keto ester diene 335, as a colorless oil and 29.0 mg (38%) of the the keto ester diene 336, as a colorless oil. Analysis of both oils by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that each oil consisted of one component.

The keto ester diene 335 exhibited IR (film): 1712, 1635, 1176, 1138, 902 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 1.17 (d, 3H, J = 7 Hz, -CHCH₃), 1.29 (t, 3H, J = 7 Hz, -OCH₂CH₃), 1.84-1.95 (m, 1H), 1.99-2.07 (m, 1H), 2.20 (s, 3H, -COCH₃), 2.27-2.45 (m, 2H), 2.53-2.59 (m, 1H, H₆), 4.14-4.23 (m, 2H, -OCH₂CH₃), 4.55 (broad q, 1H, J = 7 Hz, H₄), 4.85 (broad s, 1H, H₉), 5.03
(broad t, 1H, J ~ 1.5 Hz, H_b), 5.82 (s 1H, H_c). Irradiation at δ 1.17 converted the signal at δ 4.55 to a broad doublet (J ~ 1 Hz). Irradiation at δ 2.55 sharpened the signal at δ 1.99-2.07 and the broad quartet at δ 4.55. Irradiation at δ 4.55 converted the doublet at δ 1.17 to a singlet and the multiplet at δ 2.53-2.59 to a broad triplet (J ~ 4 Hz). NOE difference experiments: irradiation at δ 1.17 caused enhancement of the signals at δ 4.55 and δ 2.53-2.59; irradiation at δ 5.82 caused enhancement of the signal at δ 5.03. Exact Mass calcd. for C_{14}H_{20}O_3 (M^+): 236.1412; found: 236.1410.

The keto ester diene 336 exhibited IR (film): 1720, 1713, 1635, 1191, 1162, 899 cm^{-1}; ^1H NMR (CDCl_3, 400 MHz): δ 1.04 (d, 3H, J = 7 Hz, -CHCH_3), 1.25 (t, 3H, J = 7 Hz, -OCH_2CH_3), 1.62-1.74 (m, 1H), 1.99 (dq, 1H, J = 13, 4 Hz), 2.18 (s, 3H, -COCH_3), 2.29-2.39 (m, 1H), 2.48 (dd, 1H, J = 10, 4 Hz, H_e), 2.53 (dt, 1H, J = 14, 4 Hz), 2.62-2.71 (m, 1H, H_d), 4.13 (q, 2H, J = 7 Hz, -OCH_2CH_3), 4.83 (broad s, 1H, H_a), 4.94 (broad s, 1H, H_b), 5.62 (d, 1H, J = 2 Hz, H_c). Irradiation at δ 1.04 simplified the multiplet at δ 2.62-2.71 to a doublet (J = 10 Hz). Irradiation at δ 2.66 simplified the doublets at δ 1.04 and δ 5.62 to singlets and the doublet of doublets at δ 2.48 to a doublet (J = 4 Hz). NOE difference experiment: irradiation at δ 1.04 caused enhancement of the signals at δ 2.48, δ 2.62-2.71 and δ 5.62. Exact Mass calcd. for C_{14}H_{20}O_3 (M^+): 236.1412; found: 236.1420.

Both materials were refluxed in mesitylene for 1 h under an argon atmosphere and no isomerization of the double bonds was observed in either case.
Preparation of the Keto Aldehyde 337 and the Keto Ether 338
(a) In Benzene

A solution of the keto aldehyde 324 (37.0 mg, 0.189 mmol) in 2 mL of benzene was refluxed for 3 h under an argon atmosphere. The reaction mixture was cooled to room temperature and then was concentrated. TLC analysis (petroleum ether-diethyl ether, 3:1) of the residual oil showed the presence of two compounds, with a difference in Rf values of 0.39. The oil was subjected to chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions afforded the partially pure keto aldehyde 337 and keto ether 338. These products were slowly interconverting into each other. The $^1$H NMR (CDCl$_3$, 400 MHz) signals that could be assigned to the keto aldehyde 337 were the following: $\delta$ 0.97 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 2.20 (s, 3H, -COCH$_3$), 2.84 (dt, 1H, $J = 12$, 4 Hz, H$_e$), 3.00-3.08 (m, 1H, H$_d$), 5.02 (broad t, 1H, $J \sim 1$ Hz, H$_a$), 5.31 (broad t, 1H, $J \sim 1$ Hz, H$_b$), 5.99 (d, 1H, $J = 8$ Hz, H$_c$), 9.83 (d, 1H, $J = 8$ Hz, -CHO). The $^1$H NMR (CDCl$_3$, 400 MHz) signals could be assigned to the keto cyclic ether 338 were the following: $\delta$ 0.86 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 2.17 (s, 3H, -COCH$_3$), 2.53-2.62 (m, 1H, H$_c$), 2.71 (ddd, 1H, $J = 12$, 6, 3 Hz, H$_d$), 4.39-4.48 (m, 2H, -CH$_2$O-), 5.10 (d, 1H, $J = 6$ Hz, H$_b$), 6.40 (d, 1H, $J = 6$ Hz, H$_a$).
(b) In Benzene-\textit{d}_6

A solution of the keto aldehyde 324 (20.0 mg, 0.104 mmol) in 1 mL of benzene-\textit{d}_6 was refluxed for 3 h under an argon atmosphere. The reaction mixture was cooled to room temperature and a $^1$H NMR spectrum was obtained. This spectrum showed the presence of a mixture of the keto aldehyde 337 and the keto ether 338 in a ratio of 1:2, respectively. The $^1$H NMR (C\textsubscript{6}D\textsubscript{6}, 400 MHz) signals that could be assigned to the keto aldehyde 337 were the following: $\delta$ 0.60 (d, 3H, $J = 7$ Hz, -CH\textsubscript{3}), 1.63 (s, 3H, -COCH\textsubscript{3}), 4.59 (broad s, 1H, H\textsubscript{a}), 4.78 (broad s, 1H, H\textsubscript{b}), 5.80 (d, 1H, $J = 8$ Hz, H\textsubscript{c}), 9.89 (d, 1H, $J = 8$ Hz, -CHO). The $^1$H NMR (C\textsubscript{6}D\textsubscript{6}, 400 MHz) signals that could be assigned to the keto ether 338 were the following: $\delta$ 0.72 (d, 3H, $J = 7$ Hz, -CH\textsubscript{3}), 1.70 (s, 3H, -COCH\textsubscript{3}), 4.22 (d, 1H, $J = 12$ Hz, -CH\textsubscript{2}O-), 4.28 (d, 1H, $J = 12$ Hz, -CH\textsubscript{2}O-), 4.88 (d, 1H, $J = 6$ Hz, H\textsubscript{b}), 6.36 (d, 1H, $J = 6$ Hz, H\textsubscript{d}). Concentration of the solution, followed by pumping on a vacuum pump to remove traces of solvent, afforded 16.0 mg (80\%) of the mixture. This mixture exhibited IR (film): 1708, 1672, 1355, 1157 cm\textsuperscript{-1}. Exact Mass calcd. for C\textsubscript{12}H\textsubscript{16}O\textsubscript{2} (M\textsuperscript{+}): 192.1150; found: 192.1146.

Preparation of the Keto Aldehyde 339

![Diagram](339.png)
To a cold (-78°C), stirred solution of dry dimethyl sulfoxide (29.7 mg, 0.380 mmol) in 1.5 mL of dry dichloromethane under an argon atmosphere, was added oxalyl chloride (46.6 mg, 0.367 mmol). After the reaction mixture had been stirred at -78°C for 15 min, a solution of the diol diene 333 (32.3 mg, 0.165 mmol) in 0.5 mL of dry dichloromethane was added dropwise. The resulting mixture was stirred at -78°C for 15 min. Dry triethylamine (131 mg, 1.29 mmol) was added and the solution was stirred at -78°C for 5 min, and at room temperature for 30 min. Saturated aqueous ammonium chloride (5 mL) was added and the resulting mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄), and concentrated. The residual oil was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 24.6 mg (78%) of the keto aldehyde 339 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 3:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2760, 1708, 1672, 1162 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 1.00 (d, 3H,  J = 7 Hz, -CHCH₃), 1.85-1.94 (m, 2H), 2.19-2.30 (m, 1H), 2.24 (s, 3H, -COCH₃), 2.59 (dt, 1H,  J = 14, 4 Hz,  Hₐ), 2.71-2.77 (m, 1H), 4.07-4.15 (m, 1H,  Hₜ), 5.03 (broad t, 1H,  J ~ 2 Hz,  Hₐ), 5.14 (broad t, 1H,  J ~ 2 Hz,  Hₜ), 6.02 (d, 1H,  J = 8 Hz,  Hₐ), 10.12 (d, 1H,  J = 8 Hz, -CHO); ¹H NMR (C₆D₆, 400 MHz): δ 0.73 (d, 3H,  J = 7, -CHCH₃), 1.44-1.54 (m, 1H), 1.60-1.84 (m, 2H), 1.69 (s, 3H, -COCH₃), 2.02 (dt, 1H,  J = 14, 4 Hz,  Hₐ), 2.07-2.14 (m, 1H), 3.69-3.78 (m, 1H,  Hₜ), 4.63 (broad s, 1H,  Hₐ), 4.82 (broad s, 1H,  Hₜ), 6.02 (d, 1H,  J = 8 Hz,  Hₐ), 9.95 (d, 1H,  J = 8 Hz, -CHO). Exact Mass calcd. for C₁₂H₁₆O₂ (M⁺): 192.1150; found: 192.1146.
This product was refluxed in mesitylene for 1 h under an argon atmosphere and no isomerization of the double bonds was observed.

Preparation of the Diol Dienes 340 and 341

![Diagram of 340 and 341]

A solution of the keto aldehyde 324 (61.2 mg, 0.319 mmol) in 3 mL of dry toluene was refluxed under an argon atmosphere for 30 min. The reaction mixture was cooled to -78°C and a solution of diisobutylaluminum hydride (0.80 mL, 0.800 mmol) in toluene was added dropwise. The resulting mixture was stirred at -78°C for 30 min, at 0°C for 30 min and at room temperature for 2 h. Saturated aqueous ammonium chloride (5 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 2:3). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 48.7 mg (78%) of a colorless oil that consisted of a mixture of the diol dienes 340 (major isomer) and 341 (minor isomer) in a ratio of 10:3, respectively (¹H NMR analysis).

The mixture exhibited IR (film): 3347 (broad), 1376, 991, 895 cm⁻¹. The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the major diol diene 340 were the following:  δ 0.94 (d, 3H, J = 7 Hz, -CH₂CH₃), 1.23 (d, 3H, J =
6 Hz, -CHOHCH₃), 2.00-2.14 (m, 1H), 2.35-2.42 (m, 1H), 2.76-2.85 (m, 1H, Hₐ), 3.53-3.68 (m, 1H, -CHOHCH₃), 4.12 (dd, 1H, J = 12, 6 Hz, =CHCH₂OH), 4.32 (dd, 1H, J = 12, 8 Hz, =CHCH₂OH), 4.62 (broad s, 1H, Hₐ), 5.01 (broad s, 1H, Hₐ), 5.50 (dd, 1H, J = 8, 6 Hz, H₈). Irradiation at δ 2.80 simplified the doublet at δ 0.94 to a singlet. Irradiation at δ 3.62 simplified the doublet at δ 1.23 to a singlet. NOE difference experiment: irradiation at δ 5.50 caused enhancement of the signals at δ 2.76-2.85, δ 4.12 and δ 4.32. The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the minor diol diene 341 were the following: δ 0.87 (d, 3H, J = 7 Hz, -CHCH₃), 1.24 (d, 3H, J = 6 Hz, -CHOHCH₃), 4.62 (broad s, 1H, Hₐ), 5.01 (broad s, 1H, Hₐ), 5.46 (dd, 1H, J = 8, 6 Hz, H₈). Exact Mass calcd. for C₁₂H₂₀O₂ (M⁺): 196.1463; found: 196.1460.

Preparation of the Keto Aldehyde 345 and the Keto Ether 346

![Diagram of 345 and 346]

A solution of the keto aldehyde 345 (10.0 mg, 0.0520 mmol) in 0.5 mL of benzene-<sub>d6</sub> was refluxed for 3 h under an argon atmosphere. The reaction mixture was cooled to room temperature and a ¹H NMR spectrum was obtained. This spectrum showed the presence of a mixture of the keto aldehyde 345 and the
keto ether in a ratio of 1:2, respectively. The $^1$H NMR ($C_6D_6$, 400 MHz) signals that could be assigned to the keto aldehyde were the following: $\delta$ 0.70 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.65 (s, 3H, -COCH$_3$), 4.63 (broad s, 1H, H$_a$), 4.74 (broad s, 1H, H$_b$), 5.94 (dd, 1H, $J = 8$, 1.5 Hz, H$_c$), 10.02 (d, 1H, $J = 8$ Hz, -CHO). The $^1$H NMR ($C_6D_6$, 400 MHz) signals that could be assigned to the keto ether were the following: $\delta$ 0.92 (d, 3H, $J = 7$ Hz, -CHCH$_3$), 1.77 (s, 3H, -COCH$_3$), 4.30 (broad s, 2H, -CH$_2$O-), 5.10 (d, 1H, $J = 6.5$ Hz, H$_b$), 6.41 (d, 1H, $J = 6.5$ Hz, H$_a$). Concentration of the solution, followed by pumping on the vacuum pump to remove traces of solvent, afforded 7.0 mg (70%) of the mixture. This mixture exhibited IR (film): 1708, 1670, 1364, 1164 cm$^{-1}$. Exact Mass calcd. for $C_{12}H_{16}O_2$ (M$^+$): 192.1150; found: 192.1150.

Preparation of the Diol Dienes and

(a) By Thermolysis-Reduction of the Keto Aldehyde

A solution of the keto aldehyde (67.9 mg, 0.354 mmol) in 3 mL of dry toluene was refluxed under an argon atmosphere for 30 min. The reaction
mixture was cooled to -78°C and a solution of diisobutylaluminium hydride (0.88 mL, 0.88 mmol) in toluene was added dropwise. The resulting mixture was stirred at -78°C for 30 min, at 0°C for 30 min and at room temperature for 2 h. Saturated aqueous ammonium chloride (5 mL) was added and the resulting mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to chromatography on silica gel (2 g, elution with petroleum ether-ethyl acetate, 3:2). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 51.0 mg (74%) of a colorless oil that consisted of a mixture of the diol dienes 347 (major isomer) and 348 (minor isomer) in a ratio of 2:1, respectively (NMR analysis).

The mixture exhibited IR (film): 3367 (broad), 1638, 1110, 1015 cm⁻¹. The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the major diol diene 347 were the following: δ 1.11 (d, 3H, J = 7 Hz, -CHCH₃), 1.24 (d, 3H, J = 7 Hz, -CHOHCH₃), 3.96 (quintet, 1H, J = 7 Hz, -CHOHCH₃), 4.20 (dd, 1H, J = 12, 7 Hz, =CHCH₂OH), 4.29 (dd, 1H, J = 12, 7 Hz, =CHCH₂OH), 4.61 (broad s, 1H, Hₐ), 5.00 (broad s, 1H, Hₐ), 5.44 (t, 1H, J = 7 Hz, Hₐ).

The ¹H NMR (CDCl₃, 400 MHz) signals that could be assigned to the minor diol diene 348 were the following: δ 1.08 (d; 3H, J = 7 Hz, -CHCH₃), 1.19 (d, 3H, J = 6 Hz, -CHOHCH₃), 3.93 (quintet, 1H, J = 7 Hz, -CHOHCH₃), 4.18 (dd, 1H, J = 12, 7 Hz, =CHCH₂OH), 4.31 (dd, 1H, J = 12, 7 Hz, =CHCH₂OH), 4.61 (broad s, 1H, Hₐ), 5.00 (broad s, 1H, Hₐ), 5.50 (t, 1H, J = 7 Hz, Hₐ).

**Exact Mass** calcd. for C₁₂H₂₀O₂ (M⁺): 196.1463; found: 196.1456.
(b) By Reduction of the Keto Ester Diene 336

To a cold (-78°C), stirred solution of the keto ester diene 336 (21.0 mg, 0.0890 mmol) in 1 mL of dry diethyl ether under an argon atmosphere was added, dropwise, a solution of diisobutylaluminum hydride (0.31 mL, 0.31 mmol) in hexane. The reaction mixture was stirred at -78°C for 1 h and at 0°C for 1 h. Saturated aqueous ammonium chloride (3 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed with brine, dried (MgSO₄) and concentrated. The residual oil was subjected to flash chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 2:3). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 15.1 mg (87%) of a mixture of the diol dienes 347 and 348 in a ratio of 2:1, respectively (¹H NMR analysis). The ¹H NMR spectrum of this mixture was identical with that of the same material obtained as described in (a), above.
A stirred solution of the keto ether 319 (62.5 mg, 0.145 mmol) in 1.5 mL of mesitylene was refluxed for 1 h under an argon atmosphere. Dimethyl acetylenedicarboxylate (40.5 mg, 0.285 mmol) was added and the reaction mixture was refluxed for 1 h. The solution was concentrated and the crude product was subjected to chromatography on silica gel (5 g, elution first with petroleum ether, then with diethyl ether). The combined ether fractions were concentrated to afford 62 mg (74%) of a mixture of the keto ether diesters 349 and 350 in the ratio of 5:4, respectively (1H NMR analysis). The mixture was again subjected to chromatography on silica gel (2 g, elution with petroleum ether-diethyl ether, 3:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 33 mg (40%) of the keto ether diester 349, as a colorless oil and 26 mg (31%) of the keto ether diester 350, also as a colorless oil. Analysis of both oils by TLC (petroleum ether-diethyl ether, 3:1) and 1H NMR spectroscopy indicated that each oil consisted of one component.

The major keto ether diester 349 exhibited IR (film): 1719, 1655, 1431, 1270, 1113, 705 cm⁻¹; 1H NMR (CDCl₃, 400 MHz): δ 0.82 (d, 3H, J = 7 Hz, -CHCH₃), 1.03 (s, 9H, -SiCMe₃), 1.77-1.84 (m, 2H), 1.96-2.15 (m, 2H), 2.05
(s, 3H, -COCH₃), 2.57 (dt, 1H, J = 10, 5 Hz, Hₐ), 2.61-2.69 (m, 1H, Hₐ), 2.73 (dd, 1H, J = 16.5, 2 Hz, Hₜ₄), 3.10 (dd, 1H, J = 16.5, 2 Hz, Hₚ₄), 3.30-3.36 (m, 1H, Hₖ₈), 3.74 (s, 3H, -CO₂CH₃), 3.75 (dd, 1H, J = 8, 4 Hz, -CHCH₂O-), 3.82 (overlapping singlet with a doublet of doublets, 4H, -CO₂CH₃ and -CHCH₂O-, J = 8, 4 Hz), 7.34-7.49 (m, 6H, aromatic protons), 7.56-7.86 (m, 4H, aromatic protons). Irradiation at δ 0.82 sharpened the multiplet at δ 2.61-2.69. Irradiation at δ 3.33 simplified the doublets of doublets at δ 2.73, δ 3.10, δ 3.75 and δ 3.82 to doublets (J = 16.5 Hz, J = 16.5 Hz, J = 8 Hz, J = 8 Hz, respectively). NOE difference experiments: irradiation at δ 0.82 caused enhancement of the signals at δ 1.77-1.84, δ 2.61-2.69 and δ 3.30-3.36. Exact Mass calcd. for C₃₃H₉₀₅O₅Si (M⁺-OCH₃): 543.2566; found: 543.2568.

The minor keto ether diester 350 exhibited IR (film): 1723, 1656, 1431, 1267, 1112, 705 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.74 (d, 3H, J = 7 Hz, -CHCH₃), 1.01 (s, 9H, -SiCMe₃), 1.66-1.84 (m, 2H), 1.92-2.02 (m, 1H), 2.12 (s, 3H, -COCH₃), 2.13-2.19 (m, 1H), 2.53-2.63 (m, 2H, Hₐ and Hₚ₈), 2.70 (broad d, 1H, J = 16.5 Hz, Hₜ₄), 3.05 (broad d, 1H, J = 16.5 Hz, Hₚ₄), 3.33-3.39 (m, 1H, Hₖ₈), 3.62 (dd, 1H, J = 10, 6 Hz, -CHCH₂O-), 3.73 (s, 3H, -CO₂CH₃), 3.80 (dd, 1H, J = 10, 4 Hz, -CHCH₂O-), 3.83 (s, 3H, -CO₂CH₃), 7.34-7.45 (m, 6H, aromatic protons), 7.60-7.68 (m, 4H, aromatic protons). Irradiation at δ 0.74 sharpened the multiplet at δ 2.53-2.63. Irradiation at δ 3.35 sharpened the doublets at δ 2.70 and δ 3.05 and simplified the doublets of doublets at δ 3.62 and δ 3.80 to doublets (J = 10 Hz, each). NOE difference experiments: irradiation at δ 3.35 caused enhancement of the signals at δ 2.53-2.63, δ 3.62 and δ 3.80; irradiation at δ 3.62 caused enhancement of the signals at δ 0.74, δ 3.33-3.39 and δ 3.80. Exact Mass calcd. for C₃₃H₉₀₅O₅Si (M⁺-OCH₃): 543.2566; found: 543.2573.
Preparation of the Diketo Ether 351

To a cold (-78°C), stirred solution of the keto ether diene 328 (100 mg, 0.232 mmol) and methyl vinyl ketone (80.8 mg, 1.15 mmol) in 2.5 mL of dry dichloromethane under an argon atmosphere was added boron trifluoride-etherate complex (32.9 mg, 0.232 mmol). The reaction mixture was stirred at -78°C for 1 h. Saturated aqueous ammonium chloride (5 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed (water, brine), dried (MgSO4) and concentrated. The crude product was subjected to flash chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 8:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 97.1 mg (83%) of the diketo ether 351 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 40:1) and 1H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 1708, 1112, 1063, 707 cm⁻¹; 1H NMR (CDCl3, 400 MHz): δ 0.84 (d, 3H, J = 7 Hz, -CHCH₃), 1.02 (s, 9H, -SiCMe₃), 1.61-1.71 (m, 2H), 1.78-1.95 (m, 6H), 1.91 (s, 3H, -CH₂COCH₃), 2.25-2.31 (m, 1H, Hₐ), 2.32 (s, 3H, -CH₂COCH₃), 2.36 (dt, 1H, J = 15, 5 Hz, H₉), 2.60 (dt, 1H, J = 10.5, 4 Hz, H₄), 2.83-2.90 (m, 1H, H₃), 3.43 (dd, 1H, J = 11, 2 Hz, -CHCH₂O⁻), 3.66 (dd, 1H, J = 11, 8 Hz, -CHCH₂O⁻), 7.37-7.48 (m, 6H, aromatic protons), 7.67-7.75 (m, 4H, aromatic protons). Irradiation at δ 0.84 sharpened the multiplet at δ 2.25-2.31. Irradiation at δ 2.60 sharpened the
multiplet at $\delta$ 1.78-1.95 and simplified the multiplet at $\delta$ 2.83-2.90 to a broad doublet ($J \sim 8$ Hz). Irradiation at $\delta$ 2.86 sharpened the signal at $\delta$ 2.60 and simplified both doublets of doublets at $\delta$ 3.43 and $\delta$ 3.66 to two doublets ($J = 11$ Hz, each). Irradiation at $\delta$ 3.66 sharpened the multiplet at $\delta$ 2.83-2.90 and simplified the doublet of doublets at $\delta$ 3.43 to a broad doublet ($J \sim 2$ Hz). NOE difference experiments: irradiation at $\delta$ 0.84 caused enhancement of the signals at $\delta$ 1.61-1.71, $\delta$ 1.91, $\delta$ 2.25-2.31 and $\delta$ 2.83-2.90; irradiation at $\delta$ 2.60 caused enhancement of the signals at $\delta$ 1.78-1.95, $\delta$ 2.32 and $\delta$ 2.83-2.90; irradiation at $\delta$ 2.87 caused enhancement of the signals at $\delta$ 0.84, $\delta$ 2.32, $\delta$ 2.60, $\delta$ 3.43 and $\delta$ 3.66; irradiation at $\delta$ 3.43 caused enhancement of the signals at $\delta$ 2.25-2.31, $\delta$ 2.83-2.90 and $\delta$ 3.66. Exact Mass calcd. for C$_{32}$H$_{42}$O$_{3}$Si (M$^+$): 502.2903; found: 502.2908.

Preparation of the Keto Ether Aldehyde 352

![Chemical Structure](image)

To a cold (-78°C), stirred solution of the keto ether diene 328 (70.0 mg, 0.162 mmol) and acrolein (45.3 mg, 0.808 mmol) in 1.5 mL of dry dichloromethane under an argon atmosphere was added boron trifluoride-etherate complex (23.1 mg, 0.163 mmol). The reaction mixture was stirred at -78°C for 1 h. Saturated aqueous ammonium chloride (3 mL) was added and the mixture was extracted thoroughly with diethyl ether. The combined ether extracts were washed
(water, brine), dried (MgSO₄) and concentrated. The crude product was subjected to flash chromatography on silica gel (4 g, elution with petroleum ether-diethyl ether, 20:1). Concentration of the appropriate fractions, followed by pumping on a vacuum pump to remove traces of solvent, afforded 68.0 mg (86%) of the keto ether aldehyde 352 as a colorless oil. Analysis of this oil by TLC (petroleum ether-diethyl ether, 20:1) and ¹H NMR spectroscopy indicated that it consisted of one component. This material exhibited IR (film): 2728, 1725, 1709, 1113, 1068, 705 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 0.75 (d, 3H, J = 7 Hz, -CH(CH₃)₂), 1.03 (s, 9H, -SiCMe₃), 1.60-1.69 (m, 2H), 1.75-2.05 (m, 6H), 1.92 (s, 3H, -COCH₃), 2.11-2.19 (m, 1H, H₆), 2.32-2.39 (m, 1H, H₅), 2.49 (dt, 1H, J = 12, 4 Hz, H₄), 2.85-2.92 (m, 1H, H₃), 3.50 (dd, 1H, J = 12, 4 Hz, -CHCH₂O⁻), 3.63 (dd, 1H, J = 12, 9 Hz, -CHCH₂O⁻), 7.39-7.50 (m, 6H, aromatic protons), 7.65-7.75 (m, 4H, aromatic protons), 10.04 (broad s, 1H, -CHO). Irradiation at δ 0.75 sharpened the multiplet at δ 2.11-2.19. Irradiation at δ 2.49 sharpened the multiplets at δ 1.75-2.05 and δ 2.85-2.92. Irradiation at δ 2.88 simplified the doublet of triplets at δ 2.49 to a doublet of doublets (J = 12, 4 Hz) and both doublets of doublets at δ 3.50 and δ 3.63 to two doublets (J = 12 Hz, each). NOE difference experiments: irradiation at δ 0.75 caused enhancement of the signals at δ 2.11-2.19 and δ 2.85-2.92; irradiation at δ 2.88 caused enhancement of the signals at δ 0.75, δ 2.49, δ 3.50 and δ 3.63. Exact Mass calcd. for C₂₇H₃₁O₃Si (M⁺-CMe₃): 431.2040; found: 431.2043.
IV. REFERENCES


(e) K.N. Houk, private communication.


52. We thank Dr. S. Rettig for performing these X-ray structure determinations.


64. F. Frinhgeulli, L. Minsti, F. Pizzo, T. Taticchi, D. J. Halls and E.
    (1974).
    (1988).


V. APPENDIX

1. Appendix 1: X-ray Crystallographic Data

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